Clinical and histomorphometric comparison of autologous dentin graft versus a deproteinized bovine bone graft for Socket Preservation

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Abstract
Dentin has been a significant focus of research due to its potential as a bone substitute, owing to its higher mineral content than any material derived from bone. Additionally, dentin shares two key similarities with autologous bone: it is both osteocompatible and osteoconductive, providing a physical framework for the deposition of new bone. This comparative study assessed the osteoinductive and osteoconductive capabilities of various materials commonly used in "socket preservation" or alveolar ridge preservation. The results showed that the autologous dentin matrix and bovine-derived xenografts (Bio-Oss) achieved superior bone regeneration, with a greater volume of newly formed bone (measured by the BV/TV parameter) and reduced fibrous bone, which has undesirable characteristics for implant biomechanics.

Keywords: Bovine bone, Socket Preservation, Ridge Preservation, Dentin

Introduction

The human body possesses inherent mechanisms that facilitate self-healing, but complete restoration, or 'restitutio ad integrum,' is rare, particularly in the oral cavity and alveolar bone. Biomaterials can aid in enhancing the body's natural healing abilities and successfully restore various structures within the human body 1-2. Dental implants offer a predictable solution for restoring chewing function in edentulous patients, provided sufficient residual bone thickness enables their placement, primary stability, and osseointegration. When this bone thickness is insufficient, implant procedures may only be feasible through regenerative surgery, whose success depends on an accurate diagnosis and the appropriate selection of graft materials essential for proper bone formation.
Since dental implants are now the preferred method for replacing missing teeth, preserving the alveolar ridge is crucial. Following tooth extraction, dimensional changes in the residual alveolar ridge are inevitable, and pre-existing conditions such as periodontal disease and periapical lesions can accelerate this process 3. Once a tooth is lost, the absence of stimulation to the residual bone leads to a reduction in trabecular density and bone volume in the edentulous socket, along with a decrease in the width of the buccal bone and subsequent loss of alveolar process height. These risks are most pronounced during the first eight weeks post-extraction 4.
Within the first 6 months after extraction, the alveolar ridge can lose more than 50% of its original height and width 5-6. Therefore, to preserve the bone volume necessary for optimal functional and aesthetic outcomes of dental implants, it is essential to intervene concurrently with or immediately following tooth extraction. Numerous studies support using various grafting materials in post-extraction sockets as part of a "ridge preservation technique" (5-14). Techniques involving autogenous, allogeneic, and xenograft materials for alveolar ridge preservation have been extensively documented in the literature.

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An ideal bone graft should exhibit osteoconductive, osteoinductive, and osteoproliferative properties15-17 for optimal outcomes. Among the available graft options, allografts and xenografts primarily offer osteoconduction, except for demineralized freeze-dried bone allografts, which are osteoinductive. Since autologous bone possesses all three key characteristics, it remains the gold standard. However, autologous bone grafting has limitations, including the risk of infection at the donor site, limited supply, and significant resorption.

Advances in tissue engineering and stem cell research are paving the way for innovative techniques in bone regeneration within the maxillofacial region, offering new therapeutic possibilities. Dentin has garnered attention as a potential bone substitute due to its higher mineral content than any bone-derived material. Moreover, dentin shares similarities with autologous bone, being both osteoinductive and osteoconductive, providing a physical framework for new bone formation. Another kind of study tried to modify the bone with Raloxifene to improve bone formation (18-19), while a group of researchers studied the use of a static magnetic field to improve the differentiation of osteoblasts (20).

For these reasons, dentin is recognized as an ideal bioactive material for complex tissue regeneration (21). Research indicates that dental tissue contains proteins with molecular weights similar to bone morphogenetic proteins (BMPs), which aid in differentiating mesenchymal cells into odontoblasts and ameloblasts. These proteins can enhance bone substitutes' osteoinductive properties if properly preserved during graft material processing (22). Using teeth as a bone substitute originated from early research on growth factors, particularly BMPs. In 1967, U.S. orthopedic surgeon Marshall Urist discovered BMPs and was the first to demonstrate their presence in dentin. Subsequent studies successfully isolated and characterized BMPs in the dentin matrix (23-25).

Autogenous dentin grafting was developed and clinically implemented in Korea from 2008 onwards.

The patient's extracted tooth is the ideal biomaterial, as it is autologous, does not require a secondary harvesting site, possesses high osteoconductive and osteoinductive properties, and is fully remodeled and replaced by new bone. The osteoinductive properties are due to the significant presence of BMPs (bone morphogenetic proteins) within the dentin structure. These proteins remain preserved long after extraction and are not affected by storage conditions; for instance, intact BMPs have even been found in fossilized human teeth. The partial or complete demineralization treatment used in some current methods enhances the bioavailability of dentin BMPs, which the high crystallinity of hydroxyapatite would otherwise constrain. This makes dentin the most biological and osteoinductive material available, with the only exception being autologous bone. It should be noted that although enamel has good osteoconductive properties due to its higher inorganic content (96% compared to dentin's 60-70%), it is less quickly resorbed even after demineralization (19).

Many studies on using autogenous dentin as a graft material have shown favorable clinical and histological outcomes26-30). However, there is still a need for more data supporting the clinical application of autogenous tooth grafts (ATG). Avoiding autologous bone harvesting by opening another surgical site is beneficial in cases where bone volume augmentation is needed alongside tooth extraction. Additionally, using autologous materials offers cost savings compared to alternatives derived from animals or synthetic sources (31-37).

The primary objective of the present study is to clinically and radiographically evaluate the efficacy of an autologous dentin graft compared to a deproteinized bovine bone graft in alveolar ridge preservation techniques for post-extraction sites. A secondary goal was to histologically determine the bone formation potential of ATG (Autogenous Tooth Graft). The data obtained were evaluated through histomorphometry, a quantitative histological technique that provides key bone parameters, including the bone remodeling index. This technique is notably used to diagnose metabolic bone diseases through bicortical biopsies from the iliac crest.

As a quantitative technique, histomorphometry could also have broader applications in "measuring" the bone's response to biomaterials implanted during surgery (35).

Materials and methods

In this comparative study, we assessed the osteoinductive and osteoconductive potential of various materials commonly used for "socket preservation" or alveolar ridge preservation. The study was conducted on a single patient to eliminate the variables that often arise when evaluating a larger sample size. The patient, a volunteer, was a candidate for treatment and rehabilitation with implant-prosthetic therapy at the Dental Clinic of the University of L'Aquila. Additionally, the patient required dental extractions due to periodontal issues.

The patient selected for the study met the following exclusion criteria:

- History of systemic diseases contraindicating surgery
- Long-term therapy with nonsteroidal anti-inflammatory drugs
- Lack of opposing dentition in the extraction site, preventing implant placement
- Oral therapy with bisphosphonates
- Absence of adjacent teeth near the treated area
- Inability to attend follow-up visits
- Smoking more than 10 cigarettes per day.

Before participation, the patient received a detailed explanation of the study and signed an informed consent. A thorough evaluation was conducted using diagnostic models and panoramic/periapical radiographs, along with data collection on age, gender, smoking habits, indications for dental extraction based on clinical and radiographic findings, tooth location, and the presence or absence of adjacent teeth. Once the consent was obtained, the surgical procedure could proceed.

The clinical evaluation revealed multiple missing teeth in both dental arches. The following experimental protocol was designed to assess the effectiveness of autogenous dentin in alveolar ridge preservation. The patient underwent the extraction of eight teeth across both arches.

The post-extraction sites were categorized into three groups:

- **Group 1**: The socket was filled with freshly prepared autologous dentin matrix.

- **Group 2**: Deproteinized bovine bone (Geistlich Bio-Oss) was used to fill the socket.
- **Group 3**: Control group, where the alveolar bone defect was left untreated, simulating natural post-extraction conditions.

Surgical protocol

Antibiotic Prophylaxis

Following the most recent guidelines regarding antibiotic prophylaxis in oral surgery, the patient was administered prophylactic antibiotic therapy with 2g of amoxicillin one hour before the extraction. This was followed by a postoperative regimen of 1g of amoxicillin taken twice daily for four days.

Anesthesia

Local-regional and plexus anesthesia using lidocaine was performed, with adrenaline at a dilution of 1:50,000, where feasible.

Dental Extractions

The teeth numbered 1.4, 1.2, 2.2, 2.4, 3.4, 3.2, 4.2, and 4.4 were extracted utilizing manual syndesmotomes or extraction forceps. Atraumatic extraction and subsequent grafting for alveolar ridge preservation were carried out without displacing a full-thickness flap, employing the flapless technique. Special care was taken to minimize trauma to the buccal bone surface and preserve bone morphology's integrity.

Curettage of the Alveolus

To ensure the proper execution of this study, all root fragments, fibers, and soft tissue from the alveolus had to be removed before the graft material was inserted. Curettes were used to eliminate these tissues from the post-extraction socket.

Preparation of Autologous Dentin Matrix

Concurrently with the curettage, the extracted teeth were treated to create the autologous dentin matrix graft according to the manufacturer's guidelines. The Smart Dentin Grinder produced by KometaBio was selected to prepare the autologous material. The first step involved determining the teeth for processing, excluding any endodontically treated elements. A high-speed handpiece and an ultrasonic scaler were employed to remove all cavities, artificial materials (crowns or fillings of any type, amalgam, or composites), and debris until only clean elements remained. There was no need to remove the crown or enamel. The prepared teeth were dried and placed in the grinding chamber, where they were ground and sorted using the machine's functions to achieve particle sizes between 300 and 1200 microns. Any particles smaller than 300 microns were discarded.
A drawer contained particles between 300 and 1200 microns following the shredding and sorting process. The subsequent sterilization step utilized substances provided by the manufacturer (NaOH with 20% ethanol), adhering to the specified timing and procedures. This process led to the dissolution of organic residues, bacteria, and toxins in the dentin, rendering the particles ready for use.

Grafting of Biomaterials

The freshly prepared dentin matrix was utilized as an autogenous graft in Group 1, which included the post-extraction sites of teeth 1.2, 2.2, 3.2, and 4.2. In Group 2, encompassing sites 3.4 and 4.4, a deproteinized bovine bone graft (Bio-Oss, Geistlich) was employed. In contrast, Group 3, which included sites 1.4 and 2.4, did not receive any graft material and allowed the post-extraction socket to heal naturally. The graft material was compacted into the socket by gently pressing it while utilizing the patient's blood as the preferred medium for mixing.
Using a collagen membrane is essential to protect the site from gingival proliferation (tenting effect), allowing for graft integration and osteogenesis, while ensuring optimal retention of the graft material. For this purpose, the membrane was shaped appropriately according to the dimensions of the socket and then adapted by gently pushing the ends underneath the adjacent soft tissues that had been previously unglued (envelope technique).

- **Sutures**
  The mucosal margins were secured in place using sutures without achieving complete soft tissue closure. The collagen membranes remained exposed to the oral cavity, with healing occurring by secondary intention. Suture removal was scheduled for 10 days post-surgery. The patient was advised to continue antibiotic prophylaxis, take naproxen sodium in 550 mg tablets twice daily as needed, and use a 0.2% chlorhexidine mouthwash twice daily.
- **Sample**
  Approximately six months later, implants were placed by harvesting bone for analysis from the alveolar site using a full-thickness flap and core drills (hollow-toothed, internally cooled, handpiece-mounted drills) where the biomaterial graft had been placed. The implant was then positioned. The patient received the same medication regimen as during the initial surgery. The retrieved bone sample was placed in a tube with a fixative for nine days to preserve and stabilize its constituents.

The purpose of fixation is to prevent post-mortem degenerative processes in tissues while preserving their morphology, structure, and reactivity as much as possible, thereby obtaining comprehensive and accurate information about the "in vivo" condition of the examined tissue specimen. The fixative allows for the immediate inhibition of enzyme activity, preserving all tissue components without altering the structure or causing tissue displacement. This study selected formaldehyde (or formalin) at a 4% dilution (pH 7) as the fixative.
This was followed by the inclusion step, which involves allowing a substance to permeate the tissue under examination. As this substance solidifies, the tissue can be cut into thin sections of a few microns (μm) thickness using a microtome. The inclusion material chosen for this process was methacrylate. The resulting block was then prepared for longitudinal cutting using the microtome, making histological sections approximately 5 microns (μm) thick for staining and analysis.
The sections were arranged on object slides and immersed in xylol, the inclusion solvent, to facilitate rehydration and subsequent staining. Once stained, the sections were sealed using Canada balsam and a

coverslip, depending on the needs of the investigation. Multiple sections were created from each sample, with some stained with methylene blue/blue II for the analysis of structural parameters. At the same time, the remainder underwent TRAcP staining for the evaluation of bone cell parameters.

- **Histomorphometric Analysis**
  Histomorphometric analysis involved examining the entirety of the sectioned specimen, measuring the following parameters:
- Osteoclast number per bone surface area (number/mm²)
- Osteoclast surface area as a percentage of bone surface area
- Osteoblast surface area as a percentage of bone surface area
- Bone volume as a percentage of total volume

The histomorphometric indices' nomenclature, symbols, and measurement units were expressed per the recommendations of the Histomorphometry Nomenclature Committee of the American Society for Bone and Mineral Research. Cells were fixed in 3% paraformaldehyde in 0.1 M cacodylate buffer for 15 minutes and then washed with the same buffer. TRAcP activity was detected histochemically using Sigma-Aldrich kit #386, following the manufacturer's instructions.

Results

The results obtained show that both the autologous dentin matrix and bovine-derived xenografts (Bio-Oss) demonstrated superior bone regeneration, characterized by a greater volume of newly formed bone (indicated by the BV/TV parameter) and reduced amounts of fibrous bone, which is less favorable for implant biomechanics. This conclusion was drawn not only from histomorphometric analysis but also from histological sections examined via light microscopy.
The percentage of residual material, assessed through histomorphometry, was higher in the first two groups than in the third group. This finding is significant as it indicates a more tremendous potential for replacement with newly formed bone tissue (osteoconduction). For Group I, which utilized autogenous dentin grafting, the following parameters were evaluated:

- **BV/TV:** Expressing the percentage of newly formed bone
- **OC.N/micron:** Indicating the number of osteoclasts per micron
- **OCS/BS:** Representing the total number of osteoclasts observed relative to bone volume

The results obtained were as follows:

BV/TV (Bone volume/Tissue Volume) %.

Site	Section 1	Section 2	Section 3.	Average ± SEM
1.	27%.	30%.	28%.	28.3 ± 0.88
2.	55%	61%	58%	58.0 ± 1.73
3.	21%	17%	23%	20.4 ± 1.76
4.	80%	83%	88%	83.7 ± 1.30

OC.N/micron

Site	Section 1	Section 2	Section 3.	Average ± SEM
1.	8µm.	20µm.	18µm.	8µm
2.	21µm	32µm	42µm	21µm
3.	5µm	16µm	21µm	6µm
4.	1µm	0µm	2µm	1µm

OCS/BS

Site	Section 1	Section 2.	Section 3.	Average ± SEM
1.	15%.	20%.	18%.	17.6%
2.	35%	32%	42%	36.3%
3.	13%	16%	21%	16.6%
4.	3%	0%	2%	1.6%

Regarding Group 2, which included the xenograft with deproteinized bovine bone (Bio-Oss), and Group 3, which comprised sites allowed to heal naturally, the following parameters were examined:

- **BV/TV:** Expressing the amount of newly formed bone
- **Percentage of intertrabecular spaces**
- **Percentage of residual material**

The results obtained were as follows:

	No fillers	Bio-Oss
New bone	37%±3.2%	38%±1.6%
Inter-trabecular spaces	44%±1.3%	32%±1.6%
Residual material	0%	30%±1.4%

For Bio-Oss, sections from several samples demonstrated osteoblastic activity, with bone forming directly on the surfaces of the particles. Most of these particles were surrounded by newly formed, mature, and compact bone tissue, with no bone gaps evident along the interface. The bone consistently maintained close contact with the particles, and no inflammatory infiltrate was observed. Histo morphometric analysis revealed that the newly formed bone constituted **38% ± 1.6%**, intertrabecular spaces accounted for **33% ± 1.6%**, and residual material was **30% ± 1.4%**.
In contrast, sites that underwent natural healing without any graft showed evidence of new bone tissue formation accompanied by wide gaps. Again, no inflammatory infiltrate was detected. The neoformed bone in these areas was **37% ± 3.2%**, intertrabecular spaces were **44% ± 1.3%**, and residual material was recorded at **0%**.

Discussion

The presence of neoformed bone was observed in all examined samples, indicating that the biomaterials considered in this study facilitated bone neoformation. However, the mere occurrence of neoformation needs to clarify the superiority of one biomaterial over another. Consequently, our study also assessed the amount of mineralized bone, the extent of intertrabecular spaces, and the quantity of residual biomaterial.
Based on the analyzed parameters, differences emerged among the various biomaterials, particularly regarding the amount of residual material. The autologous dentin matrix proved to be the most stable biomaterial compared to Bio-Oss and traditional healing, which exhibited a higher residual percentage

despite the same elapsed time. This finding aligns with existing literature identifying Bio-Oss as the “gold standard” among grafting materials.
In terms of material replacement within bone or fibrous tissue, traditional healing resulted in the highest percentage of fibrous tissue formation. Nevertheless, significant variations were observed among different retrievals, even when the same material was used, due to individual patient factors that play a critical role, including:

- General health conditions of the patient
- Anatomical considerations
- Amount of residual bone.

Radiological studies conducted before and after surgery suggest that the post-extraction site’s anatomical shape and the residual bone’s thickness are crucial determinants of surgical success. Specifically, certain anatomical types that exhibit greater vascularization facilitated better graft integration, leading to increased bone neoformation.
The results obtained corroborate findings from the literature. The study underscores the necessity of the alveolar ridge preservation technique in maintaining the height and width of residual alveolar bone following dental extraction. Grafted sites exhibited variable alveolar ridge preservation, influenced not only by the type of graft but also by the morphological condition of the post-extraction alveolus. While more challenges were anticipated in areas with prior periodontal lesions that caused extensive bone destruction, bone resorption was also predictable in untreated alveoli that healed spontaneously.
Despite the non-deterministic nature of the results, both types of grafts yielded favorable outcomes. This suggests that extracted teeth should be utilized as autogenous grafting material instead of being discarded as biomedical waste, representing a viable alternative to many conventional grafting materials.
Regarding the limitations of this study, it is essential to note its purely experimental nature, indicating the need for further research with larger sample sizes. Additional randomized clinical trials are necessary to establish the regenerative potential of these materials across various periodontal deficiencies.

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