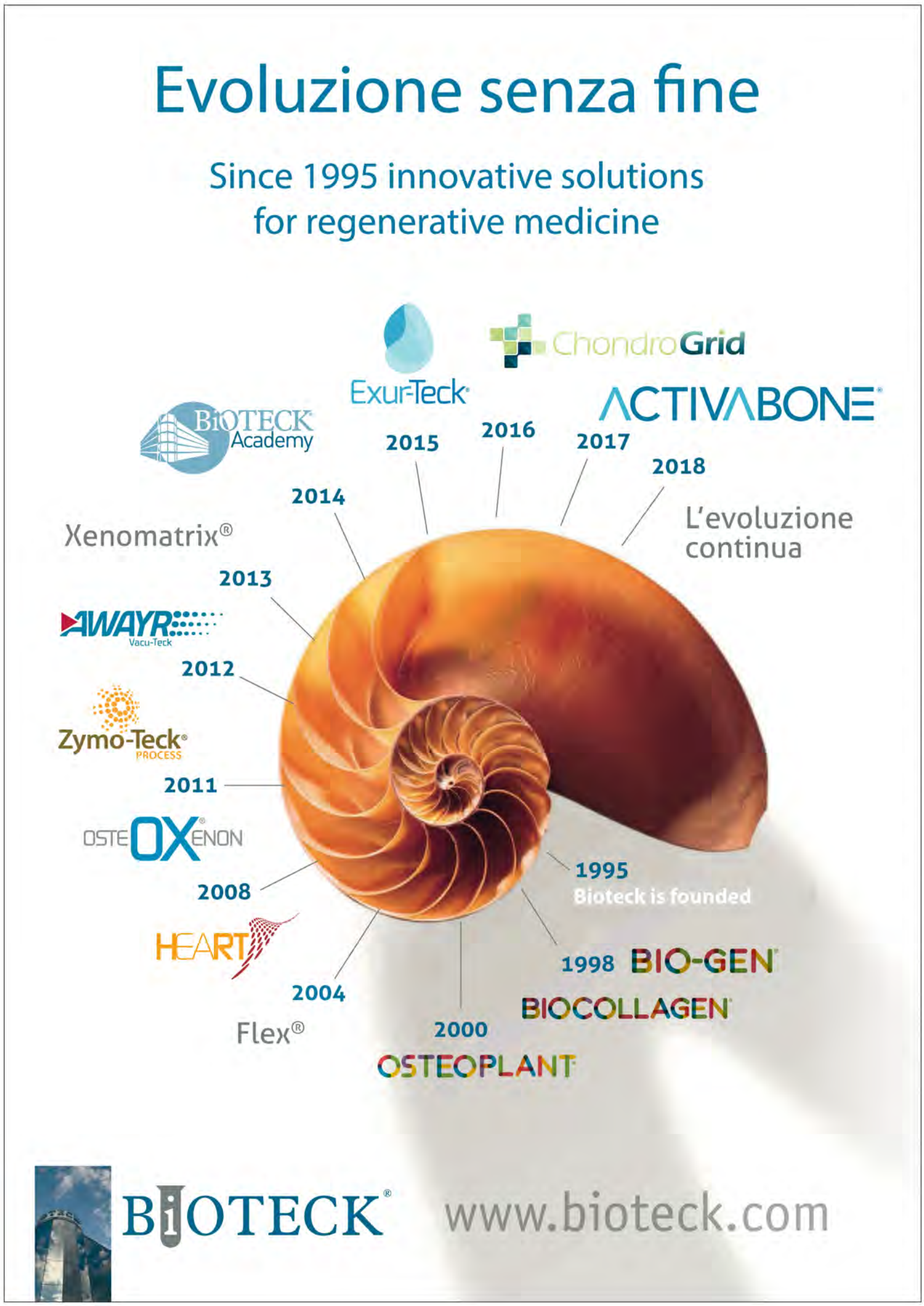
Treatment of Peri-Implantitis: Regeneration using a Slow-Resorbing Substitute

Danilo Alessio Di Stefano[1,2,3], Antonio Grimoli[2], Davide Fiori[3]

[1] *Private dental practitioner in Milan Adjunct Professor, Dental School, Vita-Salute San Raffaele University & IRCCS San Raffaele, Milan, Italy*
[2] *Dental Prosthetic Centre "Dentalnarco", Trezzano S/N, Milan, Italy*
[3] *Dental Prosthetic Centre "Civitali", Milan, Italy*



AD

Introduction

Peri-implantitis is an inflammatory process, which affects the tissues around the osseointegrated implant, leading to peri-implant bone loss. In addition, inflammation of the soft tissues is also common.

Its aetiology is infectious. The bacterial species involved, often anaerobic, are the same as those typically found in cases of periodontitis[1,2]. Other factors that may contribute to the development and worsening of the disease include an individual's predisposition, poor oral hygiene, smoking, improper implant placement, choice of an inappropriate implant in terms of morphology and size, improper prosthetic finishing, presence of foreign material such as cement, and improper implant-prosthetic passivation (in addition to occlusal trauma).

The dissemination of pro-inflammatory cytokines released by the immune system in the infected peri-implant area leads to a cascade of signals that results in the activation of proximal osteoclasts in the alveolar bone[3], leading to resorption of the peri-implant mineral matrix[4-5]. If the infection and inflammatory process are not addressed in time, erosion progressively spreads, leading to exposure of the implant body. In the most severe cases, implant loss occurs due to lack of support from the surrounding bone structure.

Once a peri-implant bone defect has occurred, even if it is properly cleansed with adequate professional dental hygiene protocols, it is often difficult to stabilise the situation. The peri-implant bone defect can, however, be the cause of a number of subsequent drawbacks: the patient will not be able to clean it properly at home; the bone cavity may favour the recurrence of peri-implantitis due to the microbial ecosystem residing within it. In addition, the absence of adequate bone support for the adjacent soft tissue may prevent the proper formation of the peri-implant seal, which may also promote recurrence of the disease.

Once the inflammatory state has been resolved and the cause eliminated, effective treatment of the peri-implant bone defect is therefore of paramount importance. Unfortunately, the decontaminated peri-implant bone defect is not able to regenerate on its own, and surgical intervention is necessary. To this end, various regenerative surgery

< page 17

< page 16

techniques have been proposed and adopted[6]. To date, there is no unanimous consensus on the best protocol to adopt. In order to optimise the decontamination of both the biological tissues and the implant surface, the opening of a flap is certainly shared as a general concept. This is followed by bone regeneration involving the grafting of biomaterials into the alveolar bone defect, which can facilitate the regeneration of the patient's bone. Furthermore, the use of membranes, absorbable or not, that separate the grafted bone defect from the mucogingival tissue is fundamental. Correct regeneration always requires optimal soft tissue healing. If this is achieved, the following occurs in the grafted area: (i) a phase of angiogenesis and infiltration of mesenchymal progenitor cells, (ii) remodelling of the graft and formation of new bone tissue, (iii) stabilisation of the tissues.

Among the bone graft substitutes that can be used, those derived from mammalian bone tissue are a viable option[7], given the similar morphology and composition of the bone tissue mineral component between the different species. Bone substitutes of animal origin must be properly processed to remove species-specific antigens that may cause unwanted immune reactions in the patient. There are several ways of removing antigens from the source bone tissue. Enzymatic treatments aim at not altering the bone mineral component and, if possible, at preserving type I collagen, a structural protein that favours the migration of the patient's cells into the bone graft.

In the case of thermal treatments, the use of temperatures of a few hundred degrees aims at eliminating the entire organic component present, including collagen. In the case of equine bone substitutes obtained by enzymatic means, it has been demonstrated that their effective colonisation by the patient's osteoblasts and osteoclasts, probably collagen-mediated, allows their remodelling in a physiological time frame[8]. In cases where the clinical conditions lead to a preference for grafts with slower resorption kinetics, bone substitutes obtained through a process of thermal antigen elimination, which slows down the resorption of the biomaterial while ensuring a good osteoconduction capacity, can be used. Equine bone substitutes obtained through an enzymatic antigen elimination process[9], as well as heat-treated bovine bone substitutes[10], have already been successfully used for the regeneration of peri-implant bone defects resulting from peri-implantitis, but in the literature there are no clinical studies comparing the two types of bone substitutes conducted on a significant number of cases and with a solid statistical analysis. The various meta-analyses that analysed currently available studies on the surgical regenerative treatment of peri-implantitis conclude that, at present, there is a lack of scientific evidence to determine the preferred type of biomaterial to be used[11-13].

This paper presents a case of peri-implantitis in two implants, which was treated with the use of a slow-absorbing equine bone substitute.

Case report

This case concerns a 53-year-old female patient, smoker, who presented for her usual periodic check-up complaining of bleeding and gingival pain caused by two implants located in position 4.6 and 4.7 during oral hygiene procedures. A cone beam computed tomography (CBCT) performed for other reasons revealed a marked peri-implant bone resorption (Fig. 1). As observed during surgery (Fig. 3), the exposure of the implant surface is greater than 50% in both fixtures, with a higher involvement in position 4.6.

Mucosal distress around the abutments of both fixtures was also observed. Following the diagnosis of peri-implantitis on both implants, the patient was proposed a treatment plan that included cleaning and decontamination of the peri-implant area, followed by guided bone regeneration (GBR) surgery consisting of the grafting of a slow-absorption bone substitute of equine origin, obtained by thermal antigen elimination (Calcitos, Bioteck S.p.A., Arcugnano, Italy), which could guarantee a prolonged temporal stability of bone profiles during regeneration, and a collagen membrane, also of equine origin (Biocollagen, Bioteck, Italy) to protect the graft.

The equine bone substitute in granules (0.5-1 mm) is made non-antigenic by thermal treatment; its porosity allows it to act as a suitable substrate for the infiltration of blood vessels and cellular elements from the patient's bone and the subsequent colonisation by endogenous bone tissue. The membrane (25 x 25 x 0.2 mm), which is composed of natural type I collagen extracted from equine Achilles tendon, is positioned, according to the principles of GBR, so as to prevent infiltration of the graft by soft tissue connective cells. The membrane ensures a protection time of 4-6 weeks, after which it is reabsorbed thanks to the action of endogenous collagenases.

The patient gave her informed consent to the treatment.

The patient underwent professional oral hygiene 5 days before surgery in order to resolve the inflammatory condition of the mucosa and prepare the peri-implant area for bone regeneration surgery, achieving an optimal state of soft tissues, consistent with the pathology shown (Fig. 2). Antibiotic therapy with Amoxicillin/Clavulanic acid (Augmentin, Glaxo-SmithKline, Verona, Italy) every 12 hours was prescribed for three days before surgery and for the following 8-10 days.

Following the pre-operative hygiene session, the patient was locally anaesthetised with Articaine 1:100,000 prior to the surgical phase. The cemented bridge and implant abutments were removed in order to open the mucoperiosteal flap and completely expose the implants and bone surface. The clinical examination confirmed the extent of bone resorption already observed on radiographic examination (Fig. 3). After removal of the granulomatous tissue that had developed around the implants (Fig. 4), a peri-implant debridement was performed with mechanical removal of the exposed threads. The implant surface was cleaned with air polishing using glycine powder, and then finally polished (Fig. 5).

> page 18

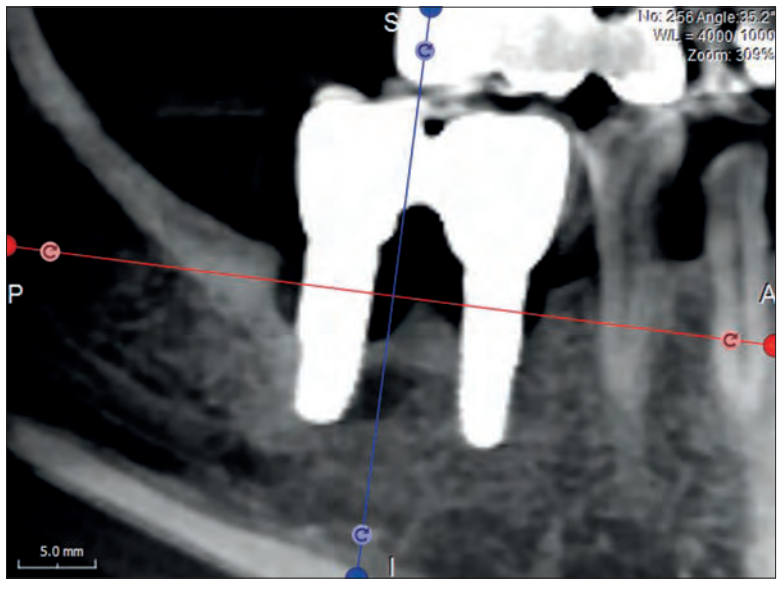


Fig. 1 - CBCT lateral view. Resorption cones involve a large portion of the implant surface.

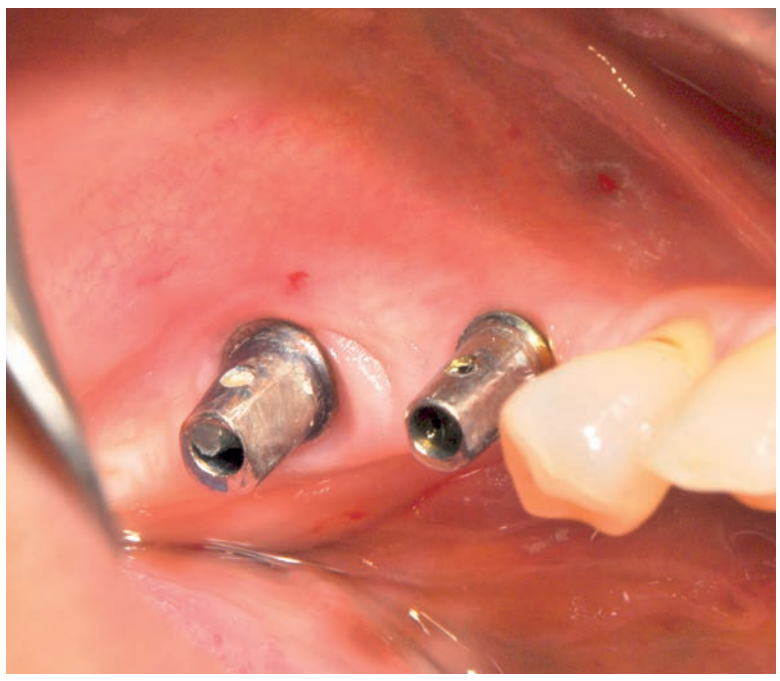


Fig. 2 – Clinical appearance of peri-implant mucosae at the time of surgery.

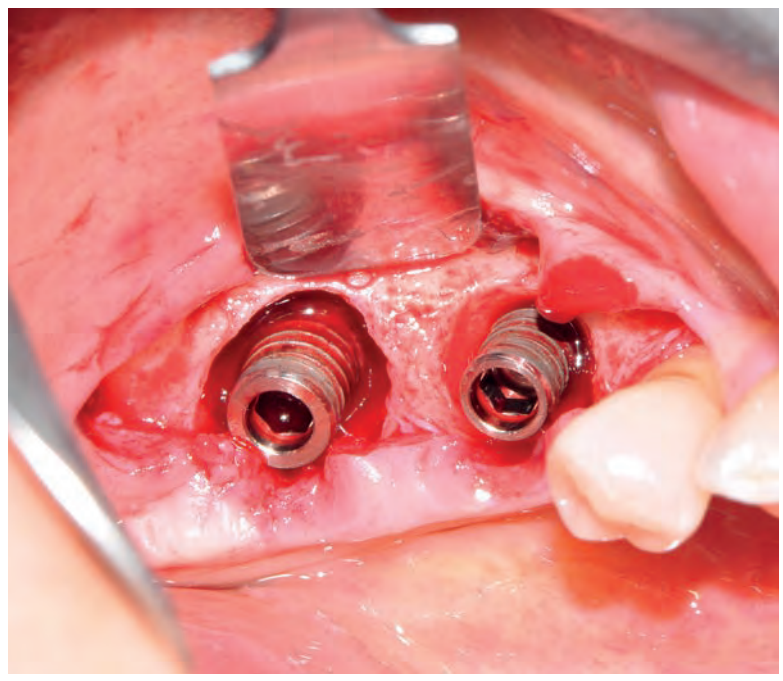


Fig. 3 - The two peri-implant defects at flap opening.

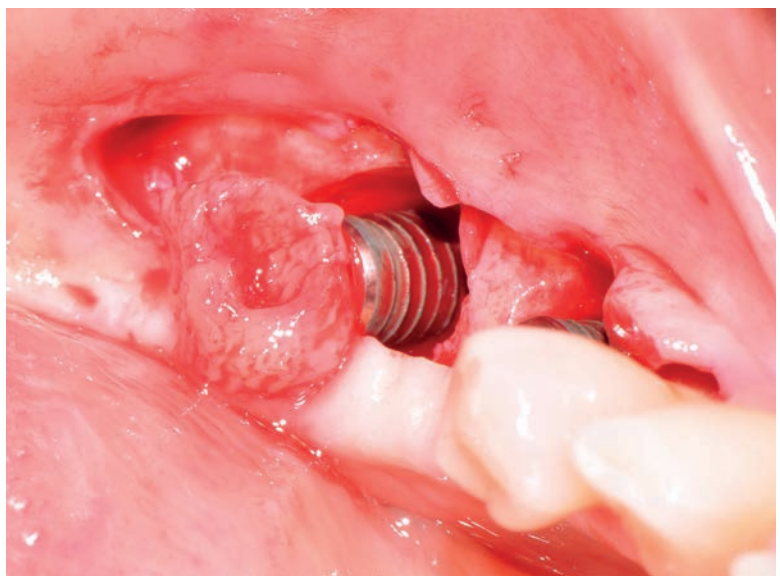


Fig. 4 – The removed granulomatous tissue surrounding the implants

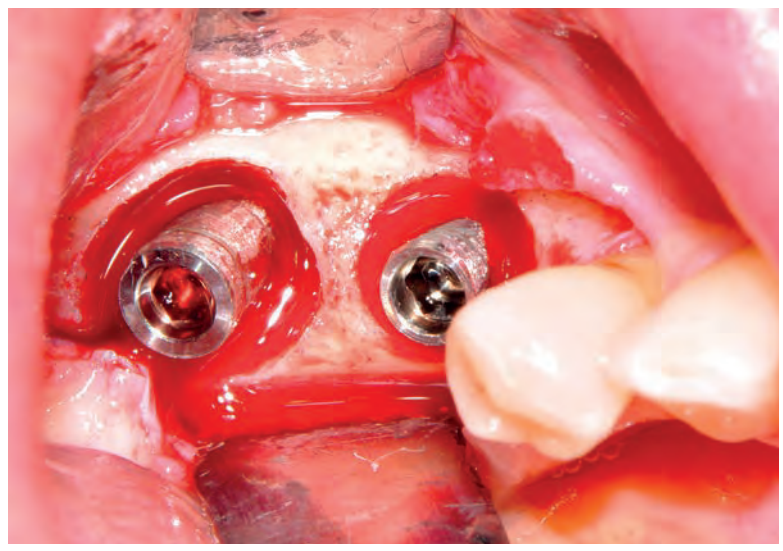


Fig. 5 – The appearance of the implant surface following removal of the threads and polishing.

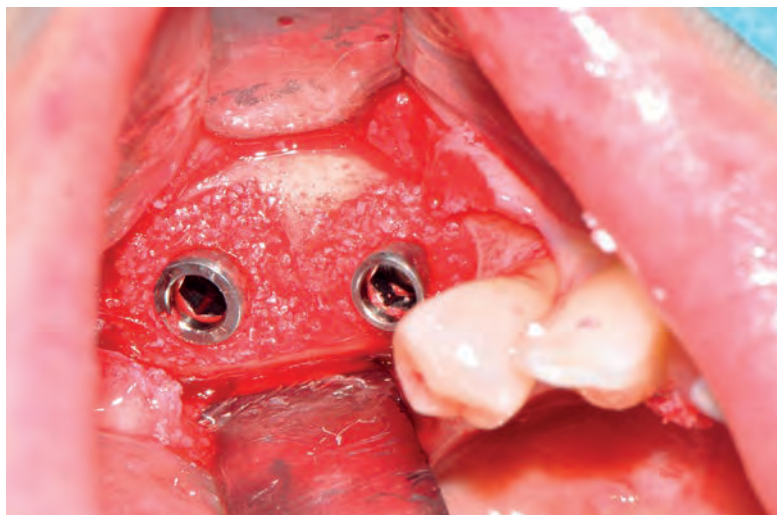


Fig. 6 - The two peri-implant defects are grafted with a slow-absorbing biomaterial

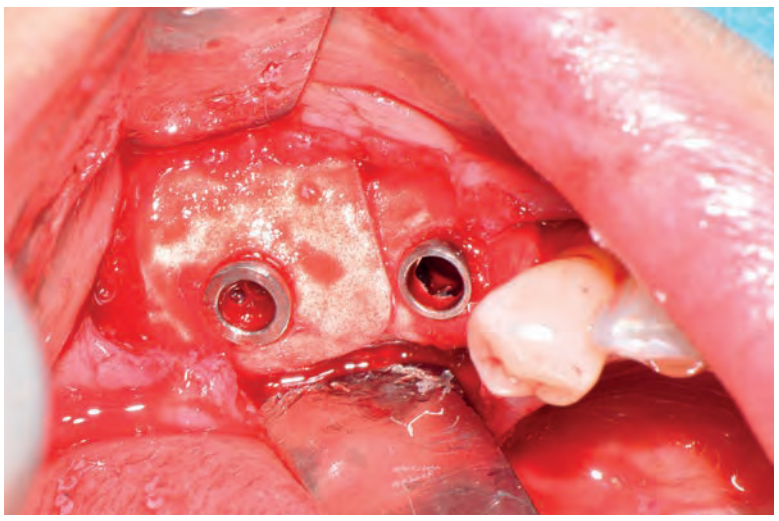


Fig. 7 - Collagen membranes are placed around the implants after proper perforation.

> page 17

To stimulate angiogenesis and integration with the graft, bleeding of the peri-implant bed was provoked. The previously hydrated granulate was grafted into the bone defect to cover the threads of the exposed surface of both implants until the original bone profile was restored (Fig. 6). The graft was protected with two membranes, suitably shaped and perforated to fit around each implant (Fig. 7).

The operation ended with the suturing of gingival flaps using non-absorbable polyamide thread (Monomyd 4-0, Butterfly, Cavenago, Italy) and the placement of two healing screws (Fig. 8). The suture was removed 12 days after surgery. A control radiograph at the end of the surgery confirmed the effective restoration of peri-implant bone volumes (Fig. 9). During the healing period and at subsequent follow-ups, no signs of gingival distress were observed (Fig. 10). The patient did not complain of any spontaneous or evoked symptoms. At the 3-month follow-up, the radiographic examination showed that peri-plantar bone profiles had been maintained (Fig. 11). The healing screws were then removed and the crowns repositioned. At the 15-month follow-up after surgery, the patient did not complain of any symptoms, and bleeding during oral hygiene had disappeared. The endoral control X-ray showed optimal maintenance of bone levels and complete stability of the peri-implant context (Fig. 12).

Conclusions and discussion

The maximum reduction of the infectious and inflammatory state of peri-implant tissues is a necessary condition for performing a GBR surgery. The strategy of peri-implant cleaning and disinfection proved satisfactory as no recurrences were observed in the post-operative period. The regeneration of resorbed bone tissue was achieved by using a slow-absorbing, non-antigenic bone granulate and isolating it with a collagen membrane that can be absorbed quickly. Both biomaterials are of equine origin.

Radiographic examinations carried out at 3 and 15 months after surgery and periodontal probing showed an almost stable state of the regenerated bone profile, the absence of defects and the maintenance of the peri-implant seal. In the absence of biopsies and histological analyses, it is not possible to determine the fraction of newly formed endogenous bone compared to the equine bone substitute, and to determine the degree of new osseointegration. When such analyses have been conducted in cases involving the use of enzymatically treated bone substitutes, they have shown a fairly rapid (several months) replacement of the graft with newly formed endogenous bone tissue, thus reproducing the kinetics of the physiological process of bone remodelling.

Although it is known that total resorption of heat-treated bovine bone grafts can take years 8, the kinetics of replacement for the equine formulation used in this case report has yet to be determined. In particular, the long-term follow-up will help us ascertain whether the bone profile is maintained and whether support to the gingival tissue continues being provided. Although collagen membranes offer a limited-in-time barrier compared to long-permanence membranes, even if absorbable (such as, for example, equine pericardium membranes), no problems have emerged regarding the infiltration of connective cells. It is hypothesised that the membrane not only plays a passive role in sealing the graft and maintaining the alveolar bone profile, but also provides a scaffold for colonisation by cell precursors and the release of factors that promote osteogenesis and graft remodelling 14. In contrast to non-absorbable membranes (e.g. expanded polytetrafluoroethylene), the use of a hydrolysable collagen membrane has avoided having to perform a new operation to remove the membrane, thus disturbing the bone regeneration process.

Even today, the clinical literature does not offer precise indications on the materials to be preferred in GBR procedures for the treatment of peri-implant defects. And the question remains open whether slow-absorbing bone substitutes should be preferred to physiological remodelling grafts, according to the rationale of a more effective maintenance of bone profiles over time, or whether the latter should be preferred to the former for their potential to achieve a real '*restitutio ad integrum*' of the alveolar bone.

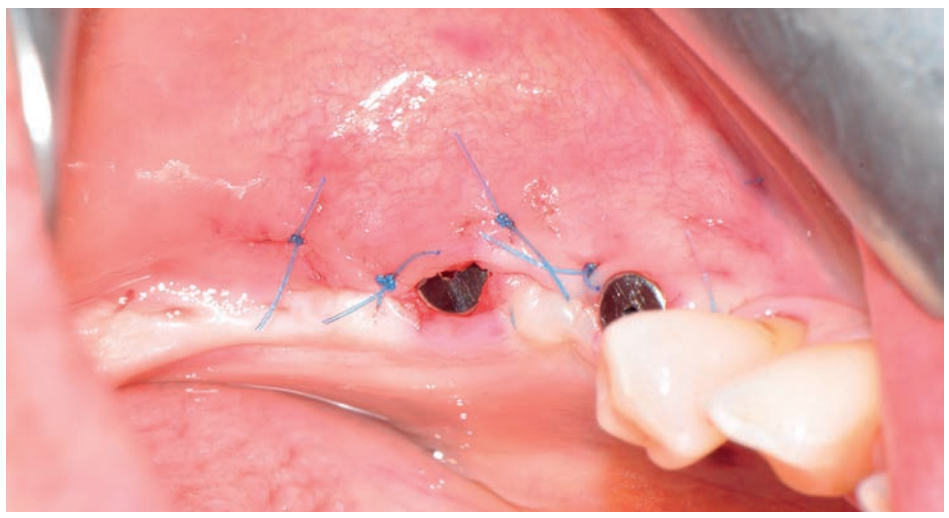


Fig. 8 - The suture at the end of surgery.

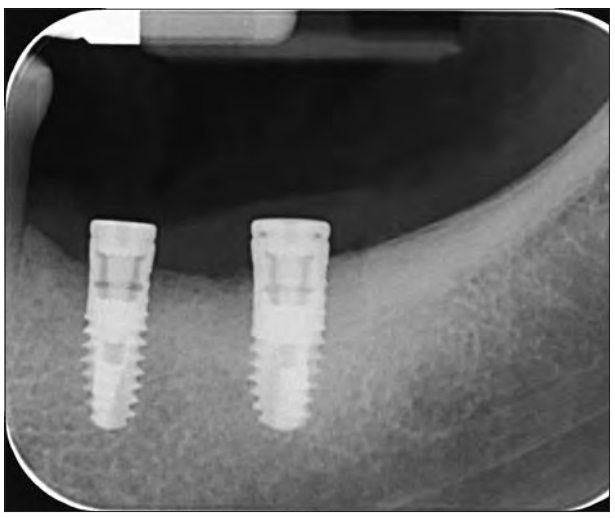


Fig. 9- Endoral control X-ray after surgery.

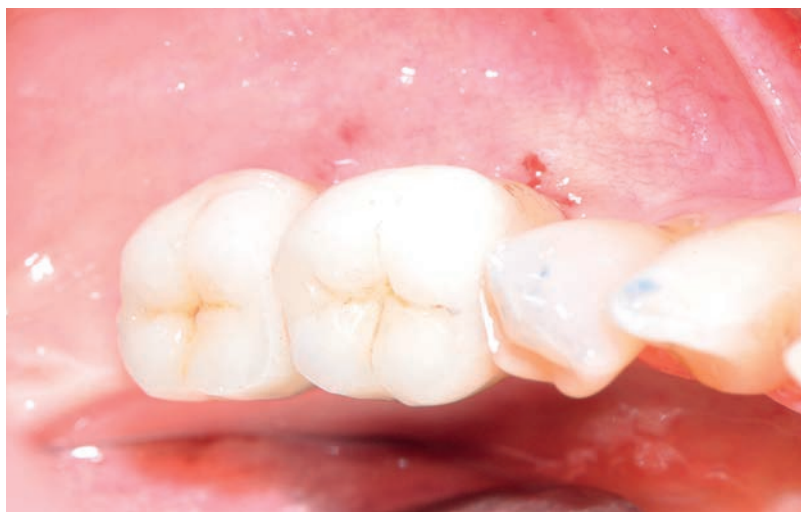


Fig. 10 - Control at 3 months, clinical aspect of rehabilitation.

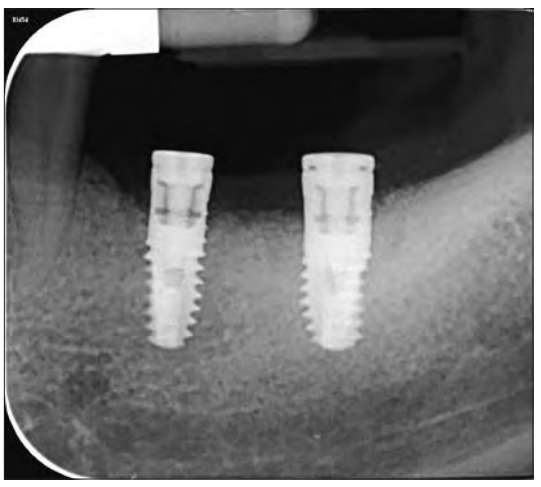


Fig. 11 - Radiographic control at 3 months: peri-implant bone levels are maintained.

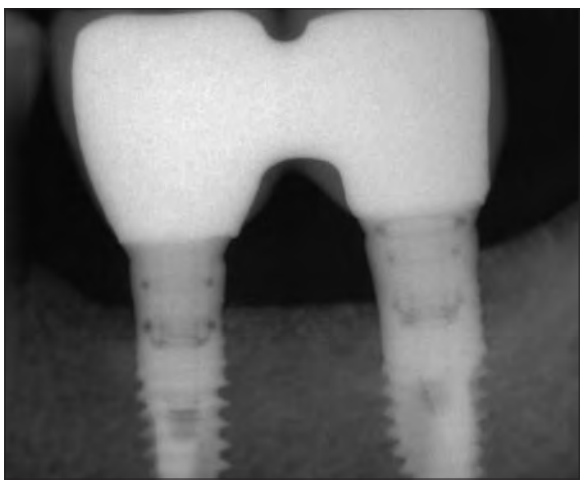


Fig. 12 - Radiographic control at 15 months: peri-implant bone levels
are maintained.

bibliography

1. Tamura N., Ochi M., Miyakawa H. & Nakazawa F. Analysis of bacterial flora associated with peri-implantitis using obligate anaerobic culture technique and 16S rDNA gene sequence. Int. J. Oral Maxillofac. Implants 28, 1521–1529 (2013).
2. Smeets R. et al. Definition, etiology, prevention and treatment of peri-implantitis – a review. Head Face Med. 10, (2014).
3. Petković A. B. et al. Proinflammatory cytokines (IL-1β and TNF-α) and chemokines (IL-8 and MIP-1α) as markers of peri-implant tissue condition. Int. J. Oral Maxillofac. Surg. 39, 478–485 (2010).
4. Schminke B. et al. The Pathology of Bone Tissue during Peri-Implantitis. J. Dent. Res. 94, 354–361 (2015).
5. Shuto T., Wachi T., Shinohara Y., Nikawa H. & Makihira S. Increase in receptor activator of nuclear factor κB ligand/osteoprotegerin ratio in peri-implant gingiva exposed to Porphyromonas gingivalis lipopolysaccharide. J. Dent. Sci. 11, 8–16 (2016).
6. Larsson L. et al. Regenerative Medicine for Periodontal and Peri-implant Diseases. J. Dent. Res. 95, 255–266 (2016).
7. Benic G. I. et al. Guided bone regeneration of peri-implant defects with particulated and block xenogenic bone substitutes. Clin. Oral Implants Res. 27, 567–576 (2016).
8. Di Stefano D. A. et al. Treatment of a bone defect consequent to the removal of a periapical cyst with equine bone and equine membranes: clinical and histological outcome. MINERVA Stomatol. 61, 15 (2012).
9. Materni A. Managing an extreme peri-implantitis: a case report. MINERVA Stomatol. 62, 295–305 (2013).
10. Schwarz F., Sculean A., Bieling K., Ferrari D., Rothamel D., Becker J. Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. J Clin Periodontol. 2008 Jan;35(1):80-7.
11. Esposito M., Grusovin MG., Worthington HV. Interventions for replacing missing teeth: treatment of peri-implantitis. Cochrane Database Syst Rev. 2012 Jan 18;1:CD004970.
12. Sahrmann P., Attin T., Schmidlin PR. Regenerative treatment of peri-implantitis using bone substitutes and membrane: a systematic review. Clin Implant Dent Relat Res. 2011 Mar;13(1):46-57.
13. Steven-Howe M., Richards D. Surgical regenerative treatment of peri-implantitis. Evid Based Dent. 2017 Oct 27;18(3):79-81.
14. Elgali I., Omar O., Dahlin C. & Thomsen P. Guided bone regeneration: materials and biological mechanisms revisited. Eur. J. Oral Sci. 125, 315–337 (2017).