

Review

The Role of Bone Decortication in Enhancing the Results of Guided Bone Regeneration: A Literature Review

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Background: Bone decortication is often performed as part of a guided bone regeneration (GBR) procedure. The biologic rationale for decortication of bone is to allow progenitor cells easy access to a GBR-treated site and to facilitate prompt angiogenesis. It also may enhance the physical connection between a bone graft and a recipient site. However, the concept of decortication prior to a GBR procedure is controversial because there are no human clinical trials to support its effectiveness, and there are opposing points of view derived from animal studies regarding its usefulness.

Methods: The literature was assessed to determine whether there are enough data to validate the rationale for using decortication of bone as an integral part of GBR procedures. Eight searches were performed seeking controlled clinical trials that addressed the ability of decortication to enhance GBR.

Results: Three controlled animal clinical trials were found that supported the use of decortication prior to performing GBR. Two controlled animal clinical trials were located that indicated decortication did not improve GBR procedures. No human controlled clinical trial was identified that addressed the ability of decortication to alter GBR procedures. The literature addressing the capacity of decortication to affect onlay grafting or wound healing also provided mixed results.

Conclusion: There is conflicting information and not enough clinical trials to make a definitive determination as to the merits of bone decortication prior to GBR procedures. *J Periodontol* 2009;80:175-189.

KEY WORDS

Bone grafting; bone regeneration; decortication; ridge augmentation.

Successful placement of a dental implant requires a recipient site with an adequate width and height of alveolar bone. Lack of bone, which could impede implant placement, can be caused by periodontitis,¹ tooth extraction,^{2,3} or trauma due to long-term use of a removable prosthesis.⁴ If a patient has a deficient ridge, a surgical procedure, referred to as guided bone regeneration (GBR), can be used to augment bone height and/or width.⁵ Decortication of bone prior to placing a bone graft is often performed as part of a GBR procedure.⁶⁻¹² It is the intentional drilling of holes through the cortical bone into the cancellous bone or the removal of cortical bone to expose cancellous bone.¹³ Sometimes, perforation of the cortical bone can be accomplished with a sharp curet.¹⁴ Decortication is done ostensibly to enhance the healing process by promoting bleeding and allowing progenitor cells and blood vessels to reach a bone-grafted site more readily.⁶⁻¹² In addition, decortication may improve the physical bond between grafted bone and a recipient site.^{15,16} However, there is controversy in the dental literature with respect to the usefulness of this procedure because its ability to accelerate or increase bone regeneration has not been substantiated in human clinical trials, and there are conflicting results derived from animal studies. Furthermore,

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decortication can have some minor negative consequences: increased operative time, additional blood loss, potentially greater postoperative pain, and some bone loss if the GBR procedure fails. Therefore, it was decided to search the literature to ascertain if there are data to support performing decortication of bone as an integral part of GBR procedures.

DATA SOURCE

This review article focuses on the ability of bone decortication to enhance GBR procedures. In addition, different issues associated with bone augmentation are discussed to provide background information. For these subjects, articles were selected from the literature to furnish general information. With regard to data pertaining to the benefits of bone decortication, a methodic review of the literature was conducted. A MEDLINE search was performed through July 2008 for studies that addressed the usefulness of bone decortication as part of GBR procedures. Searches were conducted under different headings. The reasons for the exclusion of studies for each inquiry are indicated, and the omitted papers are found in appendices correlated to each search. Cited articles were also explored for other references concerning decortication of bone.

SEARCH STRATEGIES

Search 1

The heading “decortication of bone” revealed 212 citations. The search was reduced by looking at “decortication of bone AND regeneration.” This revealed 42 citations. Nineteen were eliminated because they were not in English. Of the remaining 23 papers, four articles¹⁷⁻²⁰ were included in this review; 19 studies were excluded (Appendix 1) because they did not provide a test and control group looking at bone regeneration with and without decortication of bone or the effect of bone decortication could not be determined because of confounding factors.

Search 2

The heading “cortical perforation of bone” revealed 103 references. The search was reduced by looking at “cortical perforation of bone AND regeneration.” This revealed 19 citations. One was eliminated because it was not in English. The remaining 18 papers were assessed to see if they compared bone repair with and without decortication of bone. Seven studies were included in this review,²¹⁻²⁷ and 11 were excluded (Appendix 2).

Search 3

The heading “intramarrow penetration of bone” revealed three citations. Studies were included that

compared groups with and without intramarrow penetration of bone and assessed bone regeneration. One study was included in this review;²⁸ two were excluded (Appendix 3) because they did not clearly provide information regarding the benefits of marrow penetration.

Search 4

The heading “marrow penetration/bone regeneration” revealed 11 citations. Two studies^{28,29} were included that compared groups with and without intramarrow penetration of bone and assessed bone regeneration. Nine studies were excluded (Appendix 4) because they did not clearly provide information regarding the benefits of marrow penetration.

Search 5

The heading “bone regeneration/calvaria/augmentation/titanium/rabbits” revealed 20 citations. Two studies^{22,29} were included that assessed the use of titanium caps to induce bone regeneration and had a test and a control group to evaluate the efficacy of decortication. Eighteen investigations were excluded (Appendix 5) because they used drugs or different bone graft materials to augment bone regeneration as opposed to using only a titanium cap for regeneration, and the benefit of decortication alone could not be determined. Studies that used decortication in the test and control groups were excluded.

Search 6

The heading “guided bone generation/cortical perforation*” revealed three citations. Two references were included^{22,30} that had test and control groups with and without cortical perforations and addressed regeneration. One paper was excluded that was not pertinent to regeneration (Appendix 6).

Search 7

The heading “guided bone augmentation/decortication” revealed two citations. One reference³¹ was included. The other was excluded because it did not have a test and control group to assess the impact of decortication (Appendix 7).

Search 8

The heading “bone decortication” was searched using Google, which revealed several recent controlled studies³²⁻³⁴ that were not found under PubMed; these were included in this paper.

Because there were so few controlled clinical trials in the literature that addressed GBR procedures with and without decortication, it was decided to provide additional data from non-controlled studies that demonstrated GBR was possible without decortication. The headings in searches 9 through 11 were used to locate citations addressing this issue.

Search 9

The heading “bone regeneration/occlusive barriers” revealed nine citations. Four studies^{30,35-37} were included. Five studies were excluded because it was not possible to tell to what extent bone regeneration was due to the topography of the bone defects (Appendix 8).

Search 10

The heading “guided bone regeneration/tuberosities” revealed two citations.^{38,39} They were included in this article.

Search 11

The heading “bone regeneration/bone beyond the skeleton/animals” revealed 42 citations. Five were excluded because they were not in English. Of the remaining 37 citations, eight^{22,30,40-45} were included; 29 were excluded (Appendix 9) because they did not address bone regeneration or whether the bone regeneration could be attributed to factors other than barrier protection for cell exclusion.

GBR

GBR is based on principles of guided tissue regeneration.⁴⁶⁻⁴⁹ Melcher⁴⁶ described the concept of selective cell repopulation of defects to enhance healing. The GBR technique excludes faster growing epithelial and connective tissue cells with barriers and bone grafts to allow slower moving pluripotential and osteogenic cells to repopulate the GBR-treated site. To attain horizontal and/or vertical bone augmentation beyond the envelope of skeletal bone, four principles need to be met: exclusion of epithelium and connective tissue, space maintenance, stability of the blood clot, and primary wound closure.⁵⁰

With respect to these facets of therapy, the following facts are important in understanding their contribution to bone regeneration. Primary closure results in a greater amount of bone deposition than healing by secondary intention after a bone graft is placed. In this regard, a recent meta-analysis by Machtei⁵¹ confirmed that a GBR procedure without barrier exposure results in more bone formation than when a barrier becomes uncovered (3.01 mm versus 0.56 mm). A bioabsorbable or non-resorbable barrier can provide space maintenance and exclude epithelium and connective tissue cells, thereby facilitating repopulation of the GBR-treated area with progenitor cells.⁹ The barrier also protects the wound and provides clot stabilization. To help maintain space, the barrier may be supported with bone grafts, implants, or tenting poles.⁵⁰ GBR procedures can be successfully performed with or without a bone graft if another technique is used to maintain space under the barrier.⁵ However, bone grafts are usually used with

GBR procedures. The blood clot that forms under the barrier releases growth factors (e.g., platelet-derived growth factor) and cytokines and serves as a precursor for the vascular granulation tissue that will replace it.^{52,53}

ANGIOGENESIS: RELATIONSHIP OF BLOOD VESSELS AND NEW BONE FORMATION

Angiogenesis and blood supply are important for attaining GBR, and they follow a specific sequence of events.^{54,55} Within the first 24 hours after a GBR procedure, the created space is filled with a blood clot. Then the clot is resorbed by neutrophils and macrophages and replaced with granulation tissue. This tissue contains numerous blood vessels, which are responsible for transporting cells and nutrients involved in osteoid formation. Osteoid is unmineralized bone; upon mineralization, it is referred to as woven bone.⁵⁵ Woven bone acts as a scaffold for additional bone deposition; subsequently, it remodels converting woven bone into lamellar bone.⁵⁶

Development of bone is dependent on the creation of new blood vessels that provide progenitor cells and nourishment to the GBR-treated site.^{54,55,57,58} The temporal relationship between vascularity and bone repair was histologically monitored by several investigators.^{54,55} They reported that the creation of capillaries preceded new bone formation. Angiogenesis is a multistep process and usually proceeds from existing blood vessels.⁵⁹ Schmid et al.⁵⁵ noted that regeneration is possible after blood vessels were available, and new bone develops ~4 weeks after initiating GBR.

DECORTICATION

Many clinical studies^{6,9-12} and case reports^{7,8} used decortication as part of a GBR protocol and demonstrated successful results. Conversely, other investigations^{2,30,31,35-45} conducted in animals indicated that bone regeneration occurred without decortication. Therefore, it is questionable whether decortication of bone is necessary to attain extraskelatal bone augmentation or if it enhances results (Figs. 1 and 2).

Before discussing studies that quantified the benefits of decortication, it is advantageous to address various aspects and potential benefits that may be derived from bone decortication: increased bleeding, access for progenitor cells and blood vessels, interlocking of bone, and spatial relationships of decortications.

Drilling holes through cortical bone into more vascular cancellous bone induces bleeding that immerses the GBR site in blood.^{6,31,54,55} As the clot organizes, it releases cytokines and growth factors to attract progenitor cells, osteoblasts, and blood vessels.^{52,53,60,61} Decortication of bone is frequently

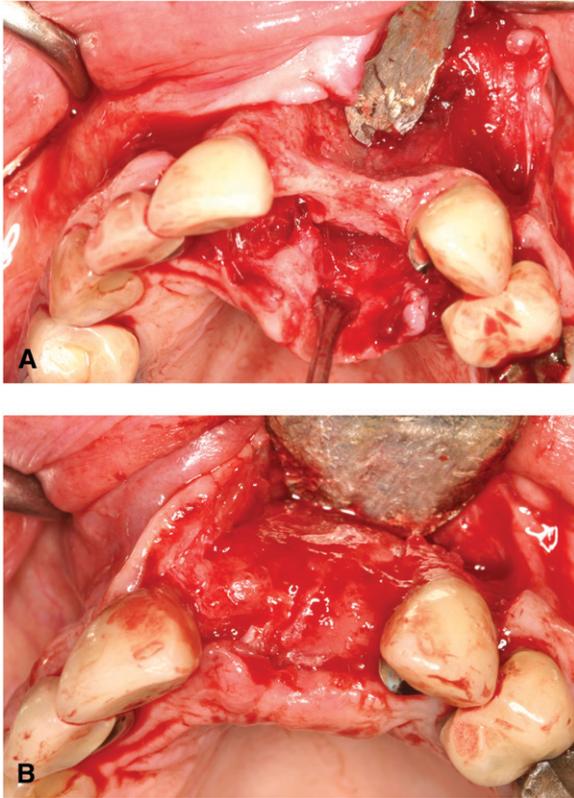


Figure 1.

A) GBR at teeth #9 and #10. Decortication was done prior to bone grafting. **B)** Healing after 6 months.

performed as part of a ridge-augmentation procedure,^{7,8,10-12} but it is not often performed when doing a socket preservation. After an extraction, bleeding from foramina in the cribriform plate usually precludes the need to induce hemorrhage. However, if a socket is not bleeding after a tooth is extracted, it has been advocated to decorticate the socket walls to provoke hemorrhaging to ensure a clot fills the alveolus.⁶² In addition, bone decortication is not usually done during the treatment of intrabony defects. Relevantly, no controlled studies were found during the literature searches on decortication that compared the treatment of intrabony defects with and without decortication of bone as an adjunctive therapy.

Decortication of bone may provide passageways for blood vessels and progenitor cells to have rapid access to a GBR-treated site.^{6,31,55} It is believed that creating perforations in the bone mimics what occurs during bone remodeling when osteoclastic cutting cones radially penetrate the bone.⁶³ Ultimately, the bone needs to resorb and create blood vessel channels or remodel around Volkmann's vascular canals to allow access for new blood vessels.³⁰ This facilitates capillary ingrowth that precedes bone deposition.^{54,55,57,58}

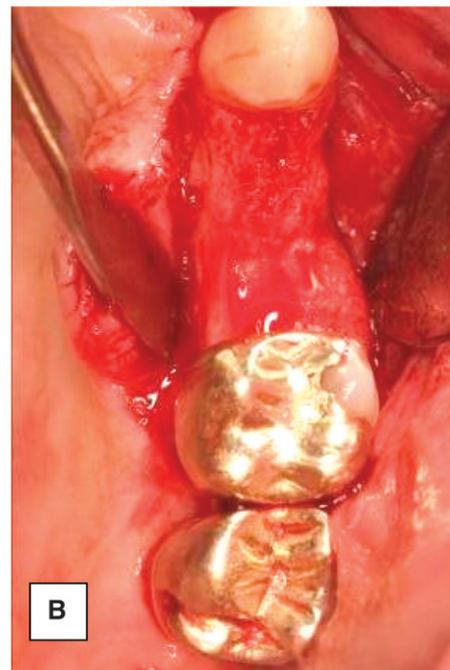


Figure 2.

A) GBR at teeth #12 and #13. Decortication was not done prior to bone grafting. **B)** Healing after 6 months.

It is recognized that osteoblasts are responsible for new bone formation and are derived from the periosteum, endosteum, and undifferentiated pluripotential mesenchymal cells in the bone marrow.⁶¹ However, during a GBR procedure, the periosteum is elevated with the flap, and a barrier is placed over the grafted bone, thereby excluding any contribution of osteoblasts from the periosteum. In addition, the cortical

bone upon which a bone graft was initially placed may impede undifferentiated pluripotential mesenchymal cells from the endosteum and bone marrow from reaching the GBR-treated site. Therefore, it was theorized that decortication of intact bone may speed up the process of getting blood vessels, osteoblasts, and pluripotential cells to grafted sites.⁶⁻¹²

Perforating the bony cortex also may increase the mechanical interlocking of a bone graft and a recipient site, which may improve its stability and provide firm linking for newly regenerated bone.^{15,16} Concerning monocortical bone blocks, it usually takes 4 to 5 months for them to bond with native bone.⁶⁴ However, clinicians have noted that when bone blocks are presumed healed, they can fracture off along the interface of the bone graft and native bone as an implant is placed.⁶⁴ This finding suggests that block grafts may be interlocked with native bone and not fully fused to it.

With respect to the spacing of bone perforations to attain the maximum benefit, this subject has never been addressed in the literature (Fig. 3). However, it is prudent to avoid over decortication when placing bone blocks because they need to be immobilized, and solid bone is needed for the lag screws that retain the bone graft.

REGIONAL ACCELERATORY PHENOMENON

Frost⁶⁵ described a phenomenon referred to as regional acceleratory phenomenon. It denotes that there is a local exuberant response to noxious stimuli, which accelerates the normal healing process. Relevantly, decortication can be considered a noxious stimulus; Winet⁶⁶ noted that vascularity peaked after trauma to the bone and declined to normal levels after healing was completed. Application of this concept is

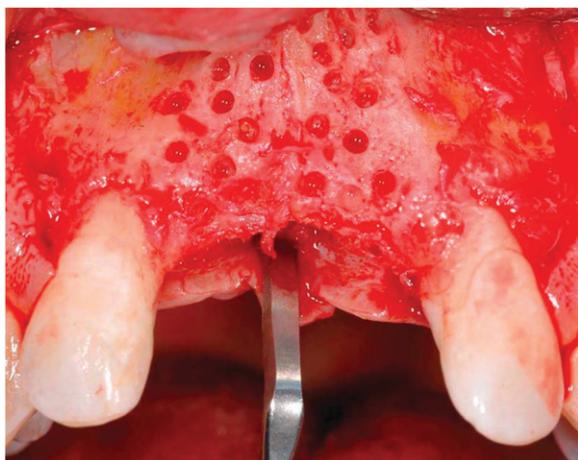


Figure 3.

An example of arbitrarily spaced decortications in buccal plate of the premaxilla.

being used as a method to facilitate rapid orthodontic movement.^{34,67} In particular, selective alveolar decortication is used to initiate local tissue repair and release of osteoprogenitor cells and osteoinductive agents.⁶⁷

EFFECT OF DECORTICATION ON INCORPORATION OF ONLAY BONE GRAFTS OR WOUND HEALING: MEDICAL AND DENTAL LITERATURE

This section addresses the use of decortication to enhance the incorporation of onlay bone grafts and wound healing.^{16-20,23-27,32,33,68-74} It does not address the intentional regeneration of bone outside the skeletal structures, which is covered in a subsequent segment of the text. The information for the medical and dental literature is presented separately to make it easier to follow the available data.

Medical Literature Related to Onlay Bone Grafting and Wound Healing

In medicine, GBR procedures are not usually performed to develop bone outside the skeletal envelope of bone. However, investigations have assessed the benefits of decortication to enhance the fusion of vertebrae^{17,18,33} and the incorporation of bone grafts to mend non-union of fractured clavicles⁶⁸ and humeruses.⁶⁹ Therefore, data from the medical literature that referred to bone decortication were reviewed to determine whether it could provide additional information with respect to the benefits of bone decortication.

In 1924, the concept of denuding bone or creating a decortication facet was described as a method to accelerate arthrodesis (spinal fusion).⁷⁰ Subsequently, clinicians conducted controlled studies^{16-18,20,33,71,72} in animals to decide if cortical bone perforations enhanced the incorporation of onlay bone grafts (Table 1). These studies were succinctly outlined because their methodologies and results were diverse. Gordh et al.¹⁶ conducted a controlled clinical trial in a rat model (N = 22) that lasted 20 weeks. Tibial or femoral grafts were placed on tibial bones that were or were not perforated. The investigators noted that there was migration of marrow components through the cortical perforations to the grafted region and increased lamellar bone apposition compared to the non-decorticated grafts. These data were descriptive in nature and did not provide quantification of monitored parameters.

Decortication of bone has also been used extensively as part of spinal fusions. Canto et al.¹⁷ found that decortication of rat vertebrae (N = 72) before grafting resulted in a larger percentage of bone formation compared to sites that were not decorticated. At 9 weeks, new bone formation ranged from 25.93% to

Table 1.**Decortication of Bone to Enhance Survival of Bone Grafts: Controlled Clinical Trials**

Investigators	Animal	Time	Result
Gordh et al. ¹⁶	22 rats	20 weeks	Decorticated grafts increased lamellar apposition of bone compared to non-decorticated graft sites.*
Canto et al. ¹⁷	72 rats	9 weeks	Statistically significant increase in the percentage formation of bone during spinal fusion was due to decortication of bone.*
Boden et al. ²⁰	60 rabbits	10 weeks	Spinal fusion was not attained in any control animals when decortication and bone grafting were omitted.*
de Carvalho et al. ⁷⁴	6 dogs	90 days	The autogenous bone grafts were incorporated with the receptor bed, mainly in the perforated and decorticated groups.*
Sandhu et al. ¹⁸	20 dogs	3 months	There were no statistically significant differences in clinical and radiographic spinal fusion rates between decorticated and non-decorticated sites treated with recombinant human BMP-2.
Huebsch et al. ¹⁹	10 dogs	10 weeks	After intentional wounding of the mandible, there was no appreciable histologic difference in healing with and without prior decortication.
Conti et al. ³³	15 dogs	3 months	Six months after spinal fusion there was no benefit if decortication was performed. Initially, 1 to 3 months, the grafts were better integrated with decortication.
Ishikawa et al. ⁷²	52 rabbits	6 weeks	The inclusion of decortication to autologous iliac grafting for spinal fusion significantly improved fusion rates in non-instrumented spines, but in instrumented spines, it did not provide a statistically significant improvement.
Adeyemo et al. ²³	12 sheep	16 weeks	Decortication provided no benefit compared to non-decorticated sites receiving mandibular onlay bone grafts.

* Better results reported with decortication were not necessarily statistically significantly better. If they were, it was stated. Otherwise, the investigators did not quantify the results and provided their interpretation of the data that decortication was beneficial.

30.6% for decorticated sites and 16.4% to 18.73% in the control group. Similarly, Boden et al.²⁰ used a rabbit model to assess the properties of the intertransverse spinal fusion healing process using autogenous iliac bone graft. Sixty rabbits were assessed after 10 weeks using different treatment methods. It was concluded that spinal fusion was not achieved in any control animals when there was omission of decortication or bone grafting. In contrast, Conti et al.³³ demonstrated in a dog model (N = 15) that decortication of vertebrae that were bone grafted resulted in better bone integration within 1 to 3 months compared to sites that were not decorticated. However, by 6 months there was no benefit with respect to the non-decorticated sites. Similarly, Ishikawa et al.⁷² noted that when spinal instrumentation and decortication were performed together in rabbits (N = 52),

decortication did not provide any benefit with regard to spinal fusion rates.

From a different perspective, Sandhu et al.¹⁸ demonstrated no statistically significant difference in spinal fusion rates (N = 20 dogs) when decortication versus applications of bone morphogenetic protein (BMP) to bone surfaces was performed before spinal fusion. Relevantly, Hsu and Wang⁷³ recently reviewed the literature to assess the use of BMPs to improve spinal fusion. They concluded that multiple commercially available recombinant BMPs demonstrate clinical success in spinal fusions, but they are too expensive to be routinely used. Therefore, it seems that the selection of a method to enhance spinal fusion is at the discretion of the clinician. One additional note concerning the use of BMPs, Issa et al.³² recently reported that combining decortication with

recombinant human BMP type 2 resulted in more bone formation in rats (N = 56) after 6 weeks than when used alone at non-decorticated sites (the evaluation was based on a radiographic densitometry technique). This concept needs further study.

Other preliminary investigations assessed if perforations of large grafts as opposed to the recipient bed would enhance the healing process. Lewandrowski et al.²⁴⁻²⁶ used lasers to perforate and demineralize bone grafts before transplanting them into rats and sheep. These studies demonstrated that osteogenesis in cortical bone grafts can be fostered through the process of partial demineralization and laser perforation. The investigators concluded that the processing of cortical bone allografts by the combination of perforation and partial demineralization resulted in better healing of transplanted bones compared to processing by partial demineralization alone. Delloye et al.²⁷ also found that perforating a bone graft itself (cortical bone) substantially improved the amount of new bone formed by the host compared to using a non-perforated bone graft.

Dental Literature Related to Onlay Bone Grafting and Wound Healing

The dental literature provided mixed results with regard to the ability of decortication to enhance the incorporation of onlay grafts or improve wound healing (Table 1).^{19,23,74} de Carvalho et al.⁷⁴ concluded after assessing the healing in six dogs after 90 days that autogenous monocortical bone grafts placed on the mandible demonstrated better healing at sites that were initially decorticated as opposed to sites that did not have initial bed preparation. The data were descriptive in nature, and the results were not quantified.

In contrast, other studies found that decortication did not enhance the incorporation of bone grafts or bone repair after intentional wounding. Adeyemo et al.²³ assessed the influence of decortication on the incorporation of onlay mandibular bone grafts in 12 sheep. After 16 weeks they noted that decortication of the recipient sites provided no advantages over non-perforated beds with respect to the rate of healing or integration of bone grafts. In another study,¹⁹ a dog model (N = 10) was used to assess healing after decortication. The investigators made a bilateral cut from the sigmoid notch to the angular process of the mandible. On one side, the fragments were decorticated and wired together. On the opposite side, the fragments were not decorticated but were overlapped and wired together. After 10 weeks, there was no appreciable histologic difference between the two sides with respect to bone healing.

In conclusion, it seems that decortication of bone is frequently used in the medical literature to enhance the incorporation of onlay bone grafts during various therapeutic procedures. However, there are animal

studies in the medical and dental literature that did not corroborate that decortication enhanced onlay grafting or the repair of intentional wounds.

ASSESSING THE EFFECT OF DECORTICATION ON REGENERATION OF BONE OUTSIDE THE SKELETAL HOUSING: ANIMAL AND HISTOLOGIC STUDIES IN THE DENTAL LITERATURE

In general, there are limited and conflicting data derived from controlled clinical trials^{22,28-31} in animal models with respect to the effects of decortications on GBR. The available data are difficult to compare because investigations used different animal models, reevaluated sites at different time intervals, attempted to regenerate different heights and widths of bone, and the results were reported as an overall percentage gain of bone, which did not differentiate between the width and height of bone. A short review of data from histologic trials pertaining to the benefits of decortication is outlined in the following sections to provide clinicians with the available information they need to make clinical decisions.

Controlled Clinical Trials in Animals: The Effect of Decortication Versus No Decortication on Bone Regeneration

Statistically significant improvement of bone regeneration after decortication. Data confirming that decortication enhanced bone regeneration has been ascertained in three studies²⁸⁻³⁰ conducted in rabbit and rat animal models (Table 2). Majzoub et al.²⁸ demonstrated in rabbits (N = 16) that 2 months after GBR the percentage of bone development in experimental titanium domes (cell occlusive barriers) placed adjacent to the calvaria was significantly greater than at sites where decortication was not performed (71.72% versus 53.58%). Similarly, Min et al.²⁹ conducted a controlled study in rabbits (N = 10). Two titanium domes were placed over the calvarium of each rabbit. Decortication was done beneath one dome, and the cortical bone was left intact under the other. At 3 months, there were more osteoblast-like cells at sites under the titanium domes that underwent decortication compared to controls (27.7 ± 3.6 versus 17.3 ± 3.6). In addition, these sites manifested a higher percentage of newly generated tissue (78.9% versus 69.8%) and a higher percentage of mineralized bone (24% versus 16.4%) at 3 months. Furthermore, in a rat model (N = 30), Rompen et al.³⁰ noted that after 4 months there was increased augmentation of bone at sites within titanium chambers that were decorticated compared to locations that were left unaltered (172.8% versus 141%, this refers to bone width with respect to thickness of the calvarium).

Table 2.**Mean Percentage of Bone Regeneration With and Without Bone Decortication: Controlled Clinical Trials**

Investigators	Animal	Time Period (months)	Increased Bone With Decortication (%)	Increased Bone With No Decortication (%)	Comment
Majzoub et al. ²⁸	16 rabbits	2	71.72*	53.58	Titanium domes had a height of 3 mm and a diameter of 4.8 mm.
Min et al. ²⁹	10 rabbits	3	78.9*	69.8	Titanium domes had a height of 4 mm and a diameter of 8 mm.
Rompen et al. ³⁰	30 rats	4	172.8*	141	Titanium chambers had a length of 5 mm, width of 4 mm, and height of 3 mm. Results evaluated with regard to the skull thickness.
Lundgren et al. ³¹	8 rabbits	3	75.5	71.2	Titanium cylinder with an inner diameter of 6 mm and inner height of 4.5 mm.
Slotte and Lundgren ²²	8 rabbits	3	64.4	64.9	Titanium cylinder with an inner diameter of 6 mm and inner height of 4.5 mm.

* Statistically significantly different compared to no decortication.

Non-significant improvements of bone regeneration after decortication. Data from clinical trials found that decortication did not enhance bone healing (Table 2).^{22,31} Lundgren et al.³¹ assessed whether removal of the outer cortical plate enhanced bone regeneration under titanium cylinders. Two cylinders were placed in eight rabbits. On one side the cortical bone was removed, whereas on the other side it was left intact. After 3 months, there was no difference in the amount of augmented bone in relation to the total experimental area at test versus control sites (75.5% versus 71.2%). The investigators concluded that removal of the outer cortical plate of bone did not enhance regeneration in a secluded space. However, the investigators mentioned two possible explanations for this finding: surgery on both sides to place the dome may have stimulated healing, and removal of the cortical plate at test sites required these locations to produce more bone than control sites to end up with a similar amount of bone. Thus, they conducted an additional study to reassess the benefits of decortication. Slotte and Lundgren²² placed two titanium cylinders in eight rabbits. The bone under one cylinder served as the test site and was perforated seven times, whereas the control site was not decorticated. After 3 months, it was found that cortical perforations did not enhance the per-

centage of bone augmentation (64.45% versus 64.9%). However, test sites demonstrated increased bone density.

Bone Regeneration in Animal Models When Bone Decortication Was Not Used as Part of the Surgical Protocol: Animal Clinical Trials

Many experimental animal studies^{22,31,35-45} examined different facets of GBR procedures without comparing the benefits of decortication versus no decortication. They demonstrated that GBR procedures could be successful without decortication of bone. Several representative investigations were selected to illustrate the efficacy of GBR procedures without decortication.

In a rabbit model, Lundgren et al.⁴⁵ placed four titanium domes (two on each side of the skull) in three rabbit calvaria to create a secluded space, with bone being the only adjoining tissue to the dome. After 3 months, histologic assessments revealed complete bone fill in all 12 domes.

In a rat model, Kostopoulos et al.³⁹ (N = 30) used a rigid polytetrafluoroethylene occlusive capsule to develop tuberosities on their rami. One side of the mandible served as the test site (periosteum left over the bone), and the other side was the control site (periosteum was removed). After 120 days, the

mean bone fill was 56% versus 52% at the test sites versus the control sites. In the same rat model (N = 30), Lioubavina et al.³⁸ assessed the long-term stability of regenerated bone. The new bone level was stable after 6 months, and the mean bone fill of capsules was 98.6% on radiographs. In another study (N = 18 rats), Kostopoulos and Karring⁷⁵ compared bone formation with and without a bioabsorbable membrane. On one side of the mandible a membrane was supported by an implant to maintain space; an implant was placed on the other side, but no membrane was used. When the barriers were removed after 6 months, the spaces under the barriers were usually filled with bone, whereas there was negligible bone formation if barriers were not placed. From a different perspective, Rasmusson et al.⁴⁴ confirmed in a rat model that GBR without decortication was able to regenerate bone around exposed implant threads. In general, it can be concluded that the above experimental animal studies demonstrated that GBR procedures were successful to different degrees without decortication. However, these investigations did not include comparisons to sites that were decorticated; therefore, they did not answer the question about whether decortication provides a benefit.

Controlled Clinical Trials in Animals: The Effect of the Size of Decortications on Regeneration of Bone

Only one controlled study was found that addressed the impact of the size of decortications on bone regeneration. Nishimura et al.²¹ evaluated whether the size of the openings through the cortex altered the outcome. Titanium mesh-reinforced expanded polytetrafluoroethylene barriers were used to create cell-occlusive domes in a rabbit model (N = 16). They created bone defects in two sizes (slits in bone): 1 × 15 mm and 3 × 15 mm. Initially, the larger slits were associated with faster and more new bone formation compared to the smaller perforations.²¹ However, no difference was noted in the amount of bone regenerated 12 weeks after therapy (12.75 mm² versus 9.70 mm²). To the best of our knowledge, no other animal study has been conducted to determine whether large perforations resulted in more new bone formation than smaller decortications.

EXTRAPOLATING ANIMAL STUDIES TO HUMANS

Rats and rabbits are often used because they are easy to anesthetize, inexpensive to buy, easy to maintain, and require little space for caging.⁷⁶ The disadvantage is that they belong to low-order phylogenetic species with a characteristically high potential for osteogenesis. The rate of osseous formation seems to vary inversely with the species' position on the phylo-

genetic scale.⁷⁶ Therefore, it is difficult to extrapolate experimental results relative to the rate and amount of bone regeneration from animal models to humans. Nevertheless, the fundamental physiology of bone repair and regeneration is similar in these animals and humans. Accordingly, it may be reasonable to suggest that the positive effects of decortication in accelerating healing or enhancing the volume of bone regeneration in experimental animal models can be obtained in humans.

ADDITIONAL LIMITATIONS OF REVIEWED STUDIES

Many experimental investigations assessing GBR procedures were done on the calvarium of rat and rabbit models. The cranial vault of these animals seems to be a reasonable experimental area for investigations regarding bone regeneration. However, outcomes in calvarial bone models may not reflect results attained with other membranous bones.

It was noted that animal studies and clinical trials that assessed the efficacy of decortication and GBR procedures did not provide information with respect to different results that may be expected in the mandible versus the maxilla. In addition, no conclusions could be drawn about how the size of the bone marrow would affect the decision to decorticate prior to performing a GBR procedure. Furthermore, no data were found that addressed how the size of the bone marrow might affect the regenerative results.

Another major limitation of the reviewed studies may pertain to the time when healing was assessed. It is possible that decortication may provide early benefits with regard to regeneration; however, these benefits cannot be clearly delineated over time. In this respect, studies that assessed histologic specimens at an earlier time point would provide additional information. Conversely, if the results are the same after 3 or 6 months, this might be interpreted to indicate that decortication is not necessary.

CONCLUSIONS

The data in the literature do not provide a clear answer about the usefulness of performing decortication to enhance GBR. However, the following conclusions can be drawn:

No human clinical trial has been done to determine whether decortication enhances ridge augmentation.

GBR using a barrier with and without decortication may result in bone regeneration.

Decortication may provide a quicker healing response; however, the data are limited to support this contention.

Decortication may facilitate regenerating more bone, as per several controlled clinical trials in animals. However, there are other investigations that

noted there was no benefit. Furthermore, successful results can be attained without decortication. Therefore, conflicting information precludes making a definitive statement that decortication results in improved outcomes.

There does not seem to be a detrimental healing effect as a result of decortication.

Decortication may help to physically interlock new bone and remaining graft material to the recipient site.

Animal models may provide information. However, healing rates are faster in animal models, and the healing response may not be the same in humans.

There is no guidance in the literature with regard to the size of holes that should be made in bone, their spatial configuration, or the amount of area that should be decorticated in relation to the size of the GBR treated site.

Growth factors and BMPs applied to grafted sites may obviate decortication procedures. However, this idea needs further testing. Additional studies also need to address the potential benefits of bone decortication done in conjunction with growth factors.

Additional controlled clinical trials (human and animal) are needed to determine whether decortication should be an integral part of GBR procedures.

The finding that decortication may have some benefits without any serious negative impact suggests that the decision to use decortication is really at the discretion of the clinician.

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REFERENCES

- Ong CT, Ivanovski S, Needleman IG, et al. Systematic review of implant outcomes in treated periodontitis subjects. *J Clin Periodontol* 2008;35:438-442.
- Lekovic V, Kenney EB, Weinlaender M, et al. A bone regenerative approach to alveolar ridge maintenance following tooth extraction. Report of 10 cases. *J Periodontol* 1997;68:563-570.
- Lekovic V, Camargo PM, Klokkevold PR, et al. Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. *J Periodontol* 1998;69:1044-1049.
- Tallgren A. The reduction in face height of edentulous and partially edentulous subjects during long-term denture wear. A longitudinal roentgenographic cephalometric study. *Acta Odontol Scand* 1966;24:195-239.
- McAllister BS, Haghight K. Bone augmentation techniques. *J Periodontol* 2007;78:377-396.
- Buser D, Bragger U, Lang NP, Nyman S. Regeneration and enlargement of jaw bone using guided tissue regeneration. *Clin Oral Implants Res* 1990;1:22-32.
- Buser D, Dula K, Belser UC, Hirt HP, Berthold H. Localized ridge augmentation using guided bone regeneration. I. Surgical procedure in the maxilla. *Int J Periodontics Restorative Dent* 1993;13:29-45.
- Buser D, Dula K, Belser UC, Hirt HP, Berthold H. Localized ridge augmentation using guided bone regeneration. II. Surgical procedure in the mandible. *Int J Periodontics Restorative Dent* 1995;15:10-29.
- Simion M, Scarano A, Gionso L, Piattelli A. Guided bone regeneration using resorbable and nonresorbable membranes: A comparative histologic study in humans. *Int J Oral Maxillofac Implants* 1996;11:735-742.
- Simion M, Jovanovic SA, Trisi P, Scarano A, Piattelli A. Vertical ridge augmentation around dental implants using a membrane technique and autogenous bone or allografts in humans. *Int J Periodontics Restorative Dent* 1998;18:8-23.
- Simion M, Dahlin C, Rocchietta I, Stavropoulos A, Sanchez R, Karring T. Vertical ridge augmentation with guided bone regeneration in association with dental implants: An experimental study in dogs. *Clin Oral Implants Res* 2007;18:86-94.
- Simion M, Rocchietta I, Kim D, Nevins M, Fiorellini J. Vertical ridge augmentation by means of deproteinized bovine bone block and recombinant human platelet-derived growth factor-BB: A histologic study in a dog model. *Int J Periodontics Restorative Dent* 2006;26:415-423.
- Jalbout Z, Tabourian G. *Glossary of Implant Dentistry*. Upper Montclair, NJ: International Congress of Oral Implantologists; 2004:24.
- Resnick DK, Haid R. *Surgical Management of Low Back Pain*. Rolling Meadows, IL: American Association of Neurological Surgeons; 2001:164.
- Alberius P, Gordh M, Lindberg L, Johnell O. Onlay bone graft behavior after marrow exposure of the recipient rat skull bone. *Scand J Plast Reconstr Surg Hand Surg* 1996;30:257-266.
- Gordh M, Alberius P, Lindberg L, Johnell O. Bone graft incorporation after cortical perforations of the host bed. *Otolaryngol Head Neck Surg* 1997;117:664-670.
- Canto FR, Garcia SB, Issa JP, Marin A, Del Bel EA, Defino HL. Influence of decortication of the recipient graft bed on graft integration and tissue neof ormation in the graft-recipient bed interface. *Eur Spine J* 2008;17:706-714.
- Sandhu HS, Kanim LE, Toth JM, et al. Experimental spinal fusion with recombinant human bone morphogenetic protein-2 without decortication of osseous elements. *Spine* 1997;22:1171-1180.
- Huebsch RF, Wellington JS. Osseous healing in dog mandibles with and without decortication. *Oral Surg Oral Med Oral Pathol* 1967;23:236-240.
- Boden SD, Schimandle JH, Hutton WC. An experimental lumbar intertransverse process spinal fusion model. Radiographic, histologic, and biomechanical healing characteristics. *Spine* 1995;20:412-420.
- Nishimura I, Shimizu Y, Ooya K. Effects of cortical bone perforation on experimental guided bone regeneration. *Clin Oral Implants Res* 2004;15:293-300.
- Slotte C, Lundgren D. Impact of cortical perforations of contiguous donor bone in a guided bone augmentation procedure: An experimental study in the rabbit skull. *Clin Implant Dent Relat Res* 2002;4:1-10.
- Adeyemo WL, Reuther T, Bloch W, et al. Influence of host periosteum and recipient bed perforation on the healing of onlay mandibular bone graft: An experimental pilot study in the sheep. *Oral Maxillofac Surg* 2008;12:19-28.

24. Lewandrowski KU, Schollmeier G, Ekkemkamp A, Uthoff HK, Tomford WW. Incorporation of perforated and demineralized cortical bone allografts. Part II: A mechanical and histologic evaluation. *Biomed Mater Eng* 2001;11:209-219.
25. Lewandrowski KU, Schollmeier G, Ekkemkamp A, Uthoff HK, Tomford WW. Incorporation of perforated and demineralized cortical bone allografts. Part I: Radiographic and histologic evaluation. *Biomed Mater Eng* 2001;11:197-207.
26. Lewandrowski KU, Tomford WW, Schomacker KT, Deutsch TF, Mankin HJ. Improved osteoinduction of cortical bone allografts: A study of the effects of laser perforation and partial demineralization. *J Orthop Res* 1997;15:748-756.
27. Delloye C, Simon P, Nyssen-Behets C, Banse X, Bresler F, Schmitt D. Perforations of cortical bone allografts improve their incorporation. *Clin Orthop Relat Res* 2002;396:240-247.
28. Majzoub Z, Berengo M, Giardino R, Aldini N, Cordioli G. Role of intramarrow penetration in osseous repair: A pilot study in the rabbit calvaria. *J Periodontol* 1999;70:1501-1510.
29. Min S, Sato S, Murai M, et al. Effects of marrow penetration on bone augmentation within a titanium cap in rabbit calvarium. *J Periodontol* 2007;78:1978-1984.
30. Rompen EH, Biewer R, Vanheusden A, Zahedi S, Nusgens B. The influence of cortical perforations and of space filling with peripheral blood on the kinetics of guided bone generation. A comparative histometric study in the rat. *Clin Oral Implants Res* 1999;10:85-94.
31. Lundgren AK, Lundgren D, Hämmerle CH, Nyman S, Sennerby L. Influence of decortication of the donor bone on guided bone augmentation. An experimental study in the rabbit skull bone. *Clin Oral Implants Res* 2000;11:99-106.
32. Issa JPM, Tiozzi R, Watanabe PC, et al. Newly formed bone in mandible decortication experimental model using rhBMP-2 evaluated by densitometric study. *Int J Morphol* 2008;26:83-88.
33. Conti OJ de, Pastorello MT, Defino, HLA. Bone decortication in spinal graft integration – An experimental study. *Acta Ortop Bras*[online] 2006;14:67-71. Available at: http://www.scielo.br/scielo.php?pid=S1413-78522006000200001&script=sci_arttext&lng=en. Accessed May 28, 2008.
34. Sebaoun JD, Kantarci A, Turner JW, Carvalho RS, Van Dyke TE, Ferguson DJ. Modeling of trabecular bone and lamina dura following selective alveolar decortication in rats. *J Periodontol* 2008;79:1679-1688.
35. Van Steenberghe D, Johansson C, Quirynen M, Molly L, Albrektsson T, Naert I. Bone augmentation by means of a stiff occlusive titanium barrier. *Clin Oral Implants Res* 2003;14:63-71.
36. Lundgren A, Lundgren D, Taylor A. Influence of barrier occlusiveness on guided bone augmentation. An experimental study in the rat. *Clin Oral Implants Res* 1998;9:251-260.
37. Lundgren AK, Sennerby L, Lundgren D. Guided jawbone regeneration using an experimental rabbit model. *Int J Oral Maxillofac Surg* 1998;27:135-140.
38. Lioubavina N, Kostopoulos L, Wenzel A, Karring T. Long-term stability of jaw bone tuberosities formed by “guided tissue regeneration.” *Clin Oral Implants Res* 1999;10:477-486.
39. Kostopoulos L, Karring T, Uraguchi R. Formation of jawbone tuberosities by guided tissue regeneration. An experimental study in the rat. *Clin Oral Implants Res* 1994;5:245-253.
40. Stavropoulos A, Nyengaard JR, Kostopoulos L, Karring T. Implant placement in bone formed beyond the skeletal envelope by means of guided tissue regeneration: An experimental study in the rat. *J Clin Periodontol* 2005;32:1108-1115.
41. Tamura T, Fukase Y, Goke E, et al. Three-dimensional evaluation for augmented bone using guided bone regeneration. *J Periodontol Res* 2005;40:269-276.
42. Lundgren AK, Lundgren D, Wennerberg A, Hämmerle CH, Nyman S. Influence of surface roughness of barrier walls on guided bone augmentation: Experimental study in rabbits. *Clin Implant Dent Relat Res* 1999;1:41-48.
43. Ito K, Nanba K, Murai S. Effects of bioabsorbable and non-resorbable barrier membranes on bone augmentation in rabbit calvaria. *J Periodontol* 1998;69:1229-1237.
44. Rasmusson L, Sennerby L, Lundgren D, Nyman S. Morphological and dimensional changes after barrier removal in bone formed beyond the skeletal borders at titanium implants. A kinetic study in the rabbit tibia. *Clin Oral Implants Res* 1997;8:103-116.
45. Lundgren D, Lundgren AK, Sennerby L, Nyman S. Augmentation of intramembraneous bone beyond the skeletal envelope using an occlusive titanium barrier. An experimental study in the rabbit. *Clin Oral Implants Res* 1995;6:67-72.
46. Melcher AH. On the repair potential of periodontal tissues. *J Periodontol* 1976;47:256-260.
47. Nyman S, Karring T, Lindhe J, Planten S. Healing following implantation of periodontitis-affected roots into gingival connective tissue. *J Clin Periodontol* 1980;7:394-401.
48. Karring T, Nyman S, Lindhe J. Healing following implantation of periodontitis affected roots into bone tissue. *J Clin Periodontol* 1980;7:96-105.
49. Dahlin C, Sennerby L, Lekholm U, Linde A, Nyman S. Generation of new bone around titanium implants using a membrane technique: An experimental study in rabbits. *Int J Oral Maxillofac Implants* 1989;4:19-25.
50. Wang HL, Boyapati L. “PASS” principles for predictable bone regeneration. *Implant Dent* 2006;15:8-17.
51. Machtei EE. The effect of membrane exposure on the outcome of regenerative procedures in humans: A meta-analysis. *J Periodontol* 2001;72:512-516.
52. Schenk RK, Buser D, Hardwick WR, Dahin C. Healing pattern of bone regeneration in membrane-protected defects: A histological study in the canine mandible. *Int J Oral Maxillofac Implants* 1994;9:13-29.
53. Tsiroidis E, Upadhyay N, Giannoudis P. Molecular aspects of fracture healing: Which are the important molecules? *Injury* 2007;38(Suppl. 1):S11-S25.
54. Hämmerle CH, Schmid J, Lang NP, Olah AJ. Temporal dynamics of healing in rabbit cranial defects using guided bone regeneration. *J Oral Maxillofac Surg* 1995;53:167-174.
55. Schmid J, Wallkamm B, Hämmerle CHF, Gogolewski S, Lang NP. The significance of angiogenesis in guided bone regeneration. A case report of a rabbit experiment. *Clin Oral Implants Res* 1997;8:244-248.
56. Hämmerle CH, Schmid J, Olah AJ, Lang NP. A novel model system for the study of experimental guided

- bone formation in humans. *Clin Oral Implants Res* 1996;7:38-47.
57. Glowacki J. Angiogenesis in fracture repair. *Clin Orthop Relat Res* 1998;355(Suppl.):S82-S89.
 58. Lu C, Miclau T, Hu D, Marcucio RS. Ischemia leads to delayed union during fracture healing: A mouse model. *J Orthop Res* 2007;25:51-61.
 59. Angiogenesis Foundation. Understanding angiogenesis. Available at: http://www.angio.org/patients/cancer/understanding_angiogenesis.html. Accessed May 30, 2008.
 60. Scheinecker C, Redlich K, Smolen JS. Cytokines as therapeutic targets: Advances and limitations. *Immunity* 2008;28:440-444.
 61. Nijweide PJ, Burger EH, Feyen JH. Cells of bone: Proliferation, differentiation, and hormonal regulation. *Physiol Rev* 1986;66:855-886.
 62. Danesh-Meyer M. Management of the extraction socket: Site preservation prior to implant placement. *Australasian Dental Practice* 2008;April:150-156.
 63. Shapiro F. Cortical bone repair. The relationship of the lacunar-canalicular system and intercellular gap junctions to the repair process. *J Bone Joint Surg Am* 1988;70:1067-1081.
 64. Rocuzzo M, Ramieri G, Bunino M, Berrone S. Autogenous bone graft alone or associated with titanium mesh for vertical alveolar ridge augmentation: A controlled clinical trial. *Clin Oral Implants Res* 2007;18:286-294.
 65. Frost HM. The regional acceleratory phenomenon: A review. *Henry Ford Hosp Med J* 1983;31:3-9.
 66. Winet H. The role of microvasculature in normal and perturbed bone healing as revealed by intravital microscopy. *Bone* 1996;19(Suppl. 1):39S-57S.
 67. Wilcko WM, Wilcko MT, Bouquot JE, Ferguson DJ. Rapid orthodontics with alveolar reshaping: Two case reports of decrowding. *Int J Periodontics Restorative Dent* 2001;21:9-19.
 68. Proubasta IR, Itarte JP, Lamas CG, Cáceres E. Midshaft clavicular non-unions treated with the Herbert cannulated bone screw. *J Orthop Surg (Hong Kong)* 2004;12:71-75.
 69. Yajima H, Maegawa N, Ota H, Kisanuki O, Kawate K, Takakura Y. Treatment of persistent non-union of the humerus using a vascularized bone graft from the supracondylar region of the femur. *J Reconstr Microsurg* 2007;23:107-113.
 70. Hibbs RA. A report of fifty-nine cases of scoliosis treated by the fusion operation. By Russell A. Hibbs, 1924. *Clin Orthop Relat Res* 1988;229:4-19.
 71. Ballmer FT, Lambert SM, Hertel R. Decortication and plate osteosynthesis for nonunion of the clavicle. *J Shoulder Elbow Surg* 1998;7:581-585.
 72. Ishikawa S, Shin HD, Bowen JR, Cummings RJ. Is it necessary to decorticate segmentally instrumented spines to achieve fusion? *Spine* 1994;19:1686-1690.
 73. Hsu WK, Wang JC. The use of bone morphogenetic protein in spine fusion. *Spine J* 2008;8:419-425.
 74. de Carvalho PS, Vasconcellos LW, Pi J. Influence of bed preparation on the incorporation of autogenous bone grafts: A study in dogs. *Int J Oral Maxillofac Implants* 2000;15:565-570.
 75. Kostopoulos L, Karring T. Augmentation of the rat mandible using guided tissue regeneration. *Clin Oral Implants Res* 1994;5:75-82.
 76. Frame JW. A convenient animal model for testing bone substitute materials. *J Oral Surg* 1980;38:176-180.
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APPENDIX I. ARTICLES EXCLUDED UNDER SEARCH DECORTICATION OF BONE AND REGENERATION

1. Kfir E, Kfir V, Eliav E, Kaluski E. Minimally invasive guided bone regeneration. *J Oral Implantol* 2007;33:205-210.
2. Yajima H, Maegawa N, Ota H, Kisanuki O, Kawate K, Takakura Y. Treatment of persistent non-union of the humerus using a vascularized bone graft from the supracondylar region of the femur. *J Reconstr Microsurg* 2007;23:107-113.
3. Kanayama M, Hashimoto T, Shigenobu K, Yamane S, Bauer TW, Togawa D. A prospective randomized study of posterolateral lumbar fusion using osteogenic protein-1 (OP-1) versus local autograft with ceramic bone substitute: Emphasis of surgical exploration and histologic assessment. *Spine* 2006;31:1067-1074.
4. Proubasta IR, Itarte JP, Lamas CG, Cáceres E. Midshaft clavicular non-unions treated with the Herbert cannulated bone screw. *J Orthop Surg (Hong Kong)* 2004;12:71-75.
5. Hou LT, Yan JJ, Tsai AY, Lao CS, Lin SJ, Liu CM. Polymer-assisted regeneration therapy with Atrisorb barriers in human periodontal intrabony defects. *J Clin Periodontol* 2004;31:68-74.
6. Rodriguez-Merchan EC, Gomez-Castresana F. Internal fixation of nonunions. *Clin Orthop Relat Res* 2004;419:13-20.
7. Martínez AA, Herrera A, Cuenca J. Marchetti nailing with decortication and bone graft in non-unions of the two upper thirds of the humerus. *Chir Main* 2002;21:28-32.
8. Wilcko WM, Wilcko T, Bouquot JE, Ferguson DJ. Rapid orthodontics with alveolar reshaping: Two case reports of decrowding. *Int J Periodontics Restorative Dent* 2001;21:9-19.
9. Lavini F, Renzi Brivio L, Pizzoli A, Giotakis N, Bartolozzi P. Treatment of non-union of the humerus using the Orthofix external fixator. *Injury* 2001;32(Suppl. 4):SD35-40.
10. David SM, Gruber HE, Meyer RA Jr., et al. Lumbar spinal fusion using recombinant human bone morphogenetic protein in the canine. A comparison of three dosages and two carriers. *Spine* 1999;24:1973-1979.
11. Siebenrock KA, Müller U, Ganz R. Indirect reduction with a condylar blade plate for osteosynthesis of subtrochanteric femoral fractures. *Injury* 1998;29(Suppl. 3):C7-15.
12. Slappey G, Toribatake Y, Ganey TM, Ogden JA, Hutton WC. Guidelines to decortication in posterolateral spine fusion. *J Spinal Disord* 1998;11:102-9.
13. Garg AK. The regional acceleratory phenomenon: An up-to-date rationale for bone decortication. *Dent Implantol Update* 1997;8:63-64.

14. Sandhu HS, Kanim LE, Toth JM, et al. Experimental spinal fusion with recombinant human bone morphogenetic protein-2 without decortication of osseous elements. *Spine* 1997;22:1171-1180.
15. Guizzardi S, Di Silvestre M, Scandroglio R, Ruggeri A, Savini R. Implants of heterologous demineralized bone matrix for induction of posterior spinal fusion in rats. *Spine* 1992;17:701-707.
16. Beckers L. Deep decortication in nonunion of shaft fractures. *Acta Orthop Belg* 1992;58(Suppl. 1):180-181.
17. Whitehill R, Stowers SF, Fechner RE, et al. Posterior cervical fusions using cerclage wires, methylmethacrylate cement and autogenous bone graft. An experimental study of a canine model. *Spine* 1987;12:12-22.
18. Kiman T, Suzuki R. Osteo-muscular decortication. *Fukushima J Med Sci* 1971;18:1-10.
19. Chang CS, Matukas VJ, Lemons JE. Histologic study of hydroxylapatite as an implant material for mandibular augmentation. *J Oral Maxillofac Surg* 1983;41:729-737.

APPENDIX 2: ARTICLES EXCLUDED UNDER SEARCH CORTICAL PERFORATION OF BONE AND REGENERATION

1. Taira H, Moreno J, Ripalda P, Forriol F. Radiological and histological analysis of cortical allografts: An experimental study in sheep femora. *Arch Orthop Trauma Surg* 2004;124:320-325.
2. Hussar P, Piirsoo A, Märtson A, Toom A, Haviko T, Hussar U. Bone healing models in rat tibia after different injuries. *Ann Chir Gynaecol* 2001;90:271-299.
3. Christiansen P. The skeleton in primary hyperparathyroidism: A review focusing on bone remodeling, structure, mass, and fracture. *APMIS Suppl* 2001;102:1-52.
4. Bondre S, Lewandowski KU, Hasirci V, et al. Biodegradable foam coating of cortical allografts. *Tissue Eng* 2000;6:217-227.
5. Rud J, Rud V, Munksgaard EC. Retrograde sealing of accidental root perforations with dentin-bonded composite resin. *J Endod* 1998;24:671-677.
6. Bataineh AB, al Qudah M. Treatment of mandibular odontogenic keratocysts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;86:42-47.
7. Leder AJ, Simon BI, Deasy M, Fenesy KE, Dunn S. Histological, clinical, and digital subtraction radiographic evaluation of repair of periodontal defects resulting from mechanical perforation of the chamber floor using ePTFE membranes. *Periodontal Clin Investig* 1997;19:9-15.
8. Mosekilde L, Weisbrode SE, Safron JA, et al. Calcium-restricted ovariectomized Sinclair S-1 minipigs: An animal model of osteopenia and trabecular plate perforation. *Bone* 1993;14:379-382.
9. Parfitt AM. Implications of architecture for the pathogenesis and prevention of vertebral fracture. *Bone* 1992;13(Suppl. 2):S41-47.
10. Bissada NF, Sears SB. Quantitative assessment of free gingival grafts with and without periosteum and osseous perforation. *J Periodontol* 1978;49:15-20.
11. Buser D, Brägger U, Lang NP, Nyman S. Regeneration and enlargement of jaw bone using guided tissue regeneration. *Clin Oral Implants Res* 1990;1:22-32.

APPENDIX 3: ARTICLES EXCLUDED UNDER SEARCH INTRAMARROW PENETRATION OF BONE

1. Hall EE, Meffert RM, Hermann JS, Mellonig JT, Cochran DL. Comparison of bioactive glass to demineralized freeze-dried bone allograft in the treatment of intrabony defects around implants in the canine mandible. *J Periodontol* 1999;70:526-535.
2. Zaner DJ, Yukna RA, Malinin TI. Human freeze-dried dura mater allografts as a periodontal biological bandage. *J Periodontol* 1989;60:617-623.

APPENDIX 4: ARTICLES EXCLUDED UNDER SEARCH MARROW PENETRATION/BONE REGENERATION

1. Yoshii T, Sotome S, Torigoe I, et al. Fresh bone marrow introduction into porous scaffolds using a simple low-pressure loading method for effective osteogenesis in a rabbit model. *J Orthop Res* 2008;27:1-7.
2. Miao X, Tan DM, Li J, Xiao Y, Crawford R. Mechanical and biological properties of hydroxyapatite/tricalcium phosphate scaffolds coated with poly(lactic-co-glycolic acid). *Acta Biomater* 2008;4:638-645.
3. Steinhagen J, Kurz B, Niggemeyer O, Bruns J. The pathophysiology of cartilage diseases. *Ortop Traumatol Rehabil* 2001;3:163-168.
4. Qian H, Yang Y, Li J, Huang J, Dou K, Yang G. The role of vascular stem cells in atherosclerosis and post-angioplasty restenosis. *Ageing Res Rev* 2007;6:109-127.
5. Murai M, Sato S, Fukase Y, Yamada Y, Komiyama K, Ito K. Effects of different sizes of beta-tricalcium phosphate particles on bone augmentation within a titanium cap in rabbit calvarium. *Dent Mater J* 2006;25:87-96.
6. Du C, Meijer GJ, van de Valk C, et al. Bone growth in biomimetic apatite coated porous Polyactive 1000PEG-T70PBT30 implants. *Biomaterials* 2002;23:4649-4656.
7. Ylänen HO, Helminen T, Helminen A, Rantakokko J, Karlsson KH, Aro HT. Porous bioactive glass matrix in reconstruction of articular osteochondral defects. *Ann Chir Gynaecol* 1999;88:237-245.
8. Ishaug SL, Crane GM, Miller MJ, Yasko AW, Yaszemski MJ, Mikos AG. Bone formation by three-dimensional stromal osteoblast culture in biodegradable polymer scaffolds. *J Biomed Mater Res* 1997;36:17-28.
9. Yamada Y, Nanba K, Ito K. Effects of occlusiveness of a titanium cap on bone generation beyond the skeletal envelope in the rabbit calvarium. *Clin Oral Implants Res* 2003;14:455-463.

APPENDIX 5: ARTICLES EXCLUDED UNDER SEARCH BONE REGENERATION/CALVARIA/AUGMENTATION/TITANIUM/RABBITS

1. Hasegawa Y, Sato S, Takayama T, Murai M, Suzuki N, Ito K. Short-term effects of rhBMP-2-enhanced bone augmentation beyond the skeletal envelope within a titanium cap in rabbit calvarium. *J Periodontol* 2008;79:348-354.
2. Ito K, Nanba K, Murai S. Effects of bioabsorbable and non-resorbable barrier membranes on bone augmentation in rabbit calvaria. *J Periodontol* 1998;69:1229-1237.

3. Jung RE, Hämmerle CH, Kokovic V, Weber FE. Bone regeneration using a synthetic matrix containing a parathyroid hormone peptide combined with a grafting material. *Int J Oral Maxillofac Implants* 2007;22:258-266.
 4. Lundgren AK, Lundgren D, Wennerberg A, Hämmerle CH, Nyman S. Influence of surface roughness of barrier walls on guided bone augmentation: Experimental study in rabbits. *Clin Implant Dent Relat Res* 1999;1:41-48.
 5. Lundgren AK, Sennerby L, Lundgren D. Guided jawbone regeneration using an experimental rabbit model. *Int J Oral Maxillofac Surg* 1998;27:135-140.
 6. Lundgren AK, Sennerby L, Lundgren D, Taylor A, Gottlow J, Nyman S. Bone augmentation at titanium implants using autologous bone grafts and a bioresorbable barrier. An experimental study in the rabbit tibia. *Clin Oral Implants Res* 1997;8:82-89.
 7. Lundgren D, Lundgren AK, Sennerby L, Nyman S. Augmentation of intramembraneous bone beyond the skeletal envelope using an occlusive titanium barrier. An experimental study in the rabbit. *Clin Oral Implants Res* 1995;6:67-72.
 8. Slotte C, Lundgren D, Burgos PM. Placement of autogeneic bone chips or bovine bone mineral in guided bone augmentation: A rabbit skull study. *Int J Oral Maxillofac Implants* 2003;18:795-806.
 9. Van Steenberghe D, Johansson C, Quirynen M, Molly L, Albrektsson T, Naert I. Bone augmentation by means of a stiff occlusive titanium barrier. *Clin Oral Implants Res* 2003;14:63-71.
 10. Maréchal M, Eyckmans J, Schrooten J, Schepers E, Luyten FP, van Steenberghe D. Bone augmentation with autologous periosteal cells and two different calcium phosphate scaffolds under an occlusive titanium barrier: An experimental study in rabbits. *J Periodontol* 2008;79:896-904.
 11. Maréchal M, Luyten F, Nijs J, Postnov A, Schepers E, van Steenberghe D. Histomorphometry and micro-computed tomography of bone augmentation under a titanium membrane. *Clin Oral Implants Res* 2005;16:708-714.
 12. Minegishi T, Kawamoto K, Yamada Y, et al. Effects of ipriflavone on bone augmentation within a titanium cap in rabbit calvaria. *J Oral Sci* 2002;44:7-11.
 13. Miyamoto I, Tsuboi Y, Takahashi K, Hyon SH, Iizuka T. Enhancement of bone volume in guided bone augmentation by cell transplants derived from periosteum: An experimental study in rabbit calvarium bone. *Clin Oral Implants Res* 2004;15:308-314.
 14. Murai M, Sato S, Fukase Y, Yamada Y, Komiyama K, Ito K. Effects of different sizes of beta-tricalcium phosphate particles on bone augmentation within a titanium cap in rabbit calvarium. *Dent Mater J* 2006;25:87-96.
 15. Nishida T, Yamada Y, Murai M, Shimizu Y, Oshikawa M, Ito K. Effects of bioactive glass on bone augmentation within a titanium cap in rabbit parietal bone. *J Periodontol* 2006;77:983-989.
 16. Tamimi FM, Torres J, Tresguerres I, Clemente C, López-Cabarcos E, Blanco LJ. Bone augmentation in rabbit calvariae: Comparative study between Bio-Oss and a novel beta-TCP/DCPD granulate. *J Clin Periodontol* 2006;33:922-928.
 17. Torres J, Tamimi FM, Tresguerres IF, et al. Effect of solely applied platelet-rich plasma on osseous regeneration compared to Bio-Oss: A morphometric and densitometric study on rabbit calvaria. *Clin Implant Dent Relat Res* 2008;10:106-112.
 18. Yamada Y, Nanba K, Ito K. Effects of occlusiveness of a titanium cap on bone generation beyond the skeletal envelope in the rabbit calvarium. *Clin Oral Implants Res* 2003;14:455-463.
- APPENDIX 6: ARTICLES EXCLUDED UNDER SEARCH GUIDED BONE GENERATION/CORTICAL PERFORATION***
1. Choi WW, Green BA, Levi AD. Computer-assisted fluoroscopic targeting system for pedicle screw insertion. *Neurosurgery* 2000;47:872-878.
- APPENDIX 7: ARTICLES EXCLUDED UNDER SEARCH GUIDED BONE AUGMENTATION/DECORTICATION**
1. Kfir E, Kfir V, Eliav E, Kaluski E. Minimally invasive guided bone regeneration. *J Oral Implantol* 2007;33:205-210.
- APPENDIX 8: ARTICLES EXCLUDED UNDER SEARCH BONE REGENERATION/OCCLUSIVE BARRIERS**
1. Maréchal M, Eyckmans J, Schrooten J, Schepers E, Luyten FP, van Steenberghe D. Bone augmentation with autologous periosteal cells and two different calcium phosphate scaffolds under an occlusive titanium barrier: An experimental study in rabbits. *J Periodontol* 2008;79:896-904.
 2. Kim TS, Knittel M, Dörfer C, Steinbrenner H, Holle R, Eickholz P. Comparison of two types of synthetic biodegradable barriers for GTR in interproximal intrabony defects: Clinical and radiographic 24-month results. *Int J Periodontics Restorative Dent* 2003;23:481-489.
 3. Eickholz P, Kim TS, Steinbrenner H, Dörfer C, Holle R. Guided tissue regeneration with bioabsorbable barriers: Intrabony defects and class II furcations. *J Periodontol* 2000;71:999-1008.
 4. Dörfer CE, Kim TS, Steinbrenner H, Holle R, Eickholz P. Regenerative periodontal surgery in interproximal intrabony defects with biodegradable barriers. *J Clin Periodontol* 2000;27:162-168.
 5. Schultz AJ. Guided tissue regeneration (GTR) of non-submerged implants in immediate extraction sites. *Pract Periodontics Aesthet Dent* 1993;5:59-65.
- APPENDIX 9: ARTICLES EXCLUDED UNDER SEARCH BONE REGENERATION/BONE BEYOND THE SKELETON/ANIMALS**
1. Artzi Z, Weinreb M, Givol N, et al. Biomaterial resorption rate and healing site morphology of inorganic bovine bone and beta-tricalcium phosphate in the canine: A 24-month longitudinal histologic study and morphometric analysis. *Int J Oral Maxillofac Implants* 2004;19:357-368.
 2. Buchman SR, Ozaki W. The ultrastructure and resorptive pattern of cancellous onlay bone grafts in the craniofacial skeleton. *Ann Plast Surg* 1999;43:49-56.

3. Chan CW, Qin L, Lee KM, Cheung WH, Cheng JC, Leung KS. Dose-dependent effect of low-intensity pulsed ultrasound on callus formation during rapid distraction osteogenesis. *J Orthop Res* 2006;24:2072-2079.
4. Hasegawa Y, Sato S, Takayama T, Murai M, Suzuki N, Ito K. Short-term effects of rhBMP-2-enhanced bone augmentation beyond the skeletal envelope within a titanium cap in rabbit calvarium. *J Periodontol* 2008;79:348-354.
5. Hunt P, Unterhauser FN, Strobel MJ, Weiler A. Development of a perforated biodegradable interference screw. *Arthroscopy* 2005;21:258-265.
6. Isidor F. Influence of forces on peri-implant bone. *Clin Oral Implants Res* 2006;17(Suppl. 2):8-18.
7. Ito K, Minegishi T, Takayama T, Tamura T, Yamada Y, Sato S. Effects of ipriflavone on augmented bone using a guided bone regeneration procedure. *Clin Oral Implants Res* 2007;18:60-68.
8. Ito K, Nanba K, Nishida T, Fujikawa K, Murai S. Osseointegration around titanium screws placed into the areas between guided bone augmented sites compared with osseointegration around guided bone graft augmented sites in rabbit tibia. *J Oral Sci* 1999;41:87-92.
9. Jin Q, Anusaksathien O, Webb SA, Printz MA, Giannobile WV. Engineering of tooth-supporting structures by delivery of PDGF gene therapy vectors. *Mol Ther* 2004;9:519-526.
10. Johnstone B, Yoo JU. Autologous mesenchymal progenitor cells in articular cartilage repair. *Clin Orthop Relat Res* 1999;(Suppl. 367):S156-S162.
11. Klein IE. The effect of thyrocalcitonin and growth hormones on bone metabolism. *J Prosthet Dent* 1975;33:365-379.
12. Kozlovsky A, Tal H, Laufer BZ, et al. Impact of implant overloading on the peri-implant bone in inflamed and non-inflamed peri-implant mucosa. *Clin Oral Implants Res* 2007;18:601-610.
13. Nociti Júnior FH, Stefani CM, Machado MA, Sallum EA, Toledo S, Sallum AW. Histometric evaluation of bone regeneration around immediate implants partially in contact with bone: A pilot study in dogs. *Implant Dent* 2000;9:321-328.
14. Parr GR, Steflik DE, Sisk AL. Histomorphometric and histologic observations of bone healing around immediate implants in dogs. *Int J Oral Maxillofac Implants* 1993;8:534-540.
15. Person P, Libbin RM, Shah D, Papierman S. Partial regeneration of the above-elbow amputated rat forelimb. I. Innate responses. *J Morphol* 1979;159:427-438.
16. Pietsch P. Effects of retinoic acid on the muscle patterns produced during forelimb regeneration in larval salamanders (*Ambystoma*). *Cytobios* 1991;66:41-61.
17. Pryor ME, Susin C, Wikesjö UM. Validity of radiographic evaluations of bone formation in a rat calvaria osteotomy defect model. *J Clin Periodontol* 2006;33:455-460.
18. Qiu YS, Shahgaldi BF, Revell WJ, Heatley FW. Observations of subchondral plate advancement during osteochondral repair: A histomorphometric and mechanical study in the rabbit femoral condyle. *Osteoarthritis Cartilage* 2003;11:810-820.
19. Reddi AH. Morphogenesis and tissue engineering of bone and cartilage: Inductive signals, stem cells, and biomimetic biomaterials. *Tissue Eng* 2000;6:351-359.
20. Schiller TD, DeYoung DJ, Schiller RA, Aberman HA, Hungerford DS. Quantitative ingrowth analysis of a porous-coated acetabular component in a canine model. *Vet Surg* 1993;22:276-280.
21. Schwartz-Arad D, Chaushu G. The ways and wherefores of immediate placement of implants into fresh extraction sites: A literature review. *J Periodontol* 1997;68:915-923.
22. Solchaga LA, Yoo JU, Lundberg M, et al. Hyaluronan-based polymers in the treatment of osteochondral defects. *J Orthop Res* 2000;18:773-780.
23. Stentz WC, Mealey BL, Nummikoski PV, Gunsolley JC, Waldrop TC. Effects of guided bone regeneration around commercially pure titanium and hydroxyapatite-coated dental implants. I. Radiographic analysis. *J Periodontol* 1997;68:199-208.
24. Stentz WC, Mealey BL, Gunsolley JC, Waldrop TC. Effects of guided bone regeneration around commercially pure titanium and hydroxyapatite-coated dental implants. II. Histologic analysis. *J Periodontol* 1997;68:933-949.
25. Sun L, Hu YY, Xiong Z, Wang WM, Pan Y. Repair of the radial defect of rabbit with polyester/tricalcium phosphate scaffolds prepared by rapid prototyping technology. *Chin J Traumatol* 2006;9:298-302.
26. Tamura T, Fukase Y, Goke E, et al. Three-dimensional evaluation for augmented bone using guided bone regeneration. *J Periodontol Res* 2005;40:269-276.
27. Turner CH. Functional determinants of bone structure: Beyond Wolff's law of bone transformation. *Bone* 1992;13:403-409.
28. Yun YH, Kim NH, Han DY, Kang ES. An investigation of bone necrosis and healing after cryosurgery, phenol cautery or packing with bone cement of defects in the dog femur. *Int Orthop* 1993;17:176-183.
29. Yamada Y, Nanba K, Ito K. Effects of occlusiveness of a titanium cap on bone generation beyond the skeletal envelope in the rabbit calvarium. *Clin Oral Implants Res* 2003;14:455-463.