

ORIGINAL ARTICLE

Autogenous DDM versus Bio-Oss granules in GBR for immediate implantation in periodontal postextraction sites: A prospective clinical study

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Funding information

National Natural Science Foundation of China, Grant/Award Number: 51672276; High-Level Talent Start-Up Research Project of Foshan University, Grant/Award Number: Gg 07002

Abstract

Purpose: Demineralized dentin matrix (DDM) from the patient's own extracted healthy tooth can be recycled as an autogenous biomaterial for reconstructive dentistry. The aim of the present study was to evaluate the clinical efficacy of autogenous DDM versus Bio-Oss granules in guided bone regeneration (GBR) for immediate implantation in periodontal postextraction sites.

Materials and methods: From November 2015 to March 2017, patients referred to the Foshan Stomatology Hospital, who had been diagnosed with severe periodontitis of the posterior mandibular tooth and agreed to dental implant treatment, were consecutively included. The patients were randomly allocated to the DDM group, treated with immediate implantation + GBR with autogenous DDM granules from the extracted tooth, or the BIO group, treated with immediate implantation + GBR with Bio-Oss granules. The implant stability and marginal bone resorption were measured immediately, at 6 and 18 months after surgery.

Results: Forty patients (45 implants) were included. Except 2 cases with wound infection, 43 implants did not have postoperative complications and achieved a satisfactory outcome after 1-year prosthetic loading. There was no statistically significant difference between the 2 groups in implant stability quotient values and marginal bone resorption.

Conclusion: The autogenous DDM granules prepared at the chairside after extractions could act as an excellent readily available alternative to bone graft material in GBR, even for implantation of severe periodontitis cases.

KEYWORDS

demineralized dentin matrix, guided bone regeneration, immediate implantation, periodontitis

1 | INTRODUCTION

Different types of bone substitutes, including autogenous bone graft, demineralized freeze-dried bone allograft, calcium sulfate, and synthetic hydroxyapatite bioglass, are used in dental implants with osseous defects and achieved favorable results in bone regeneration. However, they have some essential drawbacks including donor site morbidity, limited availability, and additional payment.¹ Tooth-derived demineralized dentin matrix (DDM) was first introduced in 1967, and several studies have shown that DDM has a chemical composition similar to bone.^{2–5} Due to chemotactic properties for osteoblasts and

osteoprogenitor cells, DDM from the patient's own extracted healthy tooth can be used for promoting the bone regeneration process at reconstructive dentistry, including extraction socket preservation, ridge augmentation, sinus bone graft, and guided bone regeneration (GBR) for implant site development.^{6–8}

There continues to be controversy regarding the medical choice of retention and removal of severely loose teeth due to periodontitis. In all cases, it should be based on patient preference. Leaders in this field have concluded that these teeth should be extracted as early as possible and reconstructed with implant restoration to prevent continuous and extensive absorption of the socket and recover tooth

function.⁹ It seems to be a reliable treatment to replace a tooth loosened by severe periodontitis with dental implant immediately after extraction.^{10–12} This method had a success rate comparable to that of delayed implant placement. In these cases, autogenous and a variety of xenogenic bone graft materials have traditionally been used to fill the osseous gap around the implant for GBR. To date, research about autogenous DDM for this type of treatment strategy has not been reported.

In this study, a series of clinical cases were used to compare the clinical and radiographic performance of DDM and traditional osseous powder at 12 months after immediate dental implantation for periodontitis that had resulted in a loose tooth. Therefore, the aim of the present study was to evaluate the GBR efficacy of autogenous DDM in periodontitis cases.

2 | MATERIALS AND METHODS

From November 2015 to March 2017, 20–60 year-old patients referred to the Foshan Stomatology Hospital, who was diagnosed with localized severe periodontitis and agreed to dental implant treatment, were consecutively included in this study.

The inclusion criteria were as follows:

1. mandibular premolar or molar, with no obvious chronic endodontic lesion;
2. the single tooth cannot be reserved, which appears severe alveolar bone resorption in excess of two-thirds of the root length in X-ray, tooth mobility 2–3°, probing depth >6 mm;
3. residual bone possesses sufficient height;
4. stable periodontal status of the rest sites; and
5. good oral hygiene, controlled systemic disorders.

The exclusion criteria were as follows:

1. generalized severe chronic periodontitis or aggressive periodontitis, or bad oral hygiene, alcohol or drug abuse;
2. active infection at extraction site; and
3. patients with systemic disease (uncontrolled diabetes mellitus, hypertension and autoimmune disease, and others) and contraindications for surgery.

The patients were randomly allocated to the DDM group with immediate implantation + GBR with autogenous DDM granules from the extracted tooth or the BIO group with immediate implantation + GBR with Bio-Oss (Geistlich Pharma AG, Wolhusen, Switzerland) cancellous granules. Patients received sufficient explanations regarding the purpose, the benefits, and possible risks of this clinical research, and informed consent was obtained from each patient. This prospective clinical research was approved by the Institutional Ethics Committee.

Two weeks before surgery, a complete periodontal treatment was prescribed to the patient. During the first surgery, the loose tooth was extracted carefully under local anesthesia. Then, 2 vertical releasing incisions mesial and distal to the extraction site were performed and a

mucoperiosteal flap was elevated. Complete debridement and curettage of the socket to remove any granulation tissue and irrigation with saline solution were performed. The patient's own DDM was prepared by a professional nurse immediately after extraction: First, the attached soft tissues, caries, enamel and cementum of the extracted tooth were removed using a dental bur. Then, the pure dentine was grinded by an automatic mill (Osteo-Mill, Tokyo Iken Co Ltd, Tokyo, Japan) at 20 000 rpm for 7–10 seconds. The crushed granules (size 0.5–1.0 mm) from 300 to 1200 µm were demineralized in 2% HNO₃ for 20 minutes to expose the dentine's organic matrix (Demineralization) and then were immersed in 5% peracetic acid and 75% ethanol for 10 minutes to remove any bacteria and smear layer (Defatting and Sterilization). Finally, the prepared DDM granules were washed twice with distilled water. Meanwhile, 2 mL injectable platelet-rich fibrin (PRF) from the patient's own venous blood (5 mL) was fabricated with routine procedure by the nurse.¹³

In parallel to the DDM preparation, an Straumann (ITI) dental implant with appropriate dimensions based on the presurgical radiographs and the clinical evaluation of the socket was placed using routine methods. The insertion torque should be ≥35 Ncm and depth of implant inside osseous tissue must reach ≥4 mm for good primary stability. Cases which do not meet these requirements were excluded from this research. After a few small perforations on the socket surface were created using a round bur, the autogenous DDM granules in the DDM group or Bio-Oss granules in BIO group were fully inserted into the gap between the implant and the osseous socket. Then, the 2 mL PRF was injected into the socket. A BioGide membrane (Osteohealth, Switzerland) was carefully used to cover the graft site. If necessary, the attached mucoperiosteal flap was released for wound closure. Postoperative prescriptions included antibiotics and digestives for 5 days and chlorhexidine oral rinse for 10 days.

All implantation surgeries and prosthodontic treatment (6 months after surgery) were performed by the same dentist (Peng Li). The implant stability quotient (ISQ) was measured by Osstell Mentor (Integration Diagnostics AB, Goteborg, Sweden), and the digital periapical radiograph of the graft site taken with paralleling technique or panoramic radiograph was performed immediately, at 6 and 18 months after surgery. The marginal bone resorption was evaluated by $D_{\text{baseline}} - D_{\text{postoperative}}$ (The distance = abutment junction to the highest point of the regenerated bone adjoined the implant in mesial and distal segment (Figure 1). Based on the length of implant, the magnification of each individual radiograph was calculated. For the minimum discrepancy, all measurements were recorded by 2 independent radiologist.

For the above 2 parameters, the descriptive statistics (average and SD, $\bar{x} \pm s$) were calculated and the Student's *t*-test was used. All statistical analysis employed the Ver. 17.0 SPSS program (SPSS Inc, Chicago, Illinois), and the statistical significance was determined to be $P < .05$.

3 | RESULTS

Forty patients (16 women and 24 men) and 45 implants (23 in DDM group, including 10 premolar, and 13 M; 22 in BIO group, including

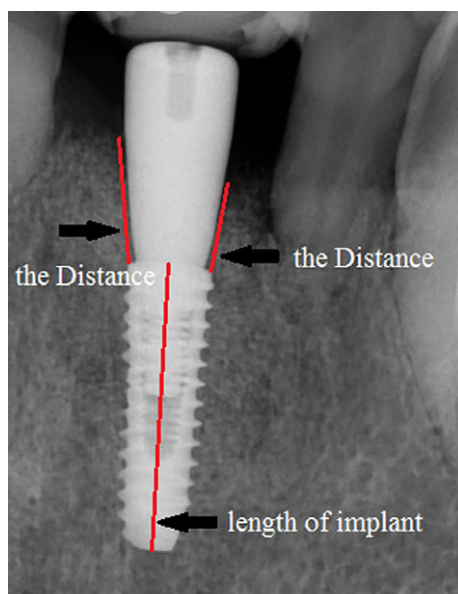


FIGURE 1 The graphic abstract of measurement of marginal bone resorption the marginal bone resorption was evaluated by $D_{\text{baseline}} - D_{\text{postoperative}}$ (the distance = abutment junction to the highest point of the regenerated bone adjoined the implant in mesial and distal segment)

9 premolar and 12 M; Tables 1 and 2) were included in this study. At 1 year follow-up, 38 patients did not have postoperative complications and achieved satisfactory outcome with implants restoration. Forty-three implants produced successful osseointegration. The ISQ values and marginal bone resorption around the implant in the

TABLE 1 Demographic information of the DDM group ($n = 22$)

Patient no.	Sex	Age	Implant site	Implant dimension (mm)	Insertion torque (Ncm)
1	M	34	46	5.3×1.0	40
2	M	21	34	4.1×1.2	40
3	F	57	46	4.5×1.0	35
			35	4.5×1.2	35
4	M	44	46	5.0×1.0	40
5	F	28	45	4.1×1.0	35
6	M	45	37	5.3×1.0	30
7	F	52	47	5.3×0.8	35
8	F	40	45	4.1×1.0	25
9	M	27	35	4.5×1.0	40
10	M	31	45	4.1×1.2	30
11	M	29	46	5.3×1.0	40
12	M	30	36	5.0×1.0	35
			44	4.1×1.0	40
13	M	38	46	4.5×1.0	40
14	F	41	37	4.5×1.0	30
15	M	33	44	3.9×1.2	35
16	F	48	46	5.0×1.0	40
17	F	23	35	4.1×1.0	40
18	M	36	36	5.3×1.0	40
19	F	40	46	4.5×1.0	35
			34	4.1×1.0	30

TABLE 2 Demographic information of the BIO group ($n = 21$)

Patient no.	Sex	Age	Implant site	Implant dimension (mm)	Insertion torque (Ncm)
1	F	23	36	5.3×1.0	40
2	M	57	44	3.9×1.2	25
3	M	26	45	4.5×1.0	40
4	F	44	46	4.5×1.0	40
5	F	45	37	5.0×1.0	40
6	M	32	46	5.3×0.8	35
7	M	38	44	4.1×1.2	35
8	F	27	37	5.3×1.0	40
9	M	31	45	4.1×1.0	40
10	M	33	35	4.1×1.0	40
11	F	20	46	4.5×1.0	35
12	M	47	44	4.1×1.0	25
13	M	26	36	5.0×1.0	40
14	F	30	35	4.5×0.8	40
15	M	54	45	4.1×1.0	20
16	M	35	34	4.1×1.0	40
17	M	29	46	4.5×1.0	35
			47	5.3×1.0	25
18	F	41	46	4.5×1.0	40
19	F	26	37	5.9×1.0	40
			35	4.1×1.2	30

2 groups are presented in Tables 3 and 4, respectively. There was no statistically significant difference between the 2 groups in the 2 parameters at each time period ($P > .05$). For most cases, there was no obvious difference in radiographic density between newly formed bone and alveolar bone.

In 2 cases (one in DDM group and one in BIO group), signs of microbial infection were observed at approximately 1 month after surgery, resulting in loosening of 2 implants in the molar region. Due to the failure of osseointegration, the 2 implants were removed and replaced with another implant of bigger diameter with additional bone graft using Bio-Oss granules after total debridement of the wound. Fortunately, after strict oral hygiene for 1 month, the wound healed without any clinical signs of infection, and the prosthodontic treatment was finished 6 months after the second implantation. However, the ISQ values from these 2 implants were excluded from the statistical calculations.

4 | CASE REPORT

A 37 year-old healthy male with severe loosening of a low right tooth was referred to our hospital. Clinical examination revealed that #47

TABLE 3 Stability ISQ values in the 2 groups ($\bar{x} \pm s$)

	Immediate postoperation	6 months	18 months
DDM group ($n = 22$)	53.6 ± 11.9	77.6 ± 7.9	79.5 ± 6.0
BIO group ($n = 21$)	54.1 ± 13.0	78.1 ± 4.2	80.2 ± 4.3
P	.14	.11	.09

TABLE 4 Marginal bone resorption around implant (mm, $x \pm s$)

	Immediate postoperation	6 months	18 months
DDM group ($n = 22$)	Baseline	1.7 ± 0.3	1.9 ± 0.6
BIO group ($n = 21$)	Baseline	1.8 ± 0.1	2.0 ± 0.5
P		.25	.18

Average of mesial and distal measurements.

was loosening to 3°, and #48 had slight pericoronitis. The panoramic radiograph showed severe alveolar resorption of #47 and perpendicular impaction of #48. The treatment plan was extraction of #47 #48, immediate #47 replacement with ITI implant and GBR using autogenous DDM and Bio-membrane. After the risks and benefits of this strategy had been explained to the patient, informed consent was obtained. This clinical research was approved by the Institutional Ethics Committee.

Six months postoperatively, clinical and radiographic assessments indicated satisfactory outcome. The implant produced clear ringing sound indicating successful osseointegration. The panoramic radiograph at 6 months indicated that the lamina dura of the socket had disappeared and the DDM granules had been completely remodeled and fused with the original socket. The details of the treatment process are shown in Figure 2A-E.

5 | DISCUSSION

In 1967, the bone-inducing property of rabbit dentin was confirmed in the intramuscular pockets.¹⁴ Many *in vitro* animal and clinical studies have been conducted since then and have confirmed the biocompatibility, biodegradability and osteoinductive and osteoconductive potency of the dentin matrix.¹⁵⁻¹⁷ For example, Gomes and couleges¹⁸ have conducted histological evaluations on the osteoinductivity of DDM with calvarial defects in rabbits and have verified that DDM have chemotactic properties for osteoprogenitor cells and osteoblasts, which may promote local bone regeneration. Murata and couleges¹⁹⁻²¹ reported the clinical usage of autogenous DDM from wisdom tooth

grafted back into the socket immediately after extraction. Six months postoperatively, 3-dimensional micro-CT and histological examinations indicated perfect bone regeneration and socket preservation. Nevertheless, the question remained if autogenous DDM material could act as an excellent readily available alternative to bone graft in severe periodontitis cases.

The osseous loss for periodontitis absorption should be reconstructed with various bone substitutes for further prosthodontic treatment. Under normal conditions, eventual hopeless teeth due to periodontitis always have to be extracted and discarded as medical waste. However, most of these teeth have healthy dental tissue. The human tooth is a rich, original source of stem cells, biopolymers, trace metal ions, and other materials. The dentin consists of 70%-75% inorganic content (hydroxyapatite and other calcium phosphate minerals such as ACP, TCP, and OCP), 20% collagen, and 10% water by weight. This is similar to the chemical composition of bone, although their tissue structures are different. After crush and demineralization, DDM become porous particles ranging in size from 300 to 1200 μm , which mainly composed of type I collagen (95%), noncollagenous proteins and growth factors, including IGF-I, TGF- β , BMP, etc. Consequently, tooth-derived DDM could be defined as acid-insoluble collagen with bone inducing molecules.^{22,23}

In the present study, 2 implants failed 1 month after surgery. Therefore, the success rate of the dental implantation for all cases in the 2 groups was 95.6% within the first year. The clinical and radiographic outcomes in this study showed that autogenous DDM could be used in GBR for immediate placement of implants in periodontal postextraction sites. There were several key aspects to the research design and management process. First, for immediate placement of implants in periodontal postextraction sites, it was reported that the failure rate was higher in maxillary than in mandible.²⁴ Therefore, we evaluated only the mandibular site because of its high success rate, and to allow comparison of the ISQ value in 2 groups. Second, PRF contains a variety of growth factors including TGF, ECGF, VEGF, FGF-2, and IGF-1, and is capable of releasing them slowly. It also contains clotting factors which may encapsulate the DDM granules in a compact form. So, the adjuvant use of injectable PRF may contribute

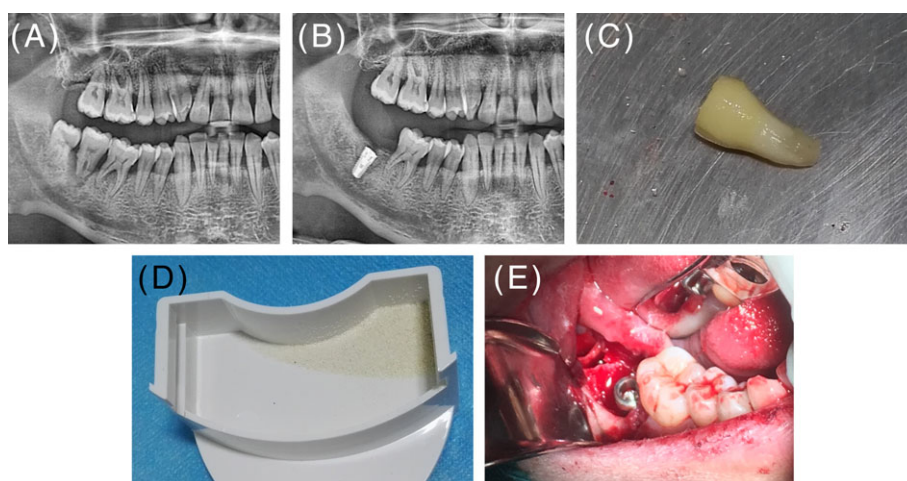


FIGURE 2 The treatment process of the case report. A, Preoperative panoramic radiograph; B, the panoramic radiograph 6 months after surgery; C, the autogenous tooth after mechanical processes; D, crushed tooth granules; and E, placement of the implant during surgery

to more predictable and favorable bone formation at the grafted site.¹³ Furthermore, a complete periodontal treatment before surgery and a total debridement of the socket intraoperatively provided a clean recipient site. For the prosthodontic treatment, the immediate loading was not employed. Finally, the primary stability of all implants was ensured in our study.

Many animal studies have demonstrated that demineralized dentin induced bone at 4 weeks, while nondemineralized dentin (so-called calcified dentin) induced bone at 8 to 12 weeks.²¹ The delayed inductive properties of the calcified dentin may be related to the inhibition of BMP release by the apatite crystals. These facts are the reason for the demineralization process of the grinded granules. Due to the high crystalline calcium phosphate of enamel hydroxyapatite, which has poor osteoconductivity, the enamel on the crown portion of the tooth was removed. Except for the demineralization, the defatting and sterilization processes were performed using commercially available materials that were relatively safe for handling DDM granules. Due to the strong oxidizing action, which causes rapid deactivation of microorganisms in the DDM granules, 5% peracetic acid and 75% ethanol were used for sterilization. The oxidation mechanism included disrupting cell wall permeability, denaturing proteins, and oxidizing sulfhydryl bonds. For the dentine grinder machine, the grinding and sieving processes were combined to save time. Through proper mechanical and chemical processes, autogenous tooth was transformed into fresh and cost-effective bone graft material at the chair side, well within the debridement and implantation period.

Previous studies histologically showed that autogenous DDM underwent gradual resorption and was replaced by new bone approximately 6 months after grafting.²⁵ In this study, radiography showed the expected results in most cases. The radiographic exam immediately after grafting indicated that DDM granules present tiny spots with high radiopacity around the implant. Gradually, the mean density of DDM granules markedly decreased, but the architecture of DDM granules became more homogeneous to the original trabecular bone. At approximately 6 months after grafting, there were no obvious differences in radiographic density between newly formed and alveolar bone. This change in radiographic characteristics distinctly indicates reabsorption of the DDM granules, new bone formation, mineralization, remodeling, and maturation at the grafted site. Therefore, in the present study the prosthodontic treatment was conducted 6 months after surgery to guarantee the stability and osseointegration of the implant.

The present study has some limitations, including small sample size ($n = 45$), nonstandardized type of implant, short follow-up period after GBR, and lack of bone biopsy for histological evidence. Moreover, 2-dimensional X-ray evaluation only provided limited information (the mesial and distal bone level) in marginal bone loss around implant. The CBCT radiographs could evaluate the changes in marginal bone more completely. Therefore, despite the favorable clinical outcomes obtained, no definitive conclusive statement can be made. Further research on the histological findings, morphometric analysis of the DDM, and long-term survival rate of the implant after prosthetic loading should be conducted to verify current result.

6 | CONCLUSION

This study showed a similar clinical and radiographic performance of DDM and traditional osseous powder in immediate placement of implants in periodontal postextraction sites. The autogenous DDM granules acted as an excellent, readily available alternative to bone graft material in GBR, even for implantation in severe periodontitis cases.

CONFLICT OF INTERESTS

No conflict of interest.

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How to cite this article: Li P, Zhu HC, Huang DH. Autogenous DDM versus Bio-Oss granules in GBR for immediate implantation in periodontal postextraction sites: A prospective clinical study. *Clin Implant Dent Relat Res.* 2018;1-6. <https://doi.org/10.1111/cid.12667>