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Treatment of periodontal defects in dogs using an injectable composite hydrogel/biphasic calcium phosphate

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Abstract An injectable composite silanized hydroxypropyl methyl cellulose/biphasic calcium phosphate (Si-HPMC/BCP) has been investigated in humans with promising results. The aim of this study was to evaluate his efficacy for treating periodontal defects (canine fenestration and premolar furcation) in dog models. At 3 months, we observed that bone formation around BCP particles in furcation model is more discernible but not statistically significant in defects filled with Si-HPMC/BCP compared to healing in control. We suggest that BCP particles sustain the bone healing process by osteoconduction, while the Si-HPMC hydrogel enhances intergranular cohesion and acts as an exclusion barrier. Furthermore, bone ingrowth is not so distinctive in superficial defects where the biomaterial appears unstable. These results with Si-HPMC/BCP are encouraging. In addition, this biomaterial is easy to use and simplifies the process of filling periodontal lesions. However, more researches are needed to improve the viscosity and hardness to adjust the material to the specificities of periodontal defects.

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1 Introduction

Many biomaterials have been studied for their application in treating the periodontal defects [1, 2]. Alloplastic biomaterials such as bioglass, hydroxyapatite (HA), β-tricalcium phosphate (β-TCP) and biphasic calcium phosphate (BCP) [3, 4] provide an alternative to allografts or xenografts [5, 6]. Indeed, the risk of viral transmission cannot be completely excluded with these latest materials but is nonexistent with synthetic materials [7]. BCP is a combination of HA and β-TCP in a 60/40 weight ratio and present a short-term absorbable phase (β-TCP) while allowing a long-term retention of the graft in a periodontal infrabony defect due to a longer absorbable phase (HA). This synthetic material has been under study for many years for its application in periodontal surgery [8, 9] and dental implant surgery [10]. BCP may be considered as a good, valuable osteoconductive scaffold for predictable bone volume gain [11–13]. However, this biomaterial can be still largely improved in terms of cohesion into the wound and easy handling during a surgical procedure in order to facilitate bone filling and periodontal regeneration. Maintaining the biomaterial "in situ" during the healing phase is one of

the most important parameters in order to obtain clinical success and a satisfactory regeneration of lost tissues. In addition, the goals of periodontal regeneration procedures are not only to obtain a bone filling of the defect but an "ad-integrum" regeneration of all the components of periodontal tissues (bone, gingiva, cementum and ligament). This "ad-integrum" regeneration is unattainable with "osteoconductive" bone graft materials alone but possible with guided tissue regeneration (GTR) or guided tissue induction (GTI). These two techniques present some limitations in their use due to the important risk of complications with GTR or the invagination of soft tissues into the lesion in large defects treated with GTI [1, 14]. New alternative biomaterials such as injectable polymer were developed to be used in combination with bone graft materials in order to facilitate surgical procedure and improve clinical results in the treatment of periodontal infrabony defects [14]. A self-reticulating polymer based on silanized hydroxypropyl methyl cellulose (Si-HPMC) has been developed in our laboratory [15–17] and may represent a potential scaffold for bone regeneration. Si-HPMC exhibits viscous and elastic properties that make its injection smooth (facilitating its injectability). Si-HPMC shows good biocompatibility and has convenient rheological properties for formation of an injectable calcium phosphate ceramics suspension. The combination of a hydrogel and a biphasic calcium/phosphate biomaterial gives consistency to the material by linking granules together in order to improve their stability in the osseous defects. On one hand, this injectable composite hydrogel/BCP has been tested for use in orthopaedic [18] and dental surgery to preserve alveolar ridge resorption prior to placement of dental implants [19, 20]. On the other hand, the addition of cellulosic polymer can also serve as a barrier on the outer edge of the periodontal defect to prevent the invagination of epithelia and soft tissues which inhibit periodontal regeneration [21, 22]. When implanted in osseous defect, hydrogel is resorbed during the initial healing process in order to promote colonization of the granules of biomaterial by osseous cells [23]. The fact that this composite treats periodontal lesions particularly due to its injectability and that hydrogel could serve as a barrier to invasion by epithelia and soft tissues is of interest.

In the present work, we investigated the bone filling and regenerative capacities of injectable Si-HPMC/BCP in periodontal defects in dogs. Three months after injection in surgically created defects (fenestration and furcation), osteoconductive properties of the composite biomaterial, biodegradation of the ceramic, and percentage of bone ingrowth were analyzed qualitatively and quantitatively using histology and histomorphometry.

2 Materials and methods

2.1 Biomaterial

2.1.1 BCP characterization

The injectable composite hydrogel/BCP is a mixture of BCP granules and Si-HPMC hydrogel [24].

2.1.2 BCP granulometry

The granulometry was measured using a scanning electron microscope (LEO 1450 VP) which showed that BCP granule diameters ranged from 80 to 200 μm.

2.1.3 BCP spectroscopy

The BCP granules (Biomatlante SARL, Vigneux de Bretagne, France) were composed of HA and β-TCP in a 62.7/37.3 weight ratio as determined by an X-ray diffraction analysis (Rietveld analysis) (Fig. 1). The BCP granules were packaged in sealed glass tubes and sintering steam sterilized at 121°C for 30 min [25].

2.1.4 Hydrogel characterization

The hydroxypropyl methyl cellulose (HPMC, Colorcon-Dow Chemical, France) presents an average molecular weight of 290 g/mol Silanol groups were grafted onto the HPMC polymer [26, 27]. The silicon percentage (0.46 wt%) grafted to HPMC was determined through inductively coupled plasma atomic emission spectroscopy (ICP-AES). The Si-HPMC powder was dissolved in NaOH (0.2 M) with constant stirring for 48 h. The resulting viscous solution of Si-HPMC (3 wt%) was dialyzed in diluted NaOH (0.09 M). The polymer solution had a pH of 12.9. Finally, it was poured into glass bottles and steam sterilized at 121°C for 30 min [28]. The basic and viscous Si-HPMC solution was hardened by adding an acidic buffer. The acidic buffered solution (pH 3.6, 100 ml) was prepared using HEPES (3.1 g), NaCl (1.46 g), and HCl (0.1 M, 30 ml) to achieve both final physiological osmotic pressure and pH.

2.1.5 Preparation of the material

The injectable composite hydrogel/BCP was prepared during surgery, under aseptic conditions. The BCP granules were mixed with the Si-HPMC hydrogel using two sterile syringes before injection into the periodontal infrabony defects.

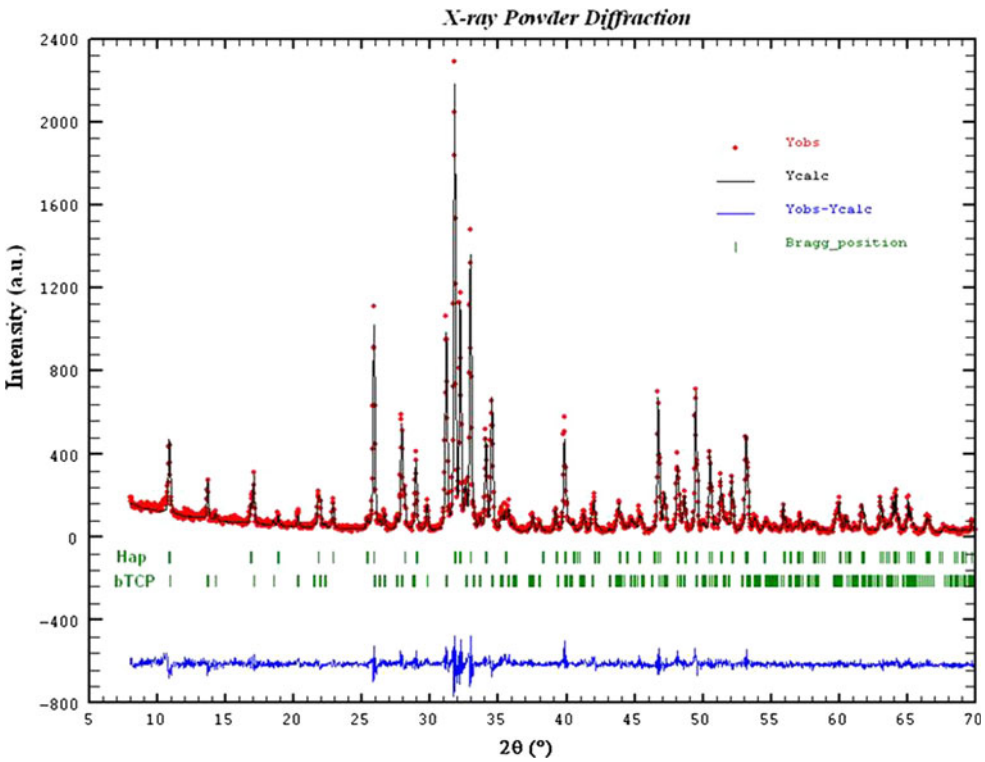

Fig. 1 Characterization of BCP granules by X-ray diffraction (Rietveld analysis). Wavelength used: copper K alpha copper. *Hap* reflection of the crystalline phase of hydroxyapatite. *B-TCP* reflection of the crystalline phase of beta-TCP

2.2 Animal model

Dog appears as the most convenient and favourite animal model in research concerning periodontal regeneration [29]. Animal handling and surgical procedures were conducted according to the European Community Guidelines for the care and use of laboratory animals (DE 86/609/CEE) and approved by the local ethics committee of Nantes Veterinary School. Four adult beagle dogs were purchased from a professional stockbreeder. Surgery was performed, under general anesthesia using an intravenous injection of diazepam (Valium®, Roche, France) 0.25 mg/kg, propofol (Rapinovet®, Schering Plough, United Kingdom) 4 mg/kg. A single dose of morphine (Morphine, Cooper, France) 0.1 mg/kg was injected subcutaneously during the surgery as an analgesic. Local anesthesia with bupivacaïne 0.50% (Bupivacaïne®, Aguettant, France) and Lidocaïne (Xylovet®, Ceva, France) 1 mg/kg was also given.

2.3 Surgical procedure

All dogs were 6 to 8 years old and exhibited spontaneous periodontal disease. They received a professional scaling 1 week prior to surgery, under general anesthesia. On the day of surgery, after general anesthesia, the gingiva was disinfected with iodine solution, and the animal was sterile draped. All defects were created on the upper jaw as described in the literature [30]. A muco-periostal buccal flap was made at the level of the maxillary canine and another at the level of the maxillary premolars. Two types of defects were surgically created: buccal fenestration on canine and furcation defect on premolars (Fig. 2). On canines, a circular critical size defect preserving bone crest (6 mm diameter) was created and the buccal bone and cementum were removed**.** On the second and third premolars (and on fourth premolar in one dog where third premolar was missing), furcation defects (6 mm high and 3 mm deep) were created. All surgical defects were made using a motor-driven drill (Aesculap, Tuttlingen, Germany) and successive burs of 2, 4 or 6 mm of diameter. During drilling, the site was irrigated with sterile saline. Each side was randomly chosen to serve as test or control. All test sites were filled with the injectable composite, Si-HPMC/BCP and the control sites were kept empty for spontaneous healing. The surgical sites were closed with absorbable sutures (Vicryl® 3.0, Ethicon, France). Prophylactic antibacterial treatment was administrated after surgery (Stomorgyl® spiramycin + Metronidazole). There was no complication during the healing period. The two experiments gave a number of defects: the fenestration-type defects on the canines were 8 (4 tests, 4 controls) and the furcation-type defects on the premolars were 15 (7 tests, 8 controls).

2.4 Preparation of the samples

After 12 weeks, the animals were anaesthetized and sacrificed by an intracardiac overdose of sodium pentobarbital.

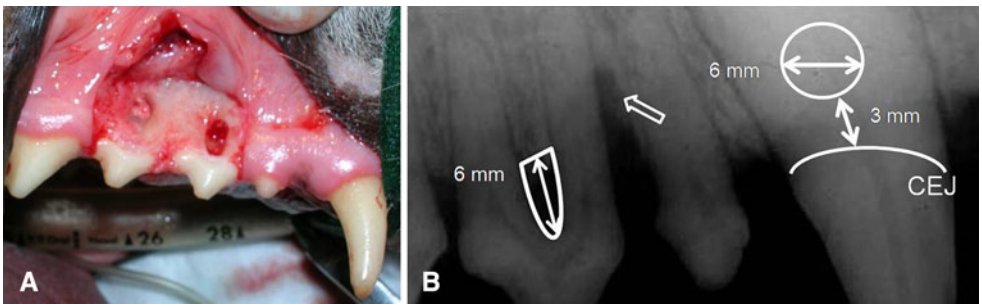

Fig. 2 Furcation defects surgically created on the second and third upper premolar (**A**). The defects are 6 mm high. Critical size fenestration defect on the buccal face of upper canine (**B**). The 6 mm circular defect was created at 3 mm from the cemento-enamel junction (CEJ). Note the presence of spontaneous periodontitis on this dog (*arrow*)

The maxillas were immediately dissected and placed in a formol solution. The non-decalcified bone samples were dehydrated in an ascending series of ethanol (70–100%) and then in pure acetone for 24 h. The samples were impregnated in methyl methacrylate (Prolabo) for 4 days and then embedded in PMMA resin. Blocks were cut into 100 µm slices with a circular diamond saw (Microtome 1600, Leica, Germany) or into 7 µm section slices using a hard tissue microtome (Leica SM 2500, Germany). The slices were examined by polarized light microscopy or light microscopy (after Goldner staining).

2.5 Histomorphometry

Three dimensional reconstructions were made, using a microscanner (SkyScan 1172, Kontich, Belgium). Samples were placed after inclusion in PMMA resin before being cut for histology. Images were obtained using a mode source at 80 kV/124 uA and signal threshold at 20. The rotation angle was of 180°. We used NRecon software (SkyScan) for three-dimensional reconstructions.

For scanning electron microscopy (SEM) observations, samples were sputtered with a thin layer of gold–palladium (EM Scope, England). SEM micrographs were taken using the backscattered electron mode at 15 kV (SEM, LEO 1450 VP).

Percentages of bone ingrowth as well as bone-to-biomaterial contact in furcation defects were calculated based on backscattered scanning electron microscopy (BSEM) images. A custom-made program developed under an image analysis system (QWin, Leica, Germany) was used. The BCP particles, bone and non-mineralized tissues were easily discriminated on BSEM images based on their respective grey levels. The area of interest was defined as the section of canine or furcation defect. The percentage of bone to biomaterial contact was measured by calculating the length of the bone in direct contact with the perimeter of BCP particles. SEM analysis through secondary electrons and backscattered electrons (BSEM) allowed a qualitative and quantitative investigation of bone formation and ceramic degradation.

2.6 Statistical analysis

The percentages of bone to biomaterial contact and bone ingrowth were expressed as mean ± standard deviation. Raw data were processed using a software (SPSS 16.0). An unpaired, non-parametric Mann–Whitney test was conducted to compare the bone ingrowth after filling by composite biomaterial and unfilled control. Differences were considered significant for *P*-value inferior to 5% ($P < 0.05$).

3 Results

No complications were observed during the surgery. During the postoperative phase, no infectious complication happened.

3.1 The canine fenestration defects

3.1.1 Histological examination

In polarized light micrograph of test condition, functional ligament fibers inserting from the cementum to the bone crest, were observed on the edge of the defect, especially the growth of a new formed bone which is significant (Fig. 3). In the central part of critical size fenestration, the bone regeneration is incomplete in all defects (test and control). At this place, only non-functional fibers were noted. BCP granules can be observed around the borders of the defects, surrounded by lamellar polarizing fibers, but also sometimes migrating into the conjunctive gingival tissue. Histological slices stained with Goldner trichrome show the presence of BCP granules, surrounded by osteoid tissue and the newly formed bone (Fig. 4). New cementum deposits along the root surface of the defect and a new

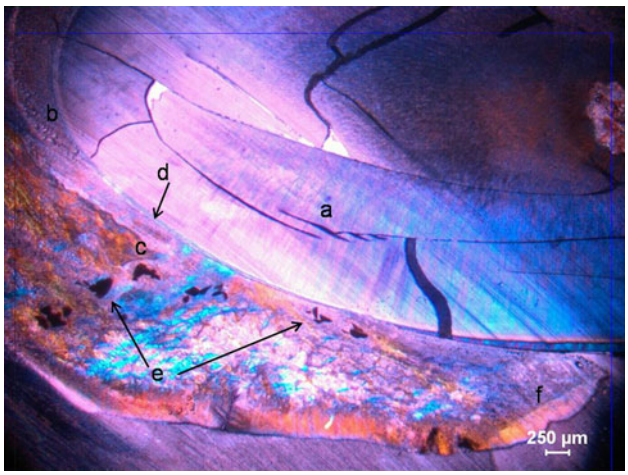

Fig. 3 Polarized light micrograph of bone fenestrations filled with composite material in canine roots after 3 months (*a* dental root, *b* cementum, *c* new formed bone, *d* periodontal ligament, *e* BCP granules, *f* gingiva)

periodontal ligament exist only if bone regeneration has occurred. We never observed ankylosis or root resorption in the test group.

3.1.2 Qualitative SEM analysis

A new formation of bone is observed at the edges of the defects as well as at the test and control sites (Fig. 5). In the test group with Si-HPMC/BCP granules, the newly formed bone is mainly in direct contact with the existing or old bone surrounding the defects. However, there is a discrete new bone formation around the dispersed BCP granules distant from the edges of the defects. In the control group, bone formation occurs only along the edges of the defects and appears less extensive compared to the test group. Furthermore, no complete healing or regeneration of fenestration defects was obtained either in the control or in test group.

3.2 The furcation defects

3.2.1 Microscanner reconstruction

A microscanner reconstruction was done for every furcation defect through an X-ray microscan. The specific anatomy of these furcation defects compared to those of the fenestration defects (in the furcation: presence of two root surfaces, higher width of the defects) made preferable the use of three dimensional reconstructions. In this way, we can obtain data concerning the maintenance of the biomaterial into the defect, as well as in a longitudinal than in a transversal axis. A partial bone regeneration occurred in both test and control groups. However, the coronal extent of the newly formed bone seemed to be more marked in the test group compared to control (Fig. 6). In transversal reconstructions of test group condition (NRecon software), bone volume was more significant in the apical part of the defects that is directly in contact of the native bone. At the top of the defects, bone regeneration was less extensive and occurred mainly at the bottom of the defect (Fig. 6B–D). The resorption of the biomaterial was always incomplete at the end of 3 months. In all these transversal reconstructions, the BCP granules were never directly in contact with the root surface and the desmodontal space was systematically re-created in all the furcation defects filled by Si-HPMC/BCP.

3.2.2 Histological examination

In polarized light micrograph (Fig. 7), a newly formed mineralized bone was observed in direct contact with the BCP granules. The density of the material was variable depending on the localization into the defect: more BCP granules were observed at the top compared to the base of the defect. A large cellular cementum was observed at the area of the roof of the furcation. A connective tissue

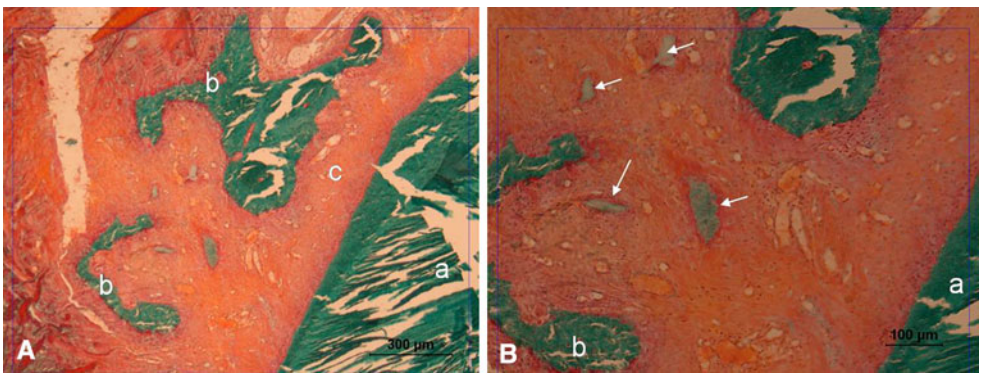

Fig. 4 Histological micrographs of bone fenestration filled with composite material in canine roots after 3 months (Goldner's trichrome staining; *a* dental root, *b* bone trabeculae, *arrow* composite material, *c* periodontal ligament)

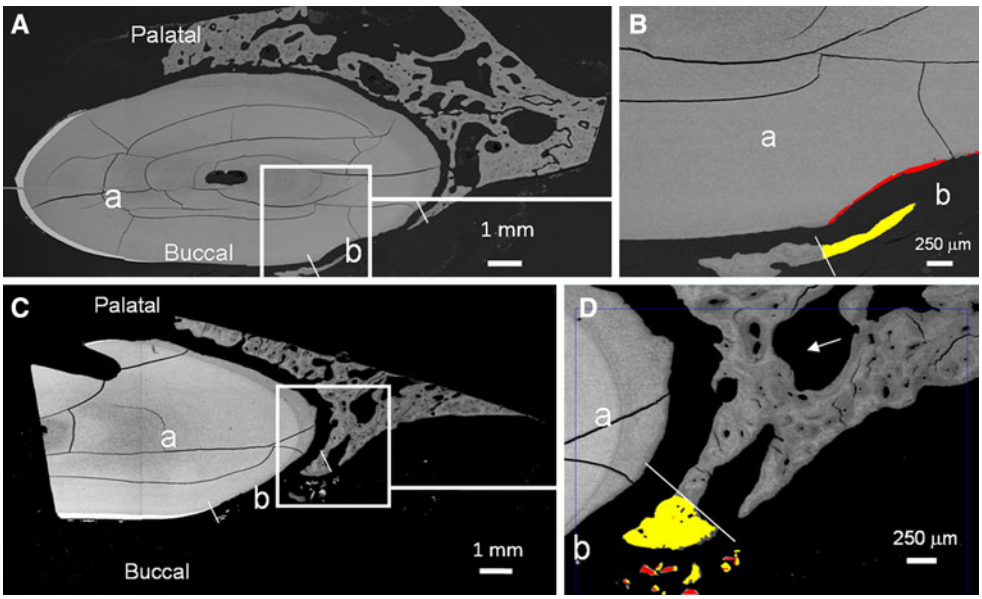

Fig. 5 BSEM pictures of bone fenestrations in canine roots after 3 months. **A** empty control and **C** test condition filled with composite material. **B** and **D** high magnification of (**A**) and (**C**). **B**: *red* dental root, *yellow* new bone. **D**: *red* composite material, *yellow* new bone; *a* dental root, *b* osseous defect, *line* limits of the defect

separated the root surface and the osseous area (Fig. 7B). Histological slices showed a well-mineralized bone with haversian systems and osteocytes lacuna in direct contact with and between BCP granules. In reconstructed figure (Fig. 8), we observed a cicatricial, long, junctional epithelium facing the cementum and subepithelial non-inflammatory connective tissue. In the coronal part of the defect, BCP granules were surrounded by the newly formed bone and we noted that trabeculae bridging the BCP granules delineated the vestibular and palatal border of defect. Interestingly, BCP granules were dispersed in a large central area and solely surrounded by osteoid tissue. In the unfilled control group, the newly formed bone was located mostly in the apical part of the defect. The space between the new bone formation and the roof of the furcation is more distinctive compared to the test group, and predominately filled by a non-structured connective tissue.

3.2.3 Qualitative SEM analysis

The qualitative SEM study was correlated to the histological examination (Fig. 7). At the areas of premolar furcation defects, the newly formed mineralized bone can be observed from the apical edge of the defects. In the control group, bone ingrowth is observed mainly in the apical and central part of the defect. In the test group filled with the injectable bone substitute, the reconstruction of the buccal cortical bone is more systematically observed. Central and coronal parts of the defects are more completely filled than in the control group. The newly formed mineralized bone was observed in direct contact with the BCP granules (Fig. 7C, D). This well-mineralized bone with mature osteocytes has formed on or between the granules. The bone shows trabeculae bridging the BCP granules.

3.2.4 Quantitative SEM analysis

In the furcation defects, the bone to biomaterial contact was $61.3 \pm 9.2\%$ ($n = 7$). The bone appositions on BCP particles were not statistically significantly different in the two groups, test and control. Bone ingrowth was $23.6 \pm 10\%$ ($n = 8$) and $35.5 \pm 13.9\%$ ($n = 7$) for left empty and biomaterial-filled defects, respectively. Although, the bone ingrowth is more in defects filled with Si-HPMC/BCP than in the left empty control, the difference was not significant (Table 1).

4 Discussion

Expecting an improvement in bone grafting, current bone regeneration strategies include the application of different bioactive factors, cell types, and biological or artificial scaffolds [31]. In the treatment of human periodontal defects, various biomaterials or bioactive agents are experimented in combination with conventional scaffolds [1]. The goal of these procedures is to obtain not only a bone filling of the periodontal defects but a complete regeneration of all the components of the periodontium. In this study, we used two models of surgical experimental

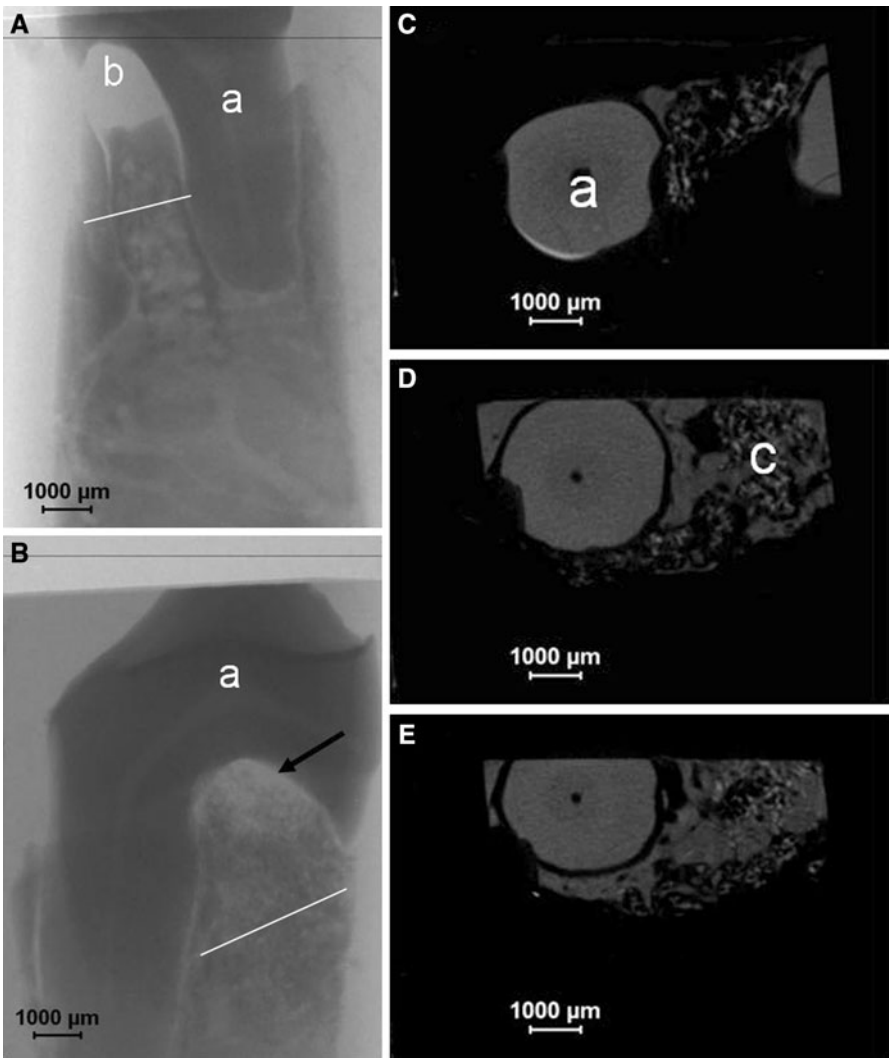

Fig. 6 Microscanner pictures of furcation defects in upper premolars after 3 months. **A** empty control and **B** test filled with composite material. Note the difference of bone regeneration in the most coronal part of the defect. Transversal reconstruction of the test condition at various levels of the defect: **C** coronal, **D** medium, **E** apical. Note that the bone reconstruction is more important at the base of the defect (**E**), due to the presence of bone apically of the defect and of a more favorable anatomy at this part of the defect. At the top, the furcation defect is incompletely regenerated (**C**); *a* dental root, *b* unfilled defect, *c* new formed bone, *line* apical limit of the defect

periodontal defects in dog. The first model was located on the vestibular face of the maxillary canine. At this place, a circular critical size defect was surgically created. The latter presented a very shallow depth due to very thin bone cortical at this anatomical level. This was an extremely unfavorable factor for maintaining the granules of biomaterial in situ. In this fenestration-type model, we evaluated the bone filling and regenerative capacities of a new composite biomaterial hydrogel/BCP. We aimed to investigate the ability of the hydrogel to promote the cohesion of the BCP granules into the wound and to prevent the migration of soft tissues along the root surface. To our knowledge, no research studied the behaviour of the BCP in these narrow defects, where the presence of bone fenestration in aesthetic anterior sectors is very difficult to manage. Regarding the bone filling of these fenestration defects, the injectable composite hydrogel/BCP material was easy to use during the surgical phase, but was unable to stay in place and we found BCP granules dispersed out of the osseous site and encapsulated into the connective gingival tissue, far away from the defect. The new bone formation was not statistically significant in the test group compared to the spontaneous healing and was never achieved in the center of the defects. The adjunction of the silanized hydroxypropyl methyl cellulose Si-HPMC as a cohesive factor for the BCP granules was ineffective in this specific periodontal defect. However, osteoconductive properties of BCP granules were still conserved and the adjunction of Si-HPMC did not affect new bone formation.

The second goal was to evaluate, in the fenestration model, the ability of the hydrogel to serve as a barrier and to promote the regeneration of all the components of the periodontium as described with GTR [21, 22] or GTI [14]. In the literature, no histological data concerning the new periodontal attachment (new bone, cementum and insertion of functional fibers from the bone to the root surface) are available on the BCP while data exist for enamel matrix derivatives [32–35]. The low viscosity of Si-HPMC led to

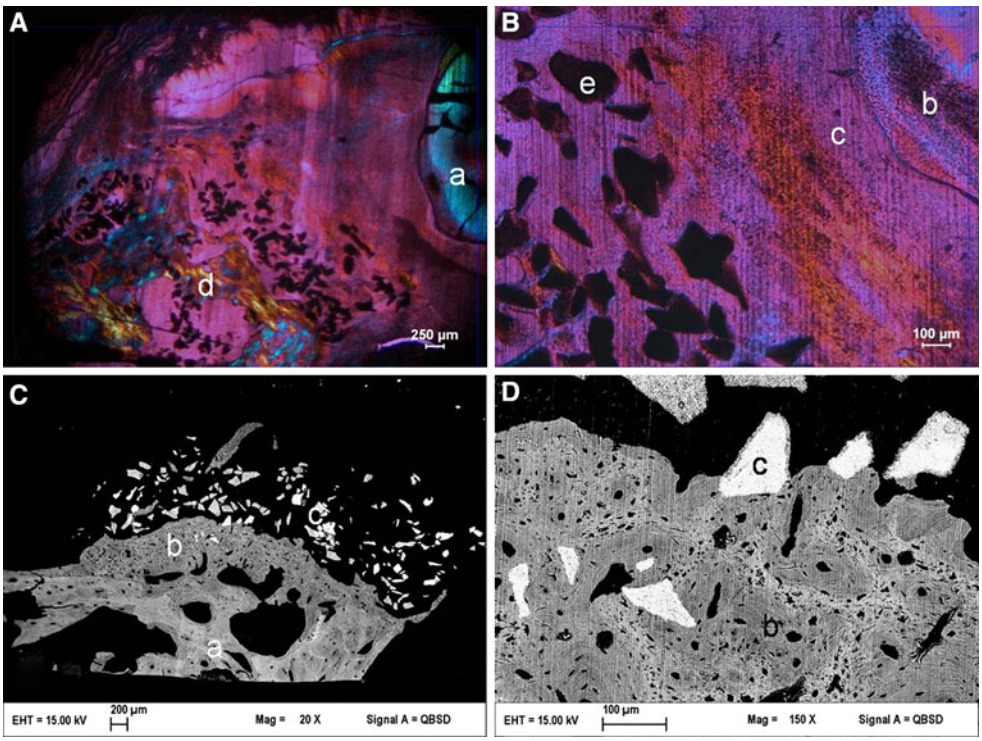

Fig. 7 **A** and **B** Polarized light micrograph of bone furcation defects in maxillary premolars filled with composite material after 3 months (*a* dental root, *b* cellular cementum, *c* periodontal ligament, *d* new formed bone, *e* BCP granules). **C** and **D**: BSEM pictures of the same furcation defect filled with composite material, at low (**C**) and high magnification (**D**); *a* bone, *b* newly formed bone, *c* BCP granules

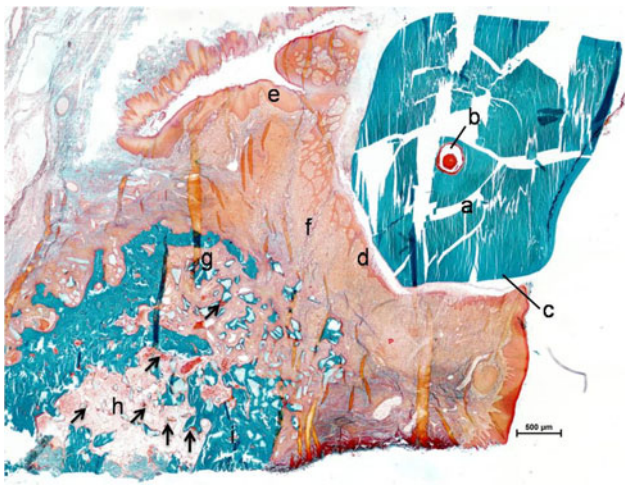

Fig. 8 Histological micrographs of bone furcation defects filled with composite material, in maxillary premolars after 3 months (Goldner's trichrome staining); *a* dentin, *b* dental pulp, *c* cementum, *d* junctional epithelium, *e* buccal gingival, *f* connective tissue, *g* BCP granules, *h* BCP granules borded by osteoid in the center of the defect (*arrows*), *i* newly formed bone

the leak of a part of the composite biomaterial during the healing and affected the periodontal regeneration. However, we never observed root resorption or ankylosis. In the center of the defect, conjunctive fibers were oriented parallel to the root surface. The use of injectable composite

Table 1 Bone healing on maxillary defects on upper second and third premolars

Furcation defects on maxillary premolars	Bone ingrowth (%)	Bone to biomaterial contact (%)
Control	23.6 ± 7 ($n = 8$)	
Test	35.5 ± 11.1 ($n = 7$)	61.3 ± 9.3 ($n = 7$)
P-value ANOVA	$P = 0.12$ NS	

hydrogel/BCP material did not induce any functionally oriented fibers and simply acted as a bone grafting material if used alone [1]. The addition of the polymer does not seem to make profits in the field of periodontal regeneration. Therefore, new research should focus on a denser polymer loaded with biologically active molecules, which is able to induce periodontal regeneration in this type of defects.

The second model was located on the maxillary premolars. At this place, a furcation critical size defect was surgically created. This model is very unfavorable in terms of healing because of the limited number of bone walls. It presents only one bone wall at the base and of the defect and the others walls are formed by the dental roots which are non-vascularized surfaces. The first goal, in this furcation model was to evaluate the ability of a new composite biomaterial hydrogel/BCP to promote new bone

formation in very unfavorable periodontal defects. The bone-fill seems qualitatively better in the group with biomaterial compared to that in the case of spontaneous healing but not statistically significant. The BCP granules are surrounded by the newly formed bone without any adverse effect after 3 months. These results are comparable with the data available from a similar study on rabbits [18]. The second goal was to investigate whether Si-HPMC could serve as a barrier to the soft tissue, enhancing bone regeneration at the external face of the defects. Previous studies [18, 23] showed that the adjunction of a silanized hydrogel Si-HPMC involved self-reticulation of the composite Si-HPMC/BCP which hardened in the bone defect forming a gel loaded with BCP ceramic particles. This self-hardening composite Si-HPMC/BCP enhances the initial stability and homogeneity of the material into open defects which can limit the gingival invagination of soft tissues into the wound during the first steps of the healing. The results seem to validate this hypothesis with a more extensive buccal new bone formation in the test group than in spontaneous healing. In the center of the defects, new bone formation seems to be retarded comparatively to peripheral areas of the defects confirming the barrier role of Si-HPMC polymer. However, BCP granules are still in place and maintain their osteoconductive properties marked by the presence of osteoid matrix around the granules. We suggest that the adjunction of Si-HPMC polymer seems to enhance material stability but delay the colonization of the intergranular spaces by osteogenic cells, and then the new bone formation. These data are in agreement with those obtained in femoral critical size defects in rabbits [18]. In furcation model, the defects are deeper and more favourable than in the fenestration model. Thus, the biomaterial can stay in place and the leak (dispersion in soft tissues) of BCP granules is less pronounced than in the fenestration model even if the viscosity of the Si-HPMC could be yet enhanced to increase the stability of the material and the clot into the defect. In this periodontal furcation model, the healing capacities are reduced because of the decreased amount of cells and vessels, only available from the apical part of the defect. In dental sockets, after tooth extraction, there are usually four bone walls and it is logical to obtain a greater bone-fill compared to the results of the present work [19, 20]. However, the new composite biomaterial hydrogel/BCP seems to offer interesting results for clinical use in periodontology or implantology. In periodontal defects, the biomaterial has to stay in place in the first steps of the healing and also to promote a quick new bone formation. New researches allowing an increase of viscosity compatible with the injectability of composite material are needed to improve the cohesiveness between the Si-HPMC and the BCP granules and so, may enhance the bone regeneration in complex defects. Use of a multilayered composite Si-HPMC/BCP (BCP granules alone in the center of the defect and composite Si-HPMC/BCP in the coronal part of the defect) may be an interesting approach more adapted to the specificities of periodontal defects, allowing to promote central bone regeneration by means of BCP's osteoconductive properties and excluding the invagination of soft tissues into the wound due to barrier effect of Si-HPMC. In the last decade, tissue engineering has evolved from the use of synthetic biomaterials, which may just replace the reduced area of damaged tissue, to the use of controlled three dimensional scaffolds in which cells can be seeded before implantation [36, 37]. In periodontal osseous defects, bone graft materials are only osteoconductive and are unable to induce periodontal regeneration. Composite biomaterials can be used as scaffolds for stem cells or bioactive agents [38]. In our laboratory, we showed that BCP granules associated with total bone marrow (TBM) provides better bone reconstruction than TBM or BCP alone in irradiated bone in rats [39] or in dogs [40, 41].The association of mesenchymal stem cells (MSCs) with BCP granules leads to a better bone reconstruction than the biomaterial alone [42]. They also can be used in periodontology to treat osseous defects [37]. The new composite biomaterial hydrogel/BCP may be a potential scaffold for bioactive agents or stem cells in order to obtain a complete periodontal regeneration.

5 Conclusion

This study described the use and results of a new injectable composite bone substitute composed of a chemically modified cellulosic polymer solution and BCP ceramic particles, in the treatment of periodontal osseous defects. This material has not been yet used with success in orthopedic surgery. In dental surgery, it has been only tested for healing of sockets after teeth extraction but never for filling of complex periodontal infrabony lesions. We demonstrated the ability of this hydrogel/BCP material to promote new bone formation, 3 months after implantation in dog's critical size furcation defects. In these large and unfavorable defects, the viscosity and texture of the injectable composite material seems to help the retention of the BCP granules in the defect during the healing phase which is a primordial factor for clinical success. However, in large and superficial defects like fenestration lesions, the viscosity of the hydrogel may be improved to increase retention capacity and the mechanical strength of the material. In our laboratory, we are actively engaged in the development of other injectable composite materials more adapted to periodontal specificities in order to increase periodontal regeneration in the treatment of infrabony defects.

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