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# Calcium Sulfate in Implantology (Biphasic Calcium Sul-Fate/Hydroxyapatite, BCS/HA, Bond Apatite®): Review of the Literature and Case Reports

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**Abstract:** Calcium sulfate is used as a synthetic graft material in orthopedics, plastic surgery, oncological surgery, and dentistry, and it has been used in a variety of clinical applications, such as the repair of periodontal defects, the treatment of osteomyelitis, maxillary sinus augmentation, and as a complement to the placement of dental implants. To carry out this systematic review, a bibliographic search was carried out. The PICO (Patient, Intervention, Comparison, Outcome) question was: Does the use of calcium sulfate as a material in guided bone regeneration in dentistry have better results compared to other bone graft materials? Finally, a case series is presented using the calcium sulfate for different procedures. Currently, the available literature on the use of calcium sulfate as a graft material in implant surgery is scarce, and what is available provides low-quality evidence. That is why more research studies on the subject are necessary to allow more comparisons and meaningful conclusions. After using Bond Apatite® in our case series, we can conclude that it is a useful and easy-to-handle material in implantology practice, but more controlled studies should be carried out in this regard to assess its long-term efficacy, especially in horizontal and/or vertical regeneration.

**Keywords:** calcium sulfate; dental implant; guided bone regeneration; sinus lift



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## 1. Introduction

The use of dental implants has become a common treatment modality and an important component of modern dentistry [1]. In many clinical situations, the edentulous areas to be rehabilitated do not offer adequate bone volume for implant placement; this may be due to different causes, such as the presence of anatomical structures that limit it (maxillary sinuses, presence of nerves or vessels, etc.) due to early bone atrophy and the traumatic extraction of a tooth or periodontal disease [2,3]. Tooth extraction is associated with the remodeling of the alveolar process and results in changes, both structural and dimensional, with horizontal losses of up to 29%–63% and vertical losses of 11%–22% at 6 months after tooth extraction [4,5].

For such defects, guided bone regeneration procedures before or in combination with implant placement are necessary [6]. These procedures are based on the use of different types of graft materials and membranes. The bone substitute must be osteoconductive, to act as a scaffold maintaining three-dimensional support during bone healing, and also osteoinductive, stimulating bone formation; the membranes act as a barrier and seal the area to be regenerated to prevent the ingrowth of soft tissue [7,8].

Historically, the most widely used grafting material was autologous bone, both extraoral and intraoral [9,10]; however, obtaining autogenous bone has several negative aspects, such as increased morbidity for the patient, limited supply, and increased duration of the intervention [11,12].

We currently have different types of bone graft materials for dental applications. Depending on the origin, they are classified as autografts, allografts, xenografts, or alloplastic grafts and can be found in the form of granules, putties, gels, and pastes, or blocks [13].

One of these alloplastic grafts is calcium sulfate, which is a common bone substitute and with a history of clinical use spanning more than 100 years, the first report of its use as a bone graft material was by the German physician Dreesman in 1892 when it was used as a treatment to seal bone defects in the long bones of eight patients with tuberculosis, according to Pelteier et al., in their work from 1957 [14]. This material is highly biocompatible and osteoconductive, undergoing practically complete resorption in vivo, and can be used as a vehicle to administer antibiotics, pharmacological agents, and growth factors [14,15].

Therefore, calcium sulfate, which is a bioactive material that produces the release of abundant calcium ions, is used as a synthetic graft material in orthopedics, plastic surgery, oncological surgery, and dentistry, and it has been used in a variety of clinical applications, such as the repair of periodontal defects, the treatment of osteomyelitis, and maxillary sinus augmentation, and as a complement to the placement of dental implants [16–19].

However, despite its many indications, it has some deficiencies that have prevented its daily use in dentistry, highlighting its rapid and complete resorption and hardening difficulties in the presence of saliva and bleeding. In 2010, Dr. Amos Yahav presented Bond Apatite® (Augma Biomaterials Ltd., Caesara Industrial Park, Israel & Microdent, Santa Eulàlia de Ronçana, Barcelona, Spain), a biphasic calcium sulfate that has proven to be more stable and with better properties than classic calcium sulfate [20,21]. It is a bone graft material composed of 2/3 biphasic calcium sulfate and 1/3 synthetic hydroxyapatite of different granulometry. Being the only one available, it is made of calcium sulfate and having the addition of hydroxyapatite. Calcium sulfate is reabsorbed and it is the hydroxyapatite particles that maintain volume during the process of new bone formation [22–24].

According to the study carried out by Yahav et al. [24], the addition of HA prolongs the resorption time and remains within the practical timeframe for dental clinical applications; most of the graft material is converted into young bone within 3 to 6 months, and the remainder is resorbed shortly thereafter.

Recent studies [19,20] have demonstrated successful results in guided bone regeneration with the use of calcium sulfate, and in addition, based on histological analysis, the percentage of graft remaining was relatively low, with no evidence of inflammatory response or graft encapsulation.

In this preparation, there are several considerations of interest. In the first place, thanks to the Biphasic Calcium Sulfate formulation (hemihydrated/dihydrated), the setting process can be reduced from about 20 min to 3, facilitating clinical management. In addition, the synthetic hydroxyapatite particles decrease the rate of graft resorption, maintaining volume; the smaller ones (90 microns) are reabsorbed after 3–4 months and the larger ones (1 mm), which represent 10% of the total hydroxyapatite, are reabsorbed after 8 months. Finally, the high porosity of the product, greater than 46%, favors the infiltration of growth factors, osteoblasts, and angiogenesis [15,25,26].

Whereas with conventional graft materials there is integration with the graft particles resulting in 20%–25% vital bone formation, with Bond Apatite®, there is no integration between the newly formed bone, and the material is completely resorbed. Instead, new vital bone is formed at the end of the regeneration process.

Biphasic calcium sulfate serves as a cement, and its rigid structure after a quick setting prevents epithelial–conjunctive cell infiltration into the material, acting as a barrier membrane. However, connective cells can multiply on the material's surface, encouraging the rapid repair of the overlying soft tissue [24].

Bond Apatite® is presented as a powder in a double barrel syringe and a sodium chloride solution. With the help of a piston, the solution is poured over the powder, obtaining a mixture that can be easily deposited in the bone deficit, since the resulting product is adhesive. Subsequently, pressure must be exerted with a dry sterile gauze for a few seconds, thus eliminating excess liquid and favoring the setting of the product. In addition, the manufacturer recommends closing the flap under tension and it is not necessary to cover the graft with any type of membrane, since when it hardens it acts as a barrier preventing the penetration of epithelial–connective cells [25,26].

This study aims to review the existing literature on calcium sulfate in oral surgery and expose various clinical cases using Bond Apatite® as a bone graft material in different situations. Therefore, the following PICO (Patient, Intervention, Comparison, Outcome) question was: Does the use of calcium sulfate as a material in guided bone regeneration in dentistry have better results compared to other bone graft materials?

## 2. Materials and Methods

To carry out this systematic review, a bibliographic search was carried out in the MEDLINE database through PubMed.

The following combinations of keywords were performed: "calcium sulfate" [MeSH Terms] AND ("surgery, oral" [MeSH Terms] OR "oral surgical procedures" [MeSH Terms]), "calcium sulfate" [MeSH Terms] AND "bone regeneration" [MeSH Terms], (calcium sulfate [MeSH Terms]) AND (bone grafting [MeSH Terms]).

The articles that were included in this systematic review had to meet the following inclusion criteria: controlled clinical trials, randomized controlled clinical trials, and case series, with more than 30 participants, carried out in humans and published within the last 10 years in English. Studies outside the field of dentistry, systematic reviews, preclinical studies, and clinical trials with insufficient information were excluded.

Finally, a case series is presented using the calcium sulfate for different procedures. Specifically, with Biphasic calcium sulfate/hydroxyapatite (BCS/HA): BCS-$CaSO_4 \cdot 1/2\ H_2O$+$CaSO_4 \cdot 2H_2O$ and HA-$Ca_{10}(PO_4)_6(OH)_2$ and liquid-NaCl 0.9%.

The selected studies were assessed following the SORT criteria [27].

## 3. Results

### *3.1. Selection of Studies*

The initial search yielded 122 articles. After applying the inclusion criteria and eliminating duplicate entries, the selected studies were 37. After reading the abstracts, 17 studies were selected and finally, after the full reading of the articles, only 7 fulfilled the criteria (Figure 1). The data obtained is summarized in Table 1.

### *3.2. Study Design*

Table (c) was created to extract data from the selected articles [28–34]. The characteristics of the studies, their objectives, and the results and conclusions obtained were assessed separately.

Three randomized controlled clinical trials (RCT) [28,30,31], three controlled clinical trials [29,33,34], and one case series [32] were included. All clinical trials had a control group comparable to the study group, and three of them used the contralateral side as the control group [28,29,31].

According to the SORT criteria [27], we can state that all RCT [28,30,31] are level 1, and the controlled clinical trials [29,33,34] can be marked as level 2, and finally the case series [32] can be staged as a level 3.

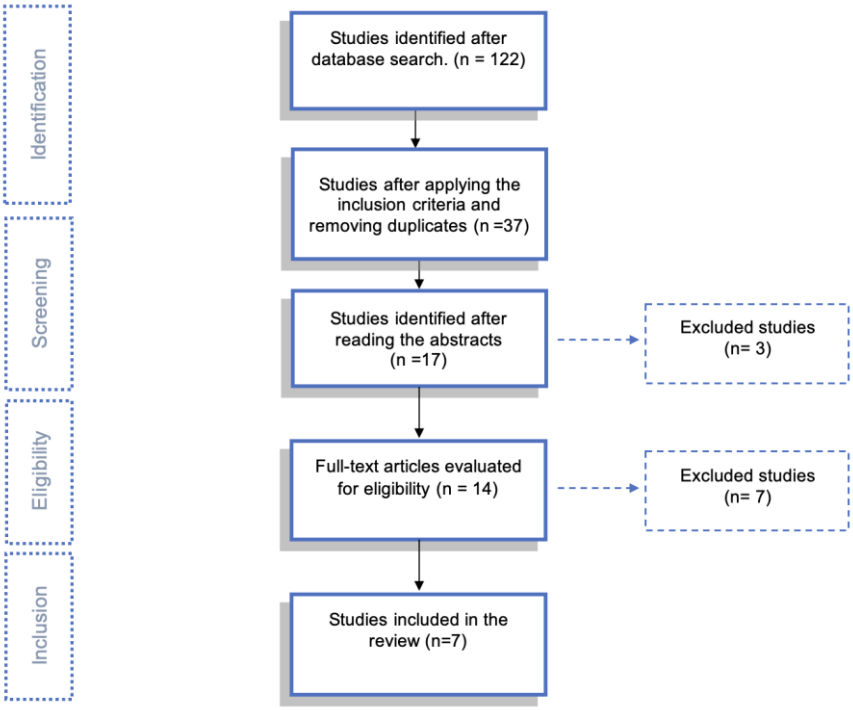



**Figure 1.** PRISMA flowchart.

### *3.3. Characteristics of the Participants*

A total of 237 patients, with a mean age of 53.95 years, were included in the studies. Only three studies [30,31,33] specify the number of participants of each gender. All the articles except one [28] collected samples from a number equal to or greater than 25 participants, with 60 participants being the maximum [33].

### *3.4. Characteristics and Results of the Studies*

In the selected studies, the applications and efficacy of the use of calcium sulfate in oral surgery were assessed. Two articles evaluated its effectiveness in the treatment of periodontal defects [28,29], three studies evaluated its use as a graft material in alveolar preservation [30,32], and one studied its application in the regeneration of maxillary bone defects after the surgical removal of radicular cysts [33] and another in sinus lifts [34].

Only two authors evaluated the efficacy of calcium sulfate in the guided bone regeneration of periodontal defects. First of all, Pandit et al. [29] obtained a decrease in probing depth of 2.67–4 mm, an increase in the clinical attachment of 1.6–2.47 mm, and a reduction in the periodontal defect of about 2 mm, without observing statistically significant differences between the groups. Secondly, Mandlik et al. [29] obtained a decrease in the probing depth and a gain in the clinical attachment level of about 5 mm in both groups without presenting statistically significant differences.

Of the three studies [30–32] that evaluated the use of calcium sulfate in alveolar preservation procedures, Horowitz et al. [32] reported that bone volume and density were maintained after extractions and after 4 months; Matchei et al. [30] and Mayer et al. [31] instead reported a slight bone loss in height of 0.65 mm [30] and 0.3 mm [31] and width of 0.5 mm [30] and 0.03 mm [31], respectively.

All of the studies performed a histopathological analysis. Matchei et al. [30] reported new bone formation in 44.4% and 16.51% of remnant calcium sulfate. Similar results were found in Mayer et al. [31], who observed that the composition of the new bone consists of 47.7% bone, 36.3% connective tissue, and 16% remaining graft material, and finally Horowitz et al. [32] reported that after 4 months the calcium sulfate graft was reabsorbed completely.

**Table 1.** Summary of the articles included. RCT: Randomized controlled clinical trial, CT: Controlled clinical trial, CS: Calcium sulfate, NG: Nanogen, DG: Dentogen, BG: BoneGen, BDX: Bovine Xenograft, BCS/HA: Calcium sulfate with hydroxyapatite.

| Author/Year<br>Type of Study | Sample Size (n)<br>Gender M/F<br>Age | Type of Study | Results | Conclusions |
|---|---|---|---|---|
| *Pandit et al.* [28]<br>*2021*<br>*RCT* | n: 16<br>20–64 years old<br>*Splitmouth*<br>**Nanogen** n: 15, **Dentogen** n: 15, **BoneGen** n: 15 | To evaluate the efficacy of calcium sulfate in the treatment of periodontal defects. Comparison of three materials Nanogen (NG), Dentogen (DG), and BoneGen (BG). | *At 6 months*<br>Probing level reduction: **NG** 3.33 mm, **DG** 2.67 mm y **BG** 4 mm.<br>Clinical insertion gain: **NG** 1.6 mm, **DG** 2.20 mm y **BG** 2.47 mm.<br>Reduction of the periodontal defect: **NG** 2 mm, **DG** 2.07 mm, **BG** 2.07 mm.<br>No statistically significant differences between groups. | Calcium sulfate is an effective material in the treatment of periodontal defects. |
| Mandlik et al. [29]<br>2012<br>CT | n: 25<br>30–50 years old<br>*Splitmouth*<br>**Group A** n: 25, **Group B** n: 25 | To compare the efficacy of phosphosilicate (Group A) and calcium sulfate (Group B) in the treatment of periodontal defects. | *At 9 months*<br>Probing level:<br>**Group A** 7.52 ± 1.074 → 2.20 ± 0.040 mm<br>**Group B** 7.20 ± 1.069 → 2.14 ± 0.351 mm<br>Clinical insertion level:<br>**Group A** 7.52 ± 1.0359 → 2.48 ± 0,614 mm<br>**Group B** 7.20 ± 1.069 → 2.32 ± 0.471<br>Bone gain: **Group A** 58.93%/Group B 48.56%<br>No statistically significant differences between groups. | No significant differences were observed between the two materials in terms of the efficacy of treating periodontal defects. |
| Machtei et al. [30]<br>2018<br>RCT | n: 11 7M/4F<br>45–80 = 64 years old | To compare the dimensional changes and bone quality of calcium sulfate (BCS/HA) and bovine xenograft (BDX) in socket preservation cases. | *At 4 months*<br>Bone height loss: BDX 0.25 mm, BCS/HA 0.65 mm, Control 1.7 mmBone width loss at −3 mm: **BDX** 1.56 ± 0.4 mm, **BCS/HA** 0.5 ± 0.4 mm **Control** 2.96 ± 0.3 mmNew bone formation: **BDX** 21,5%, **BCS/HA** 44.4% y **Control** 81,5%.<br>Remaining graft material: **BDX** 44.18%, **BCS/HA** 16.51%. | Calcium sulfate can be used as the material of choice for socket preservation with similar and sometimes even better results than bovine xenograft. |
| Mayer et al. [31]<br>2016<br>RCT | n: 36 13M/23F<br>*Splitmouth*<br>**CS** n: 14, **Control** n: 15 | To evaluate the efficacy of calcium sulfate in cases of socket preservation. | *At 4 months*<br>Bone height loss: **CS** 0.3 ± 2.01, **Control** 0.1 ± 2.03<br>Bone width loss at −3 mm: CS 0.03 ± 2.32 mm, **Control** 2.28 ± 2.36 mm<br>Histopathological analysis:<br>**CS** 47.7% bone, 36.3% connective tissue graft y 16% remaining graft material<br>**Control** 52.6% bone y 46.7% connective tissue graft | Calcium sulfate is an effective material in socket preservation cases, providing better results than natural healing. |
| Horowitz et al. [32]<br>2012<br>Case series | n: 40 | To evaluate the efficacy of calcium sulfate in cases of socket preservation. | *At 4 months*<br>*Bone volume and density were maintained. Calcium sulfate is completely reabsorbed, giving rise to new bone.* | Calcium sulfate is an effective material in cases of socket preservation before implant placement. |

**Table 1.** *Cont.*

| Author/Year<br>Type of Study | Sample Size (n)<br>Gender M/F<br>Age | | Type of Study | Results | Conclusions |
|---|---|---|---|---|---|
| Dudek et al. [33]<br>2020<br>CT | **CS**<br>n: 30 14M/16F<br>28–68 = 55.6 years old | **Xenograft**<br>n: 30 14M/16F<br>27–65 = 61.1 years old | To evaluate the efficacy of calcium sulfate in the regeneration of maxillary bone defects after surgical removal of radicular cysts compared to the use of xenografts. | Calcium sulfate achieves faster bone remodeling than bovine xenograft.<br>Virtually complete reabsorption of calcium sulfate and replacement by new bone at 3 months. | The use of calcium sulfate proved to be a simple, inexpensive, and effective reconstructive treatment of bone defects after the enucleation of odontogenic cysts. |
| Laino et al. [34]<br>2015<br>CT | n: 27<br>49–75 = 59 years old | | To evaluate the efficacy of calcium sulfate in lateral window sinus lifts. | *At 6 months*<br>Mean bone height before surgery: 4.04 ± 1.48<br>Mean bone height in regenerated sites: 12.25 ± 3.20 mm<br>Mean bone height gained: 8.21 ± 1.73 mm | The use of calcium sulfate in lateral window sinus lifts is an effective procedure. |

Dudek et al. [33] evaluated the efficacy of calcium sulfate in the regeneration of maxillary bone defects after the surgical removal of radicular cysts compared to the use of xenografts and observed that calcium sulfate achieves slightly faster bone remodeling and has almost complete resorption and a new bone replacement at 3 months.

The use of calcium sulfate as a graft material in lateral membrane sinus lifts was evaluated by Laino et al. [34], who obtained a mean bone height gain of 8.21 ± 1.73 mm after 6 months.

## 4. Clinical Cases

After reviewing the topic, six clinical cases used Bond Apatite® as bone graft material in different procedures. The characteristics of the patients and surgeries are summarized in Table 2.

**Table 2.** Description of the cases. I.M.: Intraoperative management; I.C.: Intraoperative complications; G: Good; M: Moderate.

| Patient Gender Age | Medical History of Interest [Toxic Habits] Type of Surgery | Closure by First Intention [Collagen Sponge] | I.M. | I. C. | Healing | Early Postoperative Complications | Late Postoperative Complications |
|---|---|---|---|---|---|---|---|
| **1 F 63** | NO [Tobacco: 2 cig/day] Horizontal Guided Bone Regeneration | Yes [No] | G | No | G | No | No |
| **2 M 52** | NO [-] Alveolar ridge preservation | No [Yes] | G | No | M | Graft loss and self-limited alveolitis | No |
| **3 M 61** | NO [-] Alveolar ridge preservation | Yes [No] | G | No | G | No | No osseointegration of the implant, replacement in 3 months, without problems and with good stability |
| **4 F 46** | NO [-] Alveolar ridge preservation | No [Yes] | G | No | M | Graft loss and self-limited alveolitis | No |
| **5 M 64** | NO [-] Sinus lift with lateral window | Yes [No] | G | No | G | No | No |
| **6 M 46** | NO [-] Sinus lift with lateral window | Yes [No] | G | No | G | No | No |

Without exception, informed consent was obtained from all subjects involved in the study.

In all cases, both after the extractions and after the placement of the implants, post-surgical recommendations were provided and explained, as well as Amoxicillin 750 mg every 8 h × 7 days, Dexketoprofen 25 mg every 8 h × 3–4 days alternated with Paracetamol 1g every 8 h if there was pain, in addition to rinses with Chlorhexidine 0.12% (Bexident® Post topical gel, Isdin, Barcelona Spain) every 8 h × 7 days beginning 24 h after surgery.

Periodic follow-ups were carried out after a week, after the first month, and three months after the intervention with their corresponding X-ray. In all cases except one (Patient No. 1), after 4 months and before implant placement, a biopsy of the regenerated area was performed using a histopathological study (Trefina Komet, 032, Barcelona Spain, 032, diameter 3, 2 external, and 2.6 mm internal).

### *4.1. Patient No. 1*

A 63-year-old woman with no known allergies or medical history of interest, a smoker of two cigarettes a day, came to the clinic to rehabilitate an edentulous area at levels 45 and 47. She presented with 46 with a metal-ceramic crown and cantilever towards the

mesial (Figure 2A). It was decided to cut the cantilever, keep the crown at 46 temporarily, place implants at 45 and 47 and subsequently rehabilitate with three individual metal-ceramic crowns. At the 45 level, there was a horizontal bone defect (Figure 2B), so it was decided to perform a lateral ridge augmentation with Bond Apatite® on the same day as implant placement. Surgery was performed following the manufacturer's protocol, incision, detachment of the mucoperiosteal flap, micro-perforations in the cortex, placement of a Bond Apatite® syringe, compression with dry and sterile gauze, placement of Microdent® Genius 3.5 × 12 mm implants at the level of 45 and 4.5 × 12 mm at the level of 47, following the milling of the commercial house, repositioning the flap and tension suture (Figure 3). The recommendations and postoperative pharmacological guidelines were delivered. No intra- or postoperative complications occurred. The stitches were removed a week after surgery (Figure 4A) and regular monthly check-ups were performed (Figure 4B,C). After three months, a new CBCT was requested to assess the bone gain achieved (Figure 2D). Prosthodontic rehabilitation was carried out 4 months after surgery.

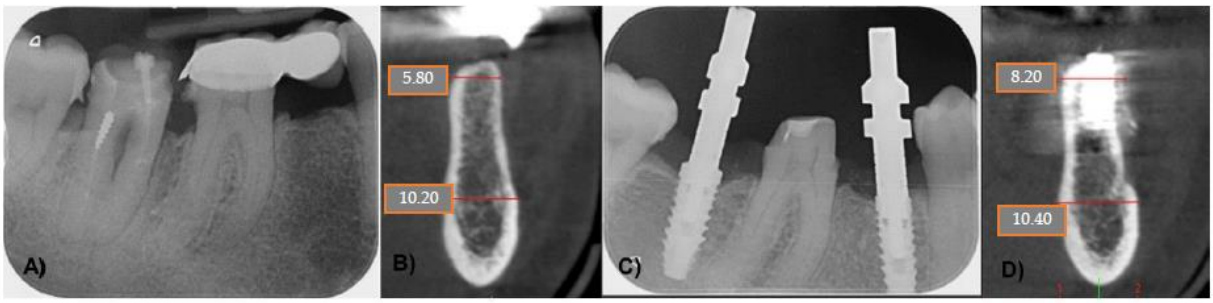



**Figure 2.** (**A**) Preoperative intraoral periapical radiograph (IOPA); (**B**) Initial CBCT; (**C**) Intraoperative IOPA; (**D**) CBCT after 4 months.

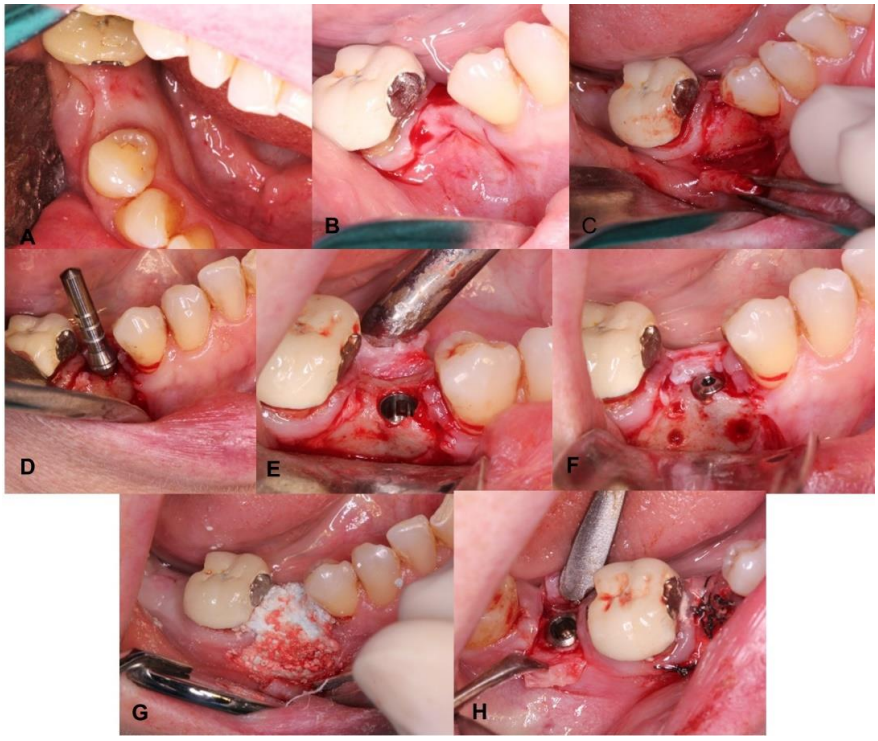



**Figure 3.** (**A**) Preoperative occlusal view; (**B**) Incision; (**C**) flap detachment; (**D**) Drilling according to protocol, check the position with the pin; (**E**) Implant placement at level 45; (**F**) Micro perforations in the vestibular; (**G**) Placement of Bond Apatite®; (**H**) Tension suture and implant placement in 47.

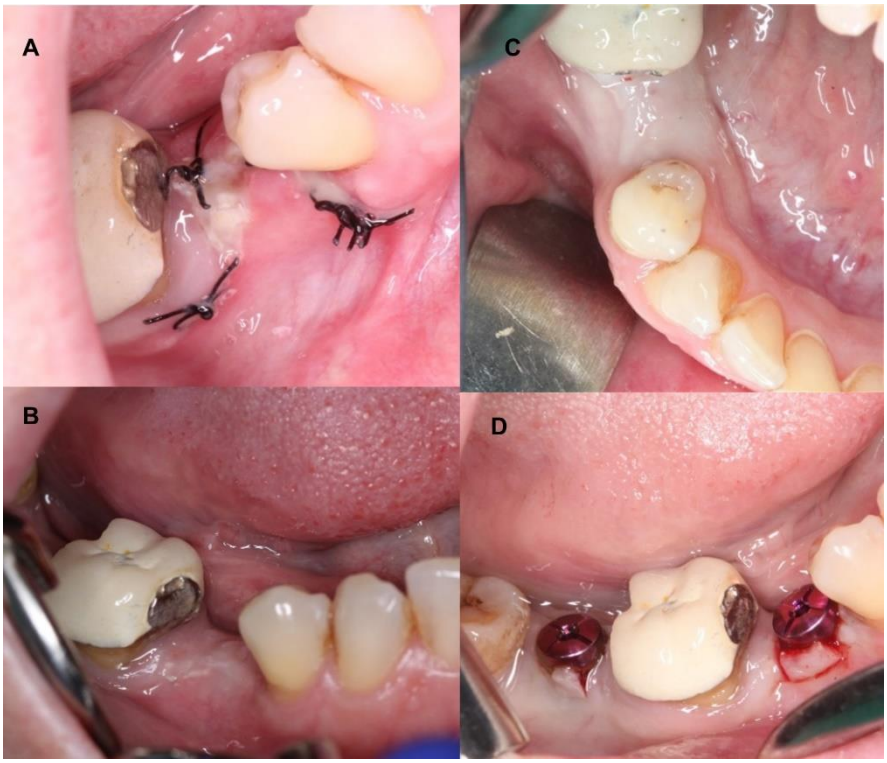



**Figure 4.** (**A**) Follow-up and removal of the suture after 7 days; (**B**) 1 month follow-up; (**C**) 2 months follow-up; (**D**) 3 months follow-up and healing abutments' placement.

### *4.2. Patient No. 2*

A 52-year-old man with no known allergies or medical or toxicological history of interest came to the clinic to assess the extraction of the 15 root remnant (Figure 5A) and placement of an implant. The case was assessed and, as there was not enough apical bone (Figure 6A), the possibility of placing an implant immediately after extraction was ruled out; it was decided to perform alveolar preservation after extraction and placement of the implant in a second surgical phase. We proceeded to the extraction of 15 and alveolar preservation with Bond Apatite® according to the manufacturer's protocol, extraction, curettage of the alveolus, placement of a Bond Apatite® syringe, compression with dry and sterile gauze, coverage with a collagen sponge and point of cross suture (Figure 7). There were no intraoperative complications. The recommendations and postoperative pharmacological guidelines were delivered. A week later, the patient attended suture removal reporting considerable pain. On examination, alveolitis and loss of graft material were observed, so the medication was changed to Amoxicillin/Clavulanic Acid 875/125 mg every 8 h × 7 days, Dexketoprofen 25mg every 8 h alternated with Metamizole 575 mg every 8 h if there was pain. Periodic monthly follow-ups were carried out (Figure 5B,C) and at 4 months a new CBCT of the area was requested (Figure 6B) for implant planning, where good healing and maintenance of bone volume were observed. On the day of surgery, a trephine biopsy was taken in the regenerated area for histopathological analysis (Figure 8) and a 3.5 × 10 mm Microdent® Genius implant was placed following the milling protocol of the commercial house (Figure 5D). The same pharmacological regimen was prescribed as on the day of the extraction and monthly follow-up visits were scheduled. Currently, he must undergo the second surgical phase and subsequent prosthodontic rehabilitation.

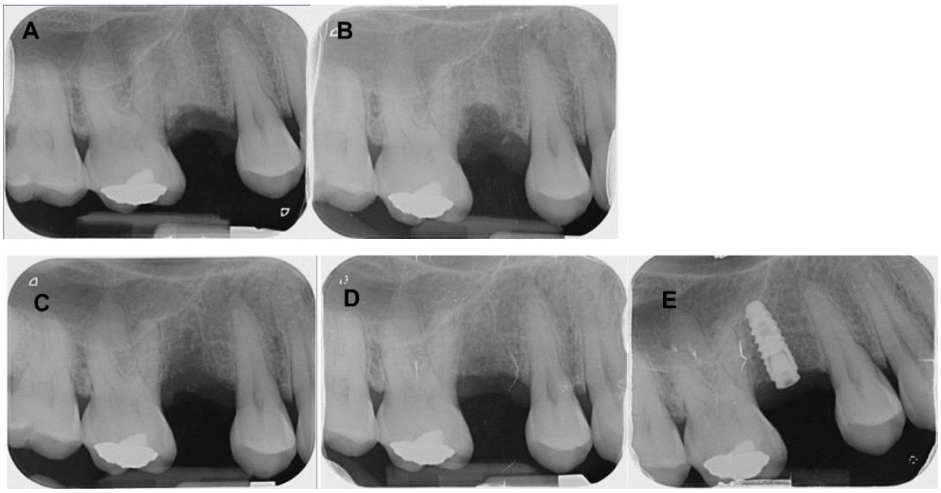
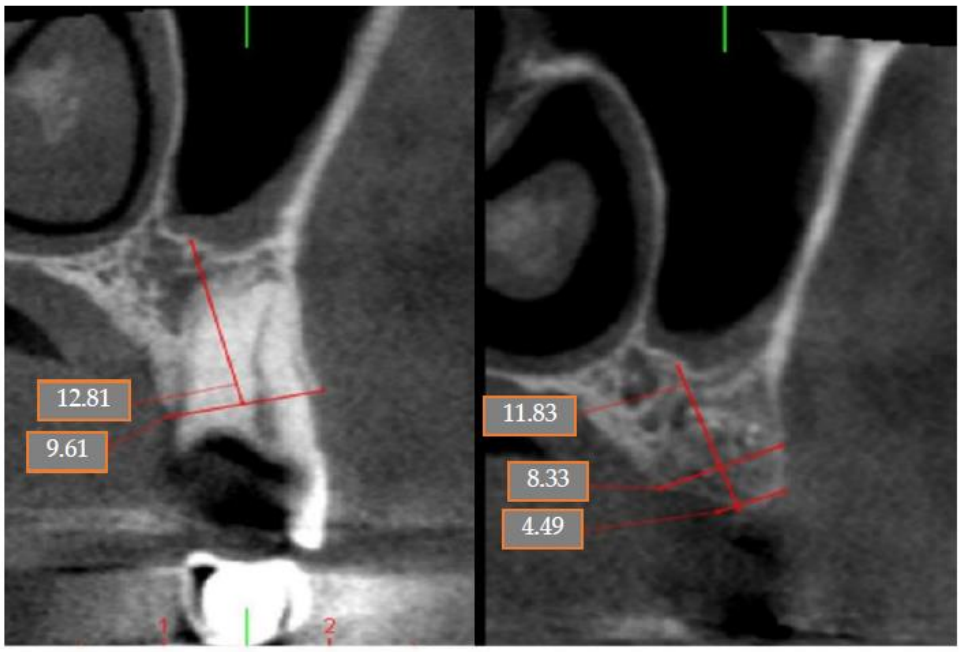



**Figure 5.** (**A**) Immediate postoperative periapical; (**B**) One week IOPA; (**C**) One month IOPA; (**D**) Two months IOPA; (**E**) IOPA after implant placement.




(**A**) (**B**)

**Figure 6.** (**A**) Previous CBCT; (**B**) CBCT after 4 months.

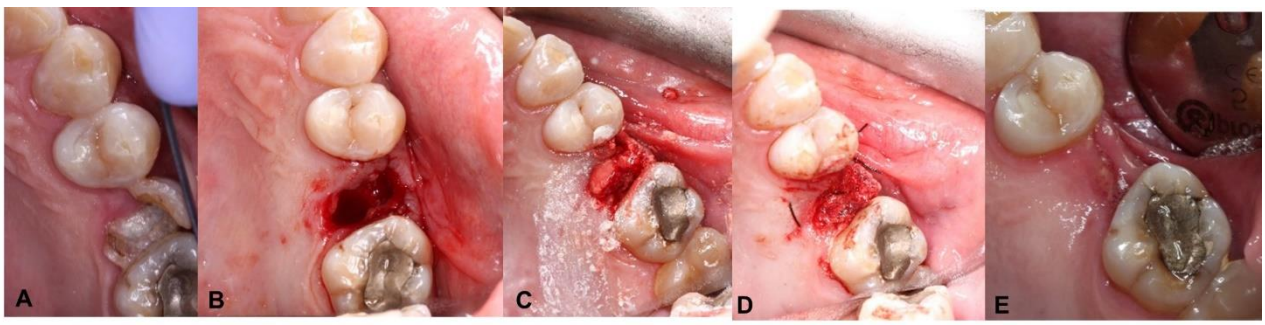



**Figure 7.** (**A**) Preoperative occlusal view; (**B**) Dental extraction of 25; (**C**) Placement of Bond Apatite®; (**D**) Postoperative occlusal view; (**E**) One-week follow-up.

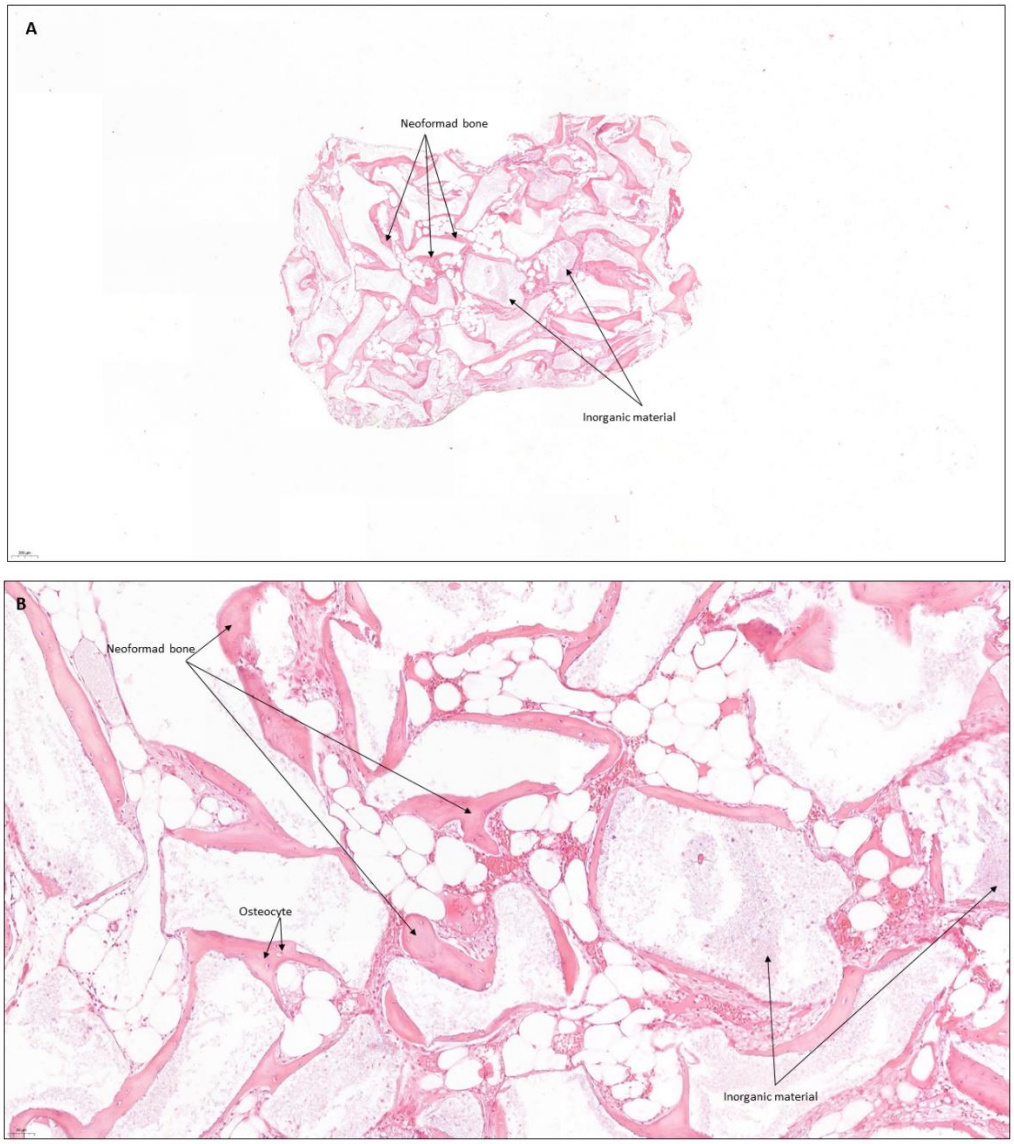



**Figure 8.** (**A**) Remains of inorganic material with newly formed bone trabeculae in (**A**) at 50× and in (**B**) at 200×. Total bone length of 5.97 mm and newformed bone of 2.98 mm.

### *4.3. Patient No. 3*

A 61-year-old male with no known allergies or relevant medical or toxicological history presented with pain in 24. He had a 24 endodontic treatment, with a filtered metal-ceramic crown in the distal part, non-restorable caries, so extraction was decided (Figure 9A). A CBCT was requested to assess the possibility of immediate implant placement, but the option was ruled out due to the presence of an apical lesion (Figure 10A). It was decided to perform alveolar preservation after extraction and placement of the implant in a second surgical phase. We proceeded to extract 24, profuse curettage of the alveolus, placement of a Bond Apatite® syringe, compression with dry and sterile gauze, and instead of placing a collagen sponge, the manufacturer's protocol was slightly changed since the closure was carried out by primary intention using a vestibular mucoperiosteal flap (Figure 11). There were no intraoperative complications. The recommendations and postoperative pharmacological guidelines were delivered. The stitches were removed a week after surgery and regular monthly check-ups were performed (Figure 9B–E). At 4 months, a new CBCT of the area was requested for implant planning, where good healing and maintenance of bone volume were observed (Figure 10C). On the day of surgery, a trephine biopsy was taken in the regenerated area for histopathological analysis (Figure 12) and a 3.5 × 12 mm

Microdent® Genius implant was placed following the milling protocol of the commercial house (Figure 9F). The same pharmacological regimen was prescribed as on the day of the extraction and monthly follow-up visits were scheduled. Four months after the placement of the implant, the second surgical phase was performed and at the time of removal of the closure plug, the implant was explanted in its entirety, showing the lack of osseointegration of it, a profuse curettage of the area and the implant replacement visit was scheduled after 3 months.

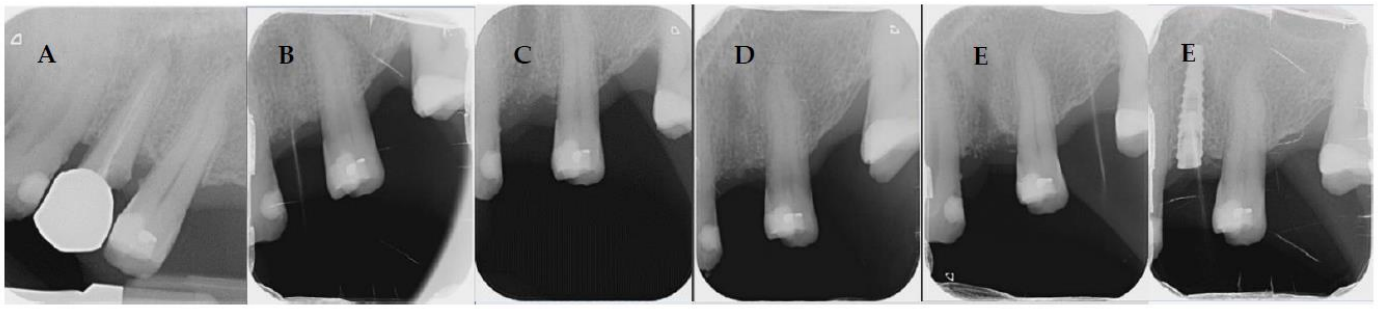
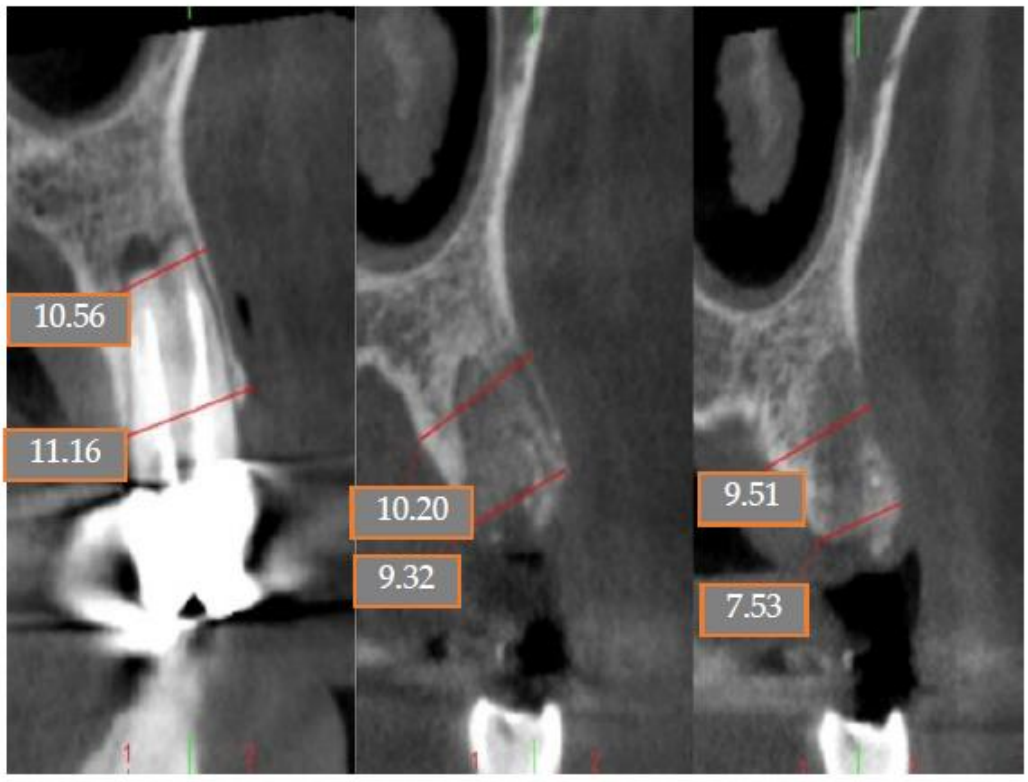



**Figure 9.** (**A**) Preoperative IOPA; (**B**) Immediate postoperative IOPA; (**C**) One week IOPA; (**D**) One month IOPA; (**E**) Two months IOPA; (**F**) IOPA after implant placement.




(**A**) (**B**) (**C**)

**Figure 10.** (**A**) Previous CBCT; (**B**) Immediate postoperative CBCT; (**C**) Postoperative CBCT after 4 months.

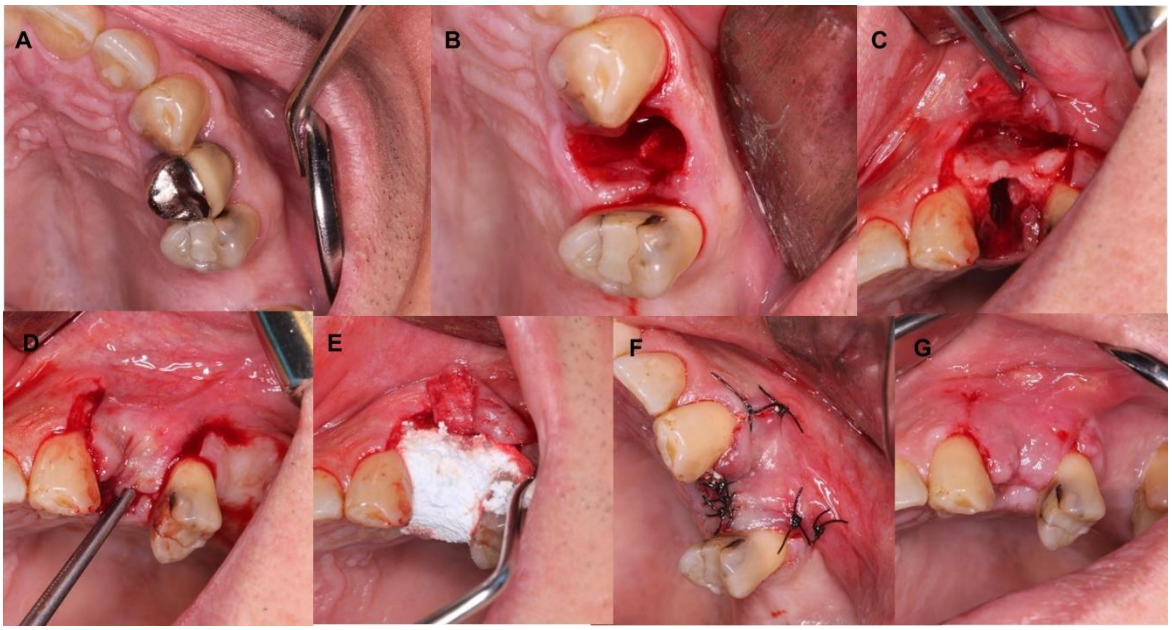



**Figure 11.** (**A**) Preoperative occlusal view; (**B**) Dental extraction of 24; (**C**) Mucoperiosteal flap; (**D**) Passivity check; (**E**) Placement of Bond Apatite®; (**F**) Closing by the first intention; (**G**) One-week follow-up.

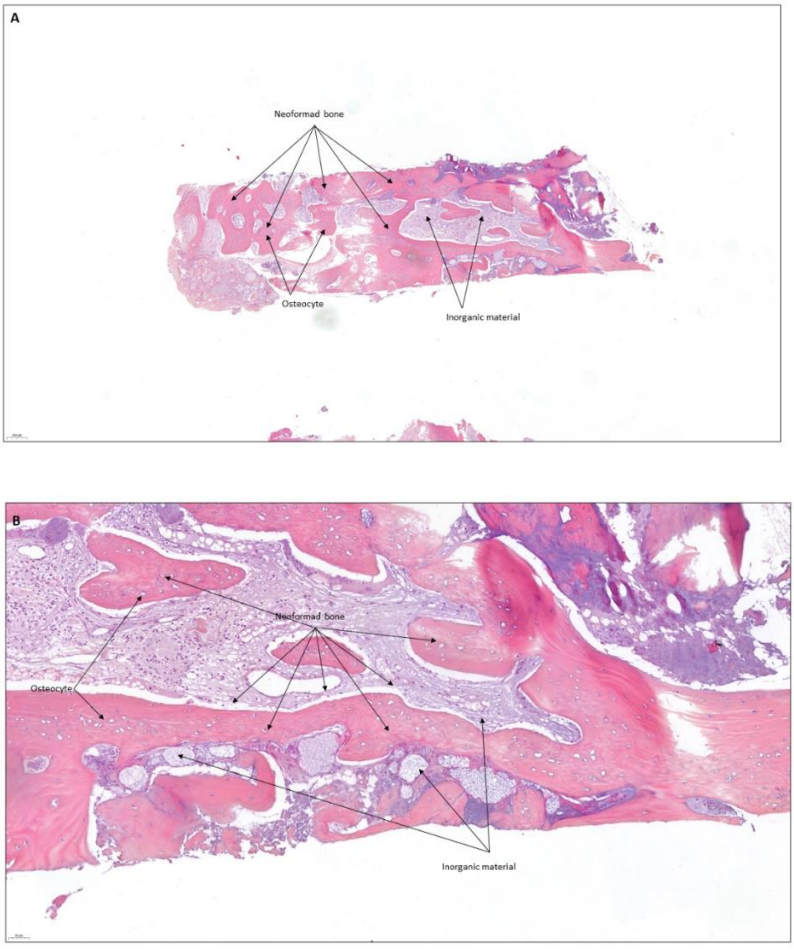



**Figure 12.** Remains of inorganic material and abundant newformed bone. Some degree of spinal cord fibrosis. (**A**) at 50× and (**B**) at 200×.Total bone length is 4.7 mm and newformed bone is 2.34 mm.

### *4.4. Patient No.4*

A 46-year-old woman with no known allergies or relevant medical or toxicological history came to the clinic due to discomfort in the upper-anterior area. She presented 12, 11, 21, and 22 with metal-ceramic crowns, endodontics, with apical lesions in all of them, and fistulas in the palatal area (Figure 13A). The patient explained that root canal retreatment had already been carried out on these teeth, so conservative treatment was ruled out and it was decided to extract all of them. A CBCT of the area was requested to assess the possible placement of immediate implants, but after observing the apical lesions (Figures 14 and 15), it was decided to place them in a second surgical phase. The 12, 11, 21, and 22 were extracted and an alveolar preservation with Bond Apatite® was performed according to the manufacturer's protocol, extraction, profuse curettage of the alveolus, placement of a Bond Apatite® syringe, compression with dry and sterile gauze, coverage with collagen sponge and cross stitches (Figure 15A–D). There were no intraoperative complications. Pharmacological recommendations and guidelines were delivered. A week later, the patient came to have the suture removed, reporting pain. On examination, alveolitis and loss of graft material were observed (Figure 15E). Amoxicillin/clavulanic acid 875/125 mg every 8 h × 7 days was prescribed. Periodic monthly check-ups were performed (Figure 13B–E) and at 4 months a new CBCT of the area was requested for implant planning, where good healing and maintenance of bone volume were observed (Figure 16). On the day of surgery, a trephine biopsy was taken in the regenerated area for histopathological analysis (Figure 17) and two 4.2 × 12 mm Microdent® Genius implants were placed in positions 12 and 22 following the drilling protocol for the commercial house (Figure 13F). The same pharmacological regimen was prescribed on the day of the extraction and monthly follow-up visits were scheduled. An immediate provisional screw-retained prosthesis was made and placed. Currently, he must undergo the second surgical phase and subsequent definitive prosthodontic rehabilitation.

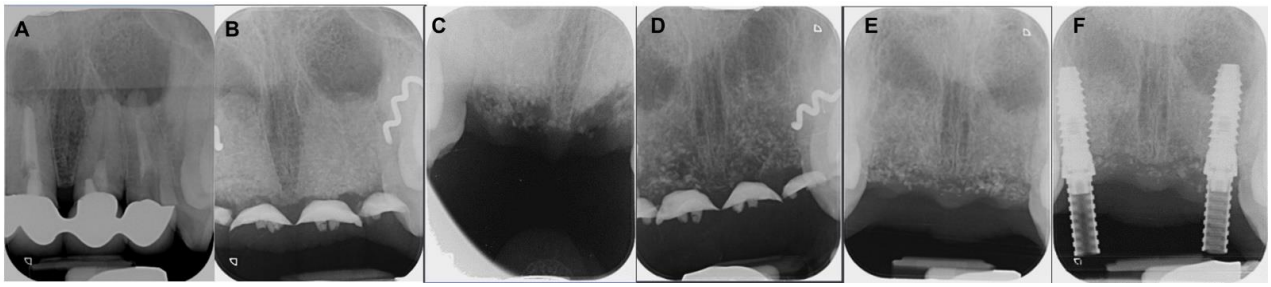



**Figure 13.** (**A**) Preoperative IOPA; (**B**) Immediate postoperative IOPA; (**C**) One-week IOPA; (**D**) One-month IOPA; (**E**) Two months IOPA; (**F**) IOPA after implant placement.

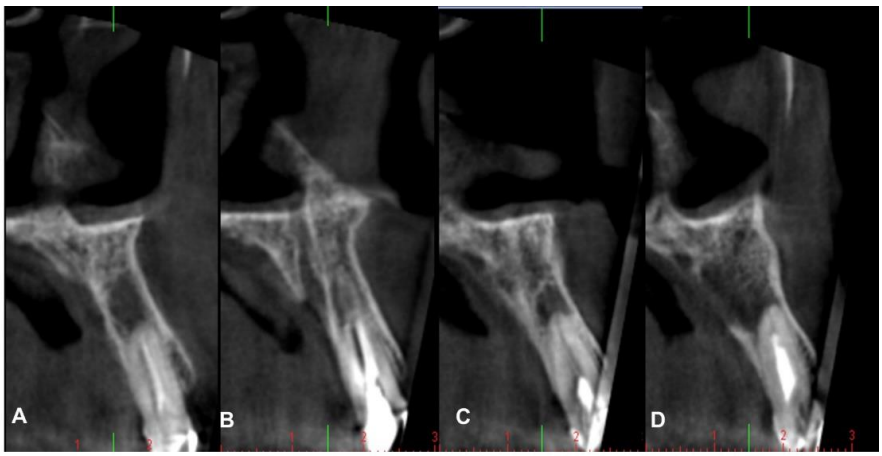



**Figure 14.** Previous CBCT. (**A**) 12 (**B**) 11 (**C**) 21 (**D**) 22.

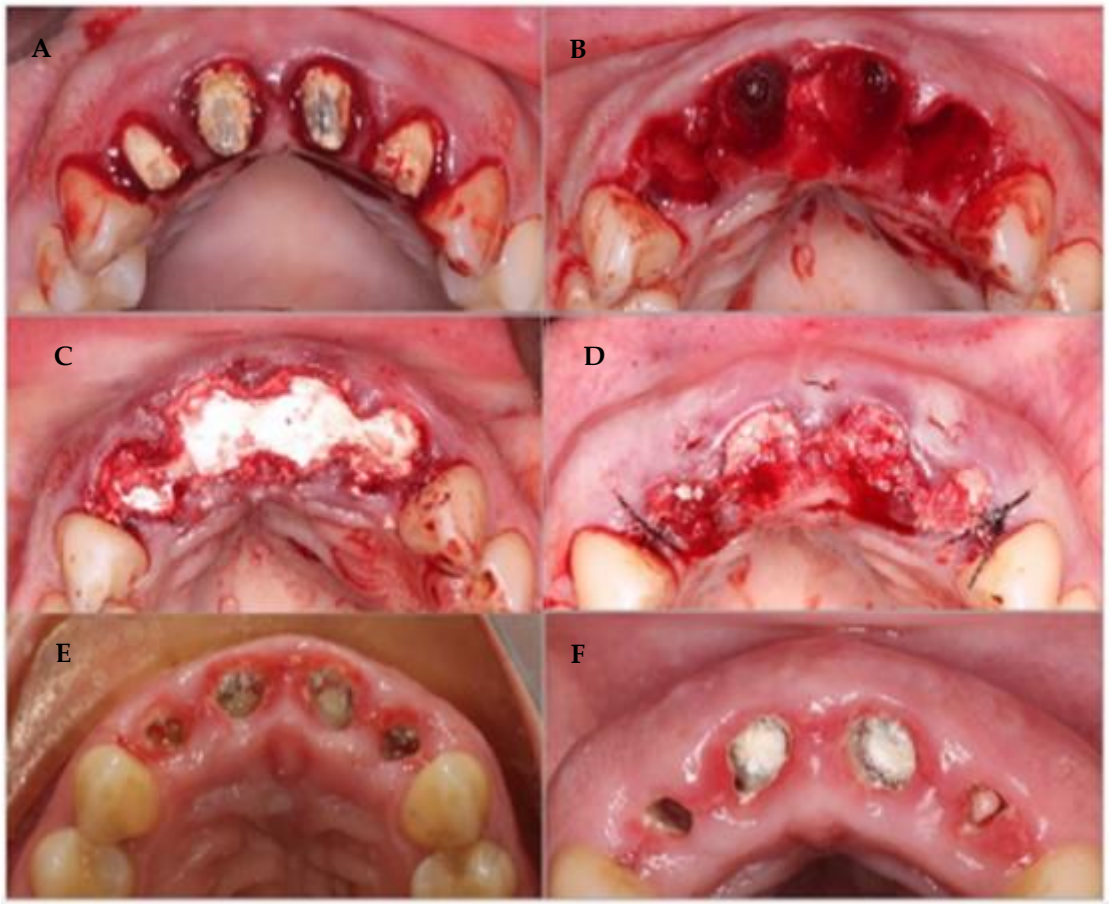



**Figure 15.** (**A**) Preoperative occlusal view; (**B**) Dental extractions; (**C**) Placement of Bond Apatite®; (**D**) Suture; (**E**) 7 days' follow-up; (**F**) 15 days' follow-up.

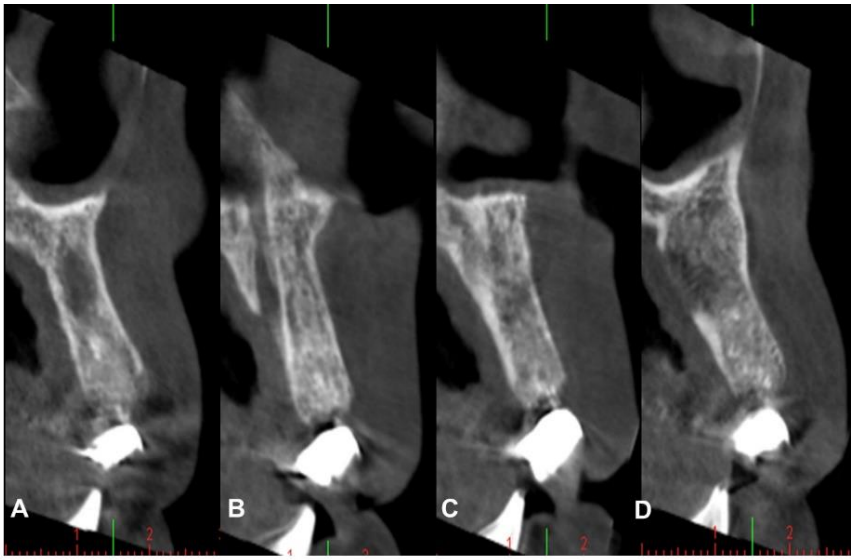



**Figure 16.** Postoperative CBCT after 4 months. (**A**) 12 (**B**) 11 (**C**) 21 (**D**) 22.

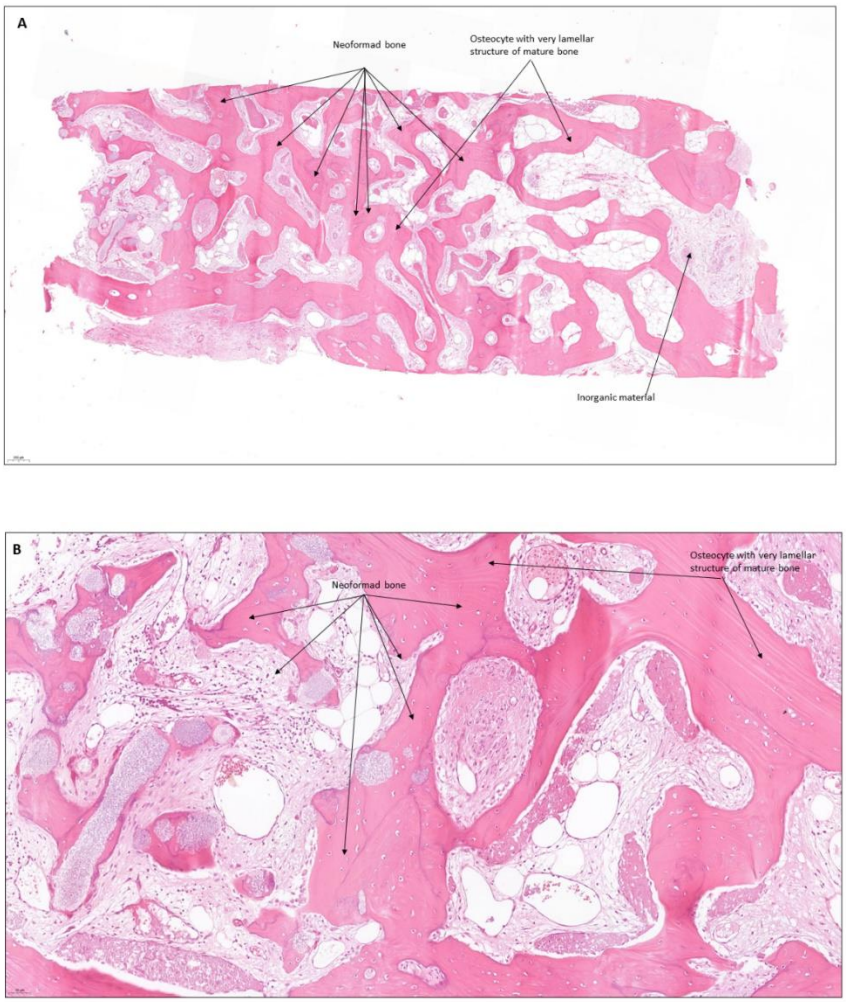



**Figure 17.** Few remains of inorganic material and abundant newly formed bone. (**A**) at 50× and (**B**) at 200×. Total bone length 6.63 mm, and clearly newformed bone indistinguishable from the rest 3.53 mm.

### *4.5. Patient No.5*

A 64-year-old male with no known allergies or medical or toxicological history of interest came to the clinic to assess rehabilitation of the second edentulous posterior quadrant by placing implants. CBCT was performed (Figure 18A) to assess bone availability in the area. It was observed that it was necessary to perform a sinus lift with a lateral window to have sufficient bone availability for the dental implant placement of 26 (3.6 mm height). It was decided to use Bond Apatite® as the bone graft material. On the day of surgery, the manufacturer's protocol was followed, detachment of the mucoperiosteal flap, preparation of the window and detachment of the sinus membrane, activation of the Bond Apatite® syringe and waiting for 1 min, placement of Bond Apatite® in the mesial area and compression with a periosteotome wrapped in a dry and sterile gauze, placement of Bond Apatite® in the distal and medial area until the cavity is filled, compression with a dry and sterile gauze from the outside of the window, reposition of the flap and suture under tension (Figure 19). Two syringes of Bond Apatite® were used. No intraoperative complications occurred and a CBCT was performed immediately after surgery (Figure 19) where a bone height gain of 12.6 mm was observed. Postoperative recommendations and pharmacological regimens were delivered. Periodic monthly check-ups were performed and at 4 months a new CBCT was requested (Figure 18C) of the area for implant planning, where good healing and bone height gain of 5.6mm were observed, a surprising result since it means that, after 4 months, more than 50% had been lost on the day of surgery.

On the day of implant placement, a trephine biopsy was taken in the regenerated area for histopathological analysis (Figure 20) and a 4.25 × 10 mm Microdent® Genius implant was placed at 26 following the drilling protocol of the commercial house. The same pharmacological regimen was prescribed as on the day of the sinus lift, and monthly follow-up visits were scheduled. Three months after the placement of the implant, the second surgical phase was carried out, and prosthodontic rehabilitation is currently being carried out.

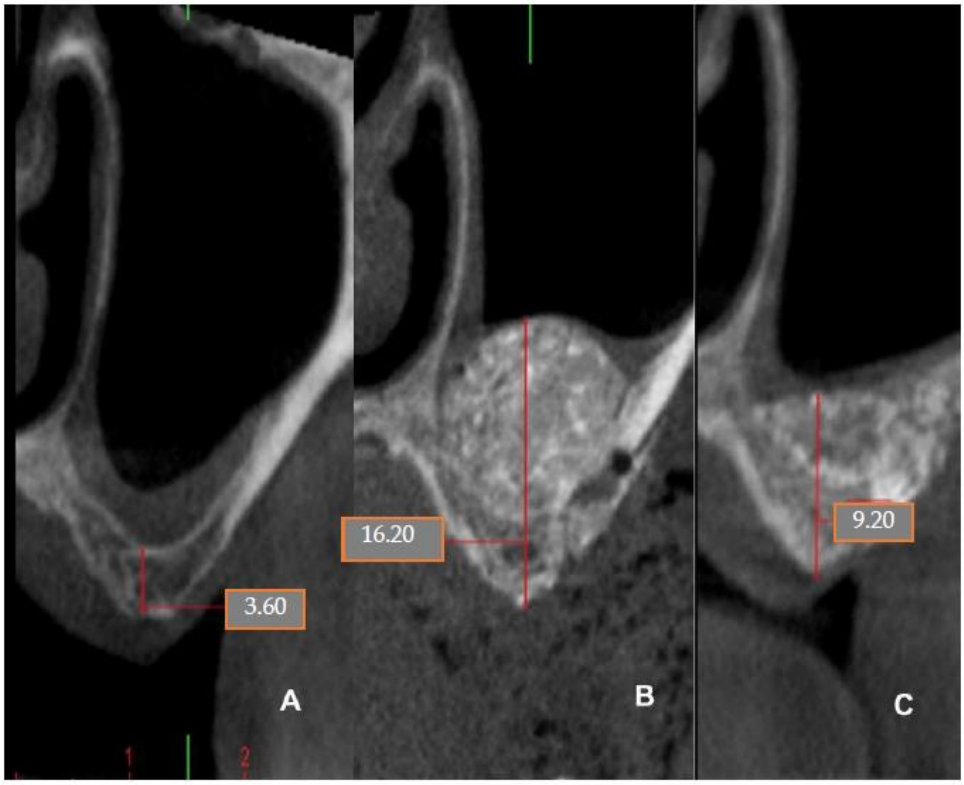



**Figure 18.** (**A**) Preoperative CBCT; (**B**) Immediate postoperative CBCT; (**C**) Postoperative CBCT after 4 months.

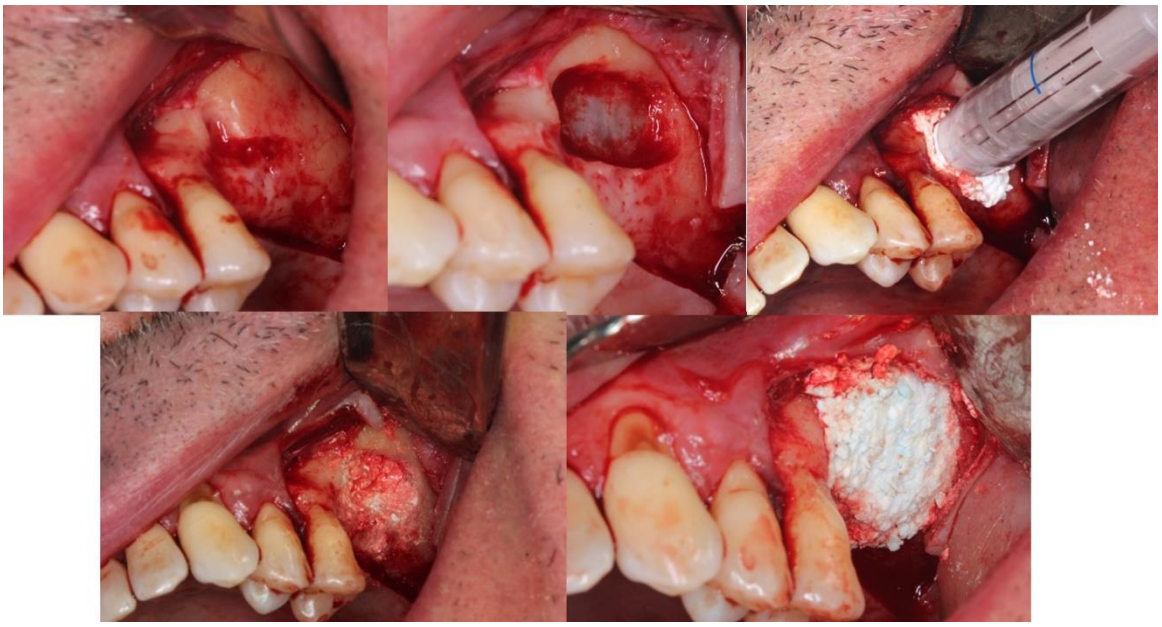


**Figure 19.** Intraoperative photographs.

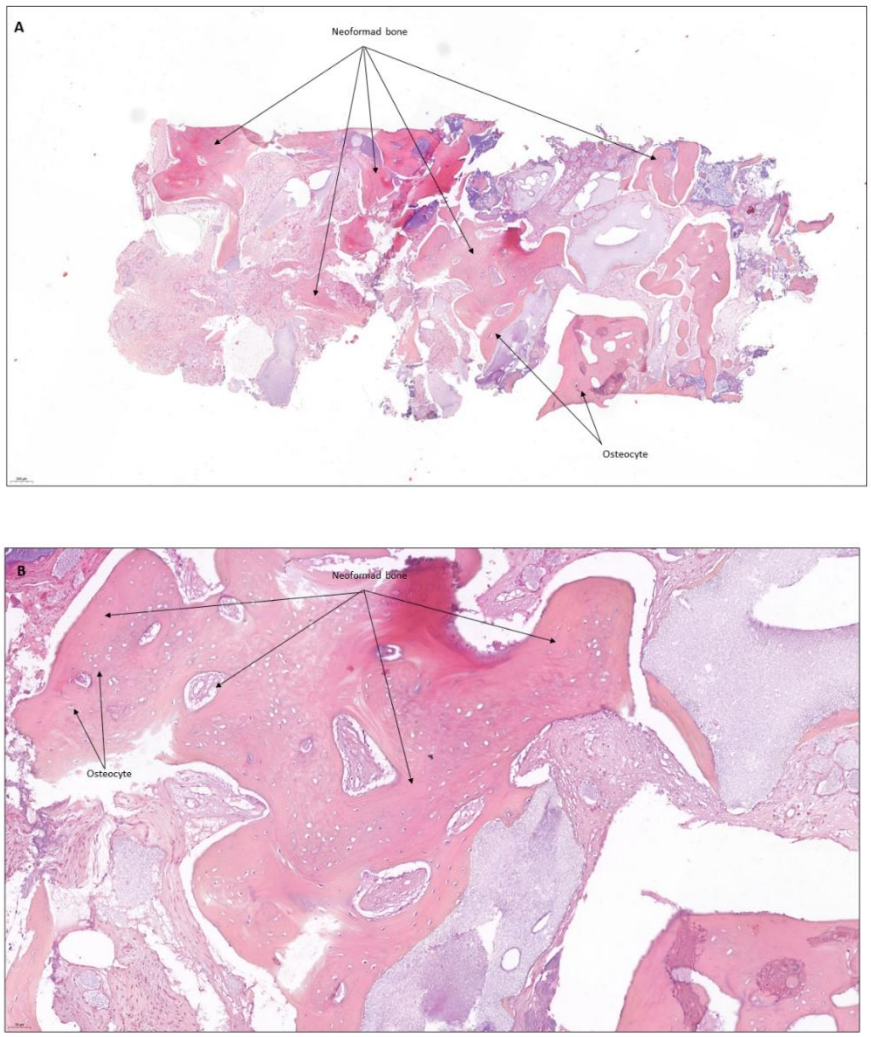



**Figure 20.** Abundant newly formed bone in (**A**) at 50× and in (**B**) at 200×. Total bone length is 7.2 mm and newly formed bone is 5.4 mm.

### *4.6. Patient No.6*

A 46-year-old man with no known allergies or relevant medical or toxicological history came to the clinic to assess rehabilitation of the edentulous second posterior quadrant by placing implants. CBCT was performed (Figure 21A) to assess bone availability in the area. It was observed that it is necessary to perform a sinus lift with a lateral window to have sufficient bone availability for implant placement since there was 6 mm in the 2.4 mm area and 2.8 mm in the 26 area. It was decided to use Bond Apatite® as the bone graft material. On the day of surgery, the manufacturer's protocol was followed, detachment of the mucoperiosteal flap, preparation of the window and detachment of the sinus membrane, activation of the Bond Apatite® syringe and waiting for 1 min, placement of Bond Apatite® in the mesial area and compression with a periosteotome wrapped in a dry and sterile gauze, placement of Bond Apatite® in the distal and medial area until the cavity is filled, compression with a dry and sterile gauze from the outside of the window, reposition of the flap and suture under tension. Two syringes of Bond Apatite® were used (Figure 22). No intraoperative complications occurred and a CBCT was performed immediately after surgery (Figure 21B) where a bone height gain of 6mm was observed in the mesial area and 9mm in the most distal part. Postoperative recommendations and pharmacological regimens were delivered. Periodic monthly check-ups were performed and at 4 months a new CBCT of the area was requested (Figure 21C) for implant planning, where good healing and bone height gain of 6mm in the mesial area and 9mm in the distal area were observed.

Currently, the patient must undergo implant placement surgery and subsequently a second surgical phase and definitive prosthodontic rehabilitation. The results of the bone biopsy are shown in Figure 23.

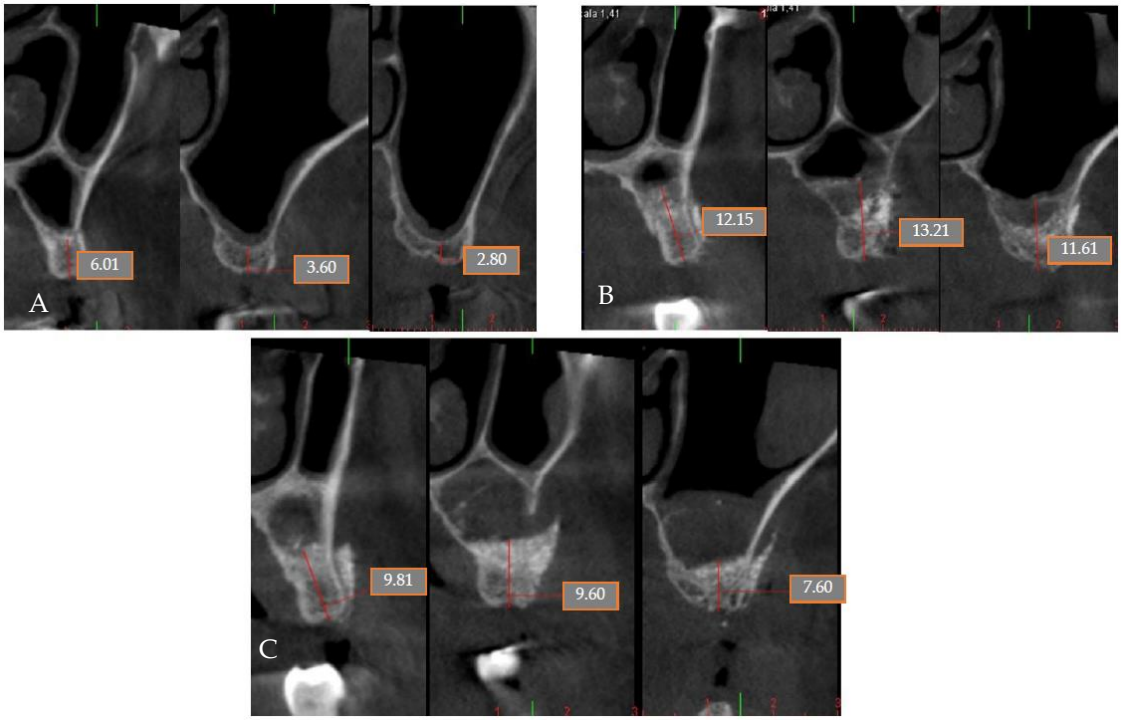



**Figure 21.** (**A**) Preoperative CBCT at level 24, 25, and 26; (**B**) Immediate postoperative CBCT at level 24, 25, and 26; (**C**) Postoperative CBCT after 4 months at level 24, 25, and 26.

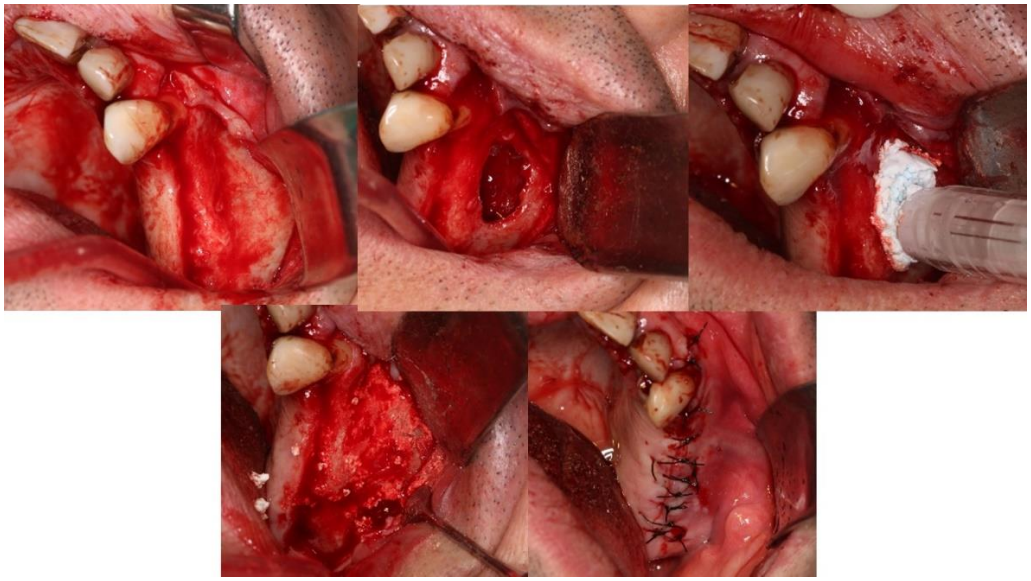


**Figure 22.** Intraoperative photographs.

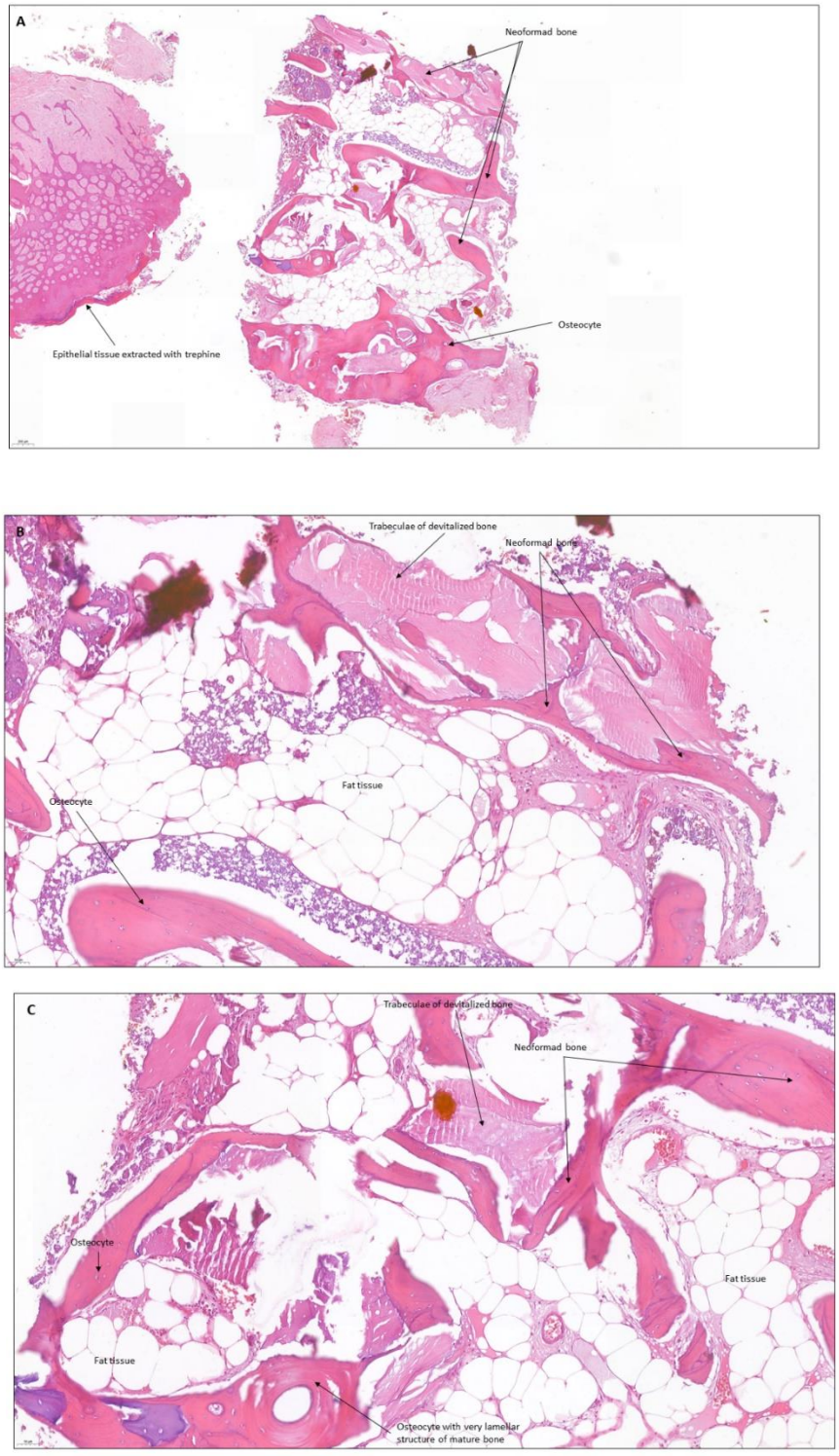



**Figure 23.** Abundant newly formed bone and some trabeculae of devitalized bone in (**A**) at 50× and in (**B**,**C**) at 200×. Total bone length of 3.56 and newly formed bone of 3.01 mm.

## 5. Discussion

In this review, the number of articles included was limited due to the limited bibliography on the subject; in addition, most of the included studies had a low level of evidence and had small samples. There was a high level of heterogeneity concerning study design, applications of calcium sulfate, and parameters studied. Due to this lack of homogeneity

that complicated the interpretation and summary of the results, it was not possible to compare and analyze the data quantitatively.

Maintaining the volume of the bone crest is important if the placement of implants in the area is subsequently planned, which is why alveolar preservation procedures require graft materials with specific characteristics [5,6].

It is important to take into account the speed and rate of resorption of the graft material, as this influences its osteoconductive capacity. Osteoconduction requires that the bone graft substitute have a rate of resorption similar to the rate of new bone formation. If the rate of resorption is faster than the rate of bone growth, the new bone will not have a scaffold to grow on. Conversely, if the graft material resorbs too slowly, it can remain in the bone defect and block new bone ingrowth [35]. In the case of calcium sulfate, it can be concluded that its resorption rate is favorable for the creation of new bone and for the maintenance of bone volume. The studies included in the review observed a 16% [30,31] residual graft after 4 months. Mahesh et al. [36] quantified its presence between 4.3% and 11.5% after 6 months and other studies [37] stated that, 12 months after the placement of calcium sulfate, it is reabsorbed in 99% and is replaced in 85% by new bone. In this regard, the works carried out by Ricci et al. [38] and, among others, Kadhim et al. [39] are very interesting. They determined that CS acts as a bioactive material when placed in a bone environment. By examining the CS during early periods, with histology, BEI, and XRM, Ricci et al. [38] observed that the CS material did not simply dissolve. As it dissolved and receded, it left behind a consistent latticework of a hydroxyapatite-like calcium phosphate mineral that was stable: in the short term, acted as an osteoconductive trellis for new bone formation, became incorporated in the new bone, and was then remodeled as the bone matured. On the other hand, the main difference between the bioactive glass (BG) and Bond Apatite (biphasic calcium sulfate/hydroxyapatite, BCS/HA) is that the latter (after activation) is injected into the site and can be molded according to the needs of the clinician. It does not require membrane coverage during the augmentation procedure [38].

The alveolar preservation cases that we performed (Case No. 2, Case No. 3, and Case No. 4) using Bond Apatite® as bone regeneration material, obtained good results in terms of maintaining bone volume. It should be noted that, in the cases where the protocol was followed, and closure was not performed by the first intention, alveolitis and partial loss of part of the material were observed after a week (Case No. 2 and Case No. 4); no difficulty was presented for the subsequent insertion of the implants.

Bone grafts continue to be one of the most widely used therapeutic strategies for the correction of periodontal bone defects. Both Trombelli et al. [40] and Reynolds et al. [41] in their systematic reviews summarized that bone substitutes were significantly more effective than open flap debridement in improving attachment levels and reducing probing depth. Both Pandit et al. [28] and Mandlik et al. [29] agree that calcium sulfate is an effective material in the treatment of periodontal defects since it is biocompatible, bioabsorbable, osteoconductive, versatile, and easy to apply. The good results of this material encourage testing its use in peri-implant treatments as it would provide a quick, comfortable, and economical solution for the follow-up of peri-implantitis. Guarnini et al. [42] propose a treatment combining the surface treatment of the implant with powdered abrasives and the use of calcium sulfate as grafting material, obtaining good results.

Laino et al. [33] studied the use of calcium sulfate as a graft in sinus lifts with a lateral window, obtaining good results, including a gain in bone height of more than 8mm, and these results coincide with those of other studies, such as that of Guarnieri et al. [42] who obtained a mean increase in bone height of 8 mm after 6 months and 2 years or that of Kher et al. [43], who reported a slightly greater gain of 10.31 mm. In our series of cases at 4 months, a bone gain of 6 mm and 9 mm was obtained depending on the area in the first case (Case No. 5) and 5.6 mm in the second case (Case No. 6). In the second case, the loss of more than 50% of bone height achieved was surprising when comparing the day of surgery with the follow-up after 4 months.

It is important to consider the size of the defect since it has been established that the width at the base of the defect facilitates space provision and influences bone repair through GBR [44]. Evidently, in tiny faults, the demand for augmentation and consequently the projected gain is slightly smaller than in bigger defects [45]. Large defect augmentation appears to be more difficult and technique-dependent.

Other factors that should be taken into consideration are the location of the defect, since the anterior and posterior mandible and maxilla segments have differing bone properties [46], and the loading timing, since according to the literature, GBR around immediate dental implant placement can improve hard tissue response during the healing period [47].

## 6. Conclusions

Calcium sulfate as a graft material in oral surgery has proven to be an effective, predictable, practical, economical, and easy-to-handle material in different areas of implant surgery.

Currently, the available literature on the use of calcium sulfate as a graft material in implant surgery is scarce, and what is available provides low-quality evidence. That is why more research studies on the subject are necessary to allow more comparisons and meaningful conclusions.

After using Bond Apatite® in our case series, we can conclude that it is a useful and easy-to-handle material in implantology practice, but more controlled studies should be carried out in this regard to assess its long-term efficacy, especially in horizontal and/or vertical regeneration.

**Author Contributions:** Conceptualization, J.L.-L. and A.M.-R.; methodology, A.T.-M.; software, B.G.-N.; validation, J.L.-L., A.T.-M. and B.G.-N.; formal analysis, A.A; investigation, A.A.; resources, R.Z.-L.G.; data curation, R.Z.-L.G.; writing—original draft preparation, A.A.; writing—review and editing, A.T.-M.; visualization, J.L.-L.; supervision, J.L.-L.; project administration, A.M.-R.; funding acquisition, R.Z.-L.G. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, the approval by the Institutional Review Board was not required since the data are properly anonymized and informed consent was obtained at the time of original data collection.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Not applicable.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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