Chapter 5

Clinical Application of Macroporous Ceramic to Promote Bone Healing in Veterinary Clinical Cases

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Additional information is available at the end of the chapter

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Abstract

Autogenous cancellous bone is the most effective material in promoting rapid healing and still considered the "gold standard" for evaluation of bone graft substitutes. The harvesting process to collect autologous bone is associated with complications and its availability is limited. Allogenic bone is another alternative with osteoconductive properties, and it act as a structural graft when applied in defects of long bones, but some disadvantages are also associated. The development of the bone grafts substitutes has gained tremendous popularity over the last two decades. Osteoconductive materials act as scaffolds were cells from the surrounding tissues with osteogenic capacities can lay new bone, and may be produced using different types of agents, such as bone products, ceramics, bioactive glasses, collagen, polymers, and composites. Bonelike® is produced by the incorporation of P_2O_5–CaO glass-based system within a hydroxyapatite matrix. Bonelike® Poro consists of polygonal granules with 2000–2800 μm and 4000–5600 μm of diameter with pore sizes range from 100 to 400 μm. This chapter will focus on the different techniques were this ceramic synthetic bone substitute was used to promote bone regeneration with special attention in both experimental and clinical cases of veterinary orthopaedics in dogs and cats, horses and ruminants, including results obtained with Bonelike®.

Keywords: bone regeneration, bone graft, bone substitutes, synthetic bone substitutes, orthopaedics, veterinary, clinical cases

1. Introduction

The bone healing process shares many similarities with soft tissues' healing, but, in contrast, the bone is the only tissue that has the capacity of healing without scar formation. Nevertheless, incomplete healing may occur, and the tissue other than the bone may be found at the healing site. Bone healing depends on adequate vascular supply and stability of the bone fragments. Proper bone healing can only occur after restoration of mechanical stability to achieve an ideal biomechanical environment. Many clinical situations may require additional osteosynthesis surgical procedures to acquire the biomechanical stability and immobilization necessary for correct bone regeneration and future functional recovery. Intrinsic mechanisms present unique histological characteristics that appear isolated or in association, depending on the bone fragment mobility [1–4]. The amount of bone *callus* produced depends on the stability of the fracture sides and usually increases with fracture instability. Spontaneous healing of complete fractures often occurs with highly unstable fragment ends and high interfragmentary strain (deformation occurring at the fracture site relative to the size of the gap), to a limit of 2% strain [1, 4]. Fracture healing under restricted motion induces an initial reduced amount of bone *callus* formation. This type of healing relies on fracture configuration and the implant's rigidity and may be achieved by external coaptation of the fracture or after gliding implant fixation with intramedullary pins and nails. With these surgical reconstructive methods, the amount of the *callus* produced is highly variable and dependent on the fracture configuration and the rigidity of the frame used [1, 3]. When the fixation is performed with a bone plate, the amount of *callus* formation will be different if the plate is not applied on the tension side of the bone, if the reduction is not perfect or when the plate lacks rigidity. In stable fractures using a rigid plate for osteosynthesis, there is significantly decreased *callus* formation between the bone fragments [1, 2]. This phenomenon is called 'primary healing', referring to the direct filling of the fracture site with the bone, without formation of significant *callus* (periosteal or endosteal). Healing under these conditions occurs by direct osteonal proliferation with interdigitation of bone fragments providing a very stable union. In opposition when the bone ends are separated by a gap inferior to 0.01 mm and the interfragmentary gap is less than 2%, the primary osteonal reconstruction results in direct formation of lamellar bone, oriented in the normal direction [1, 3]. This is termed contact healing and is initiated by osteoclasts from osteons near the fracture line. Another context for direct bone healing is observed in gaps from 800 μm to 1 mm and interfragmentary strain less than 2%, and gap healing is designated. Here, bone union and Haversian remodellation are separated by sequential process steps. Fracture site is filled directly by intermembranous bone formation, but the newly formed lamellar bone is oriented perpendicular to its long axis, and, later on, it undergoes secondary osteonal reconstruction (remodellation). In this way, the fracture repair depends on two important events: the rate of new bone growth (that replaces the stiffness and strength of the bone) and the strength and duration of the implant (maintenance of its function until it collapses and fails) [1–4]. When new bone formation is compromised and/or a risk of implant failure is expected, promotion of fracture healing is indicated, in order to enhance new bone formation, allowing for corrected bone structure formation and organization [1]. Fractures with impaired bone repair mechanisms or fixation failure will result in a non-union condition. Adequate bone repair depends on four crucial elements: an osteoconductive matrix, an

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osteoinductive signal, an osteogenic cell acting in response to that signal and an adequate blood supply [1, 3, 4]. There are several clinical situations where it is important to promote and enhance bone healing process in order to restore the original bone structure and function, both in human and veterinary medicine. These include traumatic injuries or tumour resections with substantial and irregular bone loss, gap filling following corrective osteotomy, arthrodesis or arthroplasty, spinal fusion, non-union or delayed bone union, metabolic diseases and local or systemic disease in aged patients. In these situations, bone regeneration is compromised, and the bone defect exceeds the intrinsic biological restoration mechanisms. These clinical cases occasionally result in unsatisfactory outcomes and are a challenging scenario to orthopaedic surgeons. When facing such clinical problems, different treatment strategies can be used to improve new bone formation, avoiding the formation of bone with inferior quality to the original [1, 3, 5–7].

Autogenous cancellous bone grafting (ACBG) is used in veterinary orthopaedic surgery as a bone void filler to improve bone healing in the treatment of bone defects in low-grade fractures in both mechanical and biological assessment score, arthrodesis, delayed unions or non-unions, enhancement of fracture healing, periprosthetic coating, spinal fusion procedures and void filler of bone gaps resulting from fractures, osteotomy, ostectomy, arthrodesis or tumour resection [1, 7]. The 'gold standard' when evaluating bone graft substitutes is still considered to be ACBG. Cancellous bone graft provides osteoconductive properties, acts as a scaffold for osteoprogenitor cells and delivers viable cells without the risk of immune reactions or infectious disease transmission. However, its use is associated with some limitations including the need of an additional surgery for harvesting cancellous bone, donor-site morbidity and limited amount of bone graft. The last point can result in an insufficient amount to completely fill the defect which may implicate the need for harvesting from more than one donor site. In humans, the second surgery for autologous bone graft collections is associated with 25% of morbidity, with major complications occurring in 3–4% of the patients. Complications include pain, sepsis, stress fractures, intraoperative haemorrhage, increased anaesthetic and surgical times and limited supply [8, 9]. Limited supply is more critical in small dogs and toy breeds, in cats or in animals that have been previously submitted to bone graft harvest. In those cases, the harvesting from the humerus may be the best option, because higher amounts of bone can be collected when comparing to the tibia while also presenting accelerated healing and complete restoration cancellous bone. Another drawback is its lack of strength of ACBG, hampering its use as a structural graft [1, 10]. Cortical allograft could be an alternative, which provides structural strength along with osteoinductive and osteoconductive properties. Nevertheless, the transmission of infectious diseases and adverse immune reactions are important risks to consider [11].

In the case of human patients, demineralized bone matrix (DBM) is the most common source of partially purified bone-inducting factors used. During the demineralization process, allogenic bone is chemically sterilized to preserve its osteoinductive properties from the original bone collagen network and molecular signalling. Commercial forms of DBM are also available for canine patients, where immune reactions are reduced by the removal of the periosteum, cartilage and bone marrow and by freezing process [6, 7, 12–14].

In the last decades, the well-known disadvantages of autografts and allografts have encouraged the development of bone synthetic substitutes to be employed as bone grafts, reflecting in the increase of the clinical application of these types of biomaterials. An ideal bone substitute should be biocompatible/safe; should be resorbable, with a similar mechanical resistance as the cortical bone; should have osteoconductive, osteoinductive and osteogenic properties; and should be easily handled and sterilized. The bone substitute should not cause any adverse systemic or local reaction; should provide a favourable environment to be colonized by blood vessels, cells and growth factors; and should be obtained at a low cost [7, 9].

These biomaterials are available for use in veterinary orthopaedics, alone or in combination with other strategies, such as osteoinductive bone morphogenetic proteins (BMPs) or cell-based treatments [6, 7, 11, 14]. They are composed of different materials with osteoconductive properties, such as bone products, ceramics, polymers and composites. The clinical application of each material is defined by its properties, which depend on composition and physical characteristics (e.g. granulometry, shape, pore size and interconnective porosity). The latter is determined by the manufacturing technique used [7, 9]. The synthetic bone substitutes offer an ideal substrate for bone cell colonization and consequent new bone formation [7].

Osteoconductive materials are grouped in two main categories. The first category includes ceramic-based bone substitutes, and the second category includes polymer-based bone graft substitutes (less commonly used). The most popular ceramic-based bone substitutes are calcium sulphate, bioactive glass and calcium phosphate. Calcium sulphate was the first material used as a bone graft substitute in clinical field, where it showed to be user-friendly, inexpensive, readily available and stable for filling-in bone defects, without a negative effect in bone healing. However, it presents fast absorption rates, leading to the loss of mechanical properties before equivalent new bone formation, constituting its main disadvantage and limiting its use in relevant clinical cases. Bioactive glass was designed as a bone graft for dental applications. Its use in orthopaedic surgery seems to be limited by its brittleness, radiopacity (which compromises radiographic evaluation of bone healing) and prolonged resorption times. Compared to bioactive glass, calcium phosphate is less radiopaque with faster reabsorption, but its osteointegration rate is highly variable, depending on its crystal size and stoichiometry. Tricalcium phosphate compounds are available in different presentations, including tricalcium phosphate, hydroxyapatite and a combination of the two.

Regardless of the mineral detail of its composition, the final formulations/presentation forms are of extreme relevance, concerning both its external shape and internal architecture. External shape and granule size will determine its suitability for particular lesion applications, considering effective size and ease of access for implantation. Its architecture is determinant for the resolution of the bone defect since bone ingrowth is dependent on the pore size. According to Ragetly et al., a minimum pore size of 100 μm is required for bone ingrowth and for optimal promotion of ingrowth pores should have a granulometry between 300 and 500 μm [7, 9, 15].

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2. Preclinical trials

A series of regulatory steps are essential in the development of biomaterials, requiring its physical-chemical characterization; in vitro validation, and at an intermediate stage, in vivo suitability; safety; and performance assessment: biocompatibility, osteoconduction, osteointegration and osteoinduction [16]. In sight of the ethical issues associated to the use of animals for experimental purposes, extensive efforts aim at refining in vitro methods as valid alternatives. Unfortunately, current in vitro models still underachieve in replicating the tissue response of a live animal to a bone substitute [16–18].

The preparation and conduction of preclinical studies are bound to a number of sequential phases. First, the proposed materials ought to be tested in noncritical-sized defects, allowing for the preliminary assessment of multiple material samples' behaviour in defined in vivo conditions. This feature is very important on the initial screening of a biomaterial's in vivo behaviour, enabling the choice of the chemical composition and format of the biomaterial with the most potential for more challenges [19–21]. Furthermore, noncritical-sized defect ensures fast and reliable healing process, allowing for the observation of the various stages of bone healing and biomaterial degradation [21, 22]. Once the ideal composition is chosen and biocompatibility is analyzed, the material may be used directly in clinical trials, or if found necessary, in increasingly critical defects, to confirm the results obtained in the first approach with noncritical defects, and to determine its limits of efficiency and performance [21].

One of the fundamental aspects when choosing the most adequate animal models to test bone replacement materials is the size of the bone defect amenable to assess [23, 24]. A critical-sized bone defect (CSBD) is defined as the smallest bone defect that will not heal spontaneously during the lifetime in a particular bone and species of animal [23, 25]. In a more detailed description, a CSBD has been referred to as a defect that has less than 10% bony regeneration during the lifetime of the animal or duration of the experiment [26, 27]. Although the smallest size that creates a defect designated as 'critical' is not a well-established concept, it has been defined as a segmental bone deficiency of length exceeding 2–2.5 times the diameter of the affected bone [28]. Some animal studies suggest that CSBD in sheep could be approximately three times the diameter of the diaphysis. Therefore, a critical defect in long bone cannot simply be defined by its size, but may also be dependent on the species phylogenetic scale, the location in the skeleton, the surrounding soft tissue envelope and the load bearing on the affected limb.

Bone colonization of macroporous biphasic calcium phosphate (MBCP) ceramics implanted in different sites (femur, tibia and calvaria) on a critical-sized defect in two animal models (rats and rabbits) showed bone ingrowth in all MBCP-implanted sites but with distinct rates. Bone colonization appeared statistically higher in the femur of the rabbits (48.5%) compared to the tibia (12.6%) and calvaria (22.9%) sites. As such, the comparison of results between animals or different bone defect locations is subject to bias, so a well-conducted study and fully validated animal models are essential in the development of new synthetic bone substitutes [29]. Furthermore, the host's age, metabolic and systemic conditions and comorbidities also affect the defect's healing potential [30].

Attempts to repair a CSBD only lead to the formation of fibrous connective tissue rather than the bone [31]. For practical purposes, if there is no more than 30% of the mineralization area after 52 weeks, lifelong incomplete bone healing is to be assumed [32]. The incapacity of natural healing when left untreated represents the negative control, so that the osteogenic potential of the material being tested can be considered unequivocal. Furthermore, CSBD should heal with appropriate treatment, and the autologous cancellous bone grafts are still named as the gold standard or positive control. Any new treatment based on bone tissue engineering should be tested and compared with these two landmarks [25]. Given the clinical targets of such applications (mostly aged or health-impaired patients), animals should be skeletally mature, in order to avoid misleading results deriving from the superior potential of the young animals to regenerate bone defects [23].

Recently, the osteoinductive ability of porous calcium phosphate ceramics was studied in four animal species through the implantation of cylinders of hydroxyapatite/tricalcium phosphate (HA/TCP) (in the proportion of 60 and 40%, respectively) in dorsal muscles in dogs, rabbits, rats and mice. After 1 year, the implants were removed, and histopathology tests were conducted with haematoxylin/eosin staining and Masson's trichrome staining to observe the new bone tissue formation. The study concluded that the material is biocompatible and biologically safe (no tumour or any atypical cells were present) and would be considered as a potential for bone substitute. Apart from the rat's groups, there was new bone and bone marrow tissue development in large amounts. The osteogenic ability of the implant was superior in mice, followed by dog and rabbit [33].

Small rodents, rabbits, dogs and small ruminants are the most popular model species for bone regeneration studies, bracing several of the target species for veterinary clinical applications. Allografts and bone graft substitutes have not been fully evaluated in cats, and for that reason, Dorea et al. compared the efficacy and safety of a Bioglass® with that of autogenous and allogeneic cancellous bone graft in this species. Four defects in the lateral diaphyseal cortex of the femur with a diameter of 4.0 mm were created in each animal. One hole was filled with autogenous CBG, another with allogeneic CBG and a third one with Bioglass®. The fourth defect was left unfilled. The healing process was monitored every 2 weeks by X-ray. After 6 weeks, cats were euthanized, and the resolution of the defects was appreciated. The study indicated an acceptable bone regeneration in all defects. Although with a slower healing rate, Bioglass® showed to be an acceptable alternative to ACBG in cats [34].

3. Clinical cases

The use of synthetic bone grafts, in veterinary medicine, has been increasing in the last years, but even so its application is substantially lower than in human medicine. This is mainly due to the costs involved in the use of biomaterials, but nowadays with the development of society and consequent attention given to the animals, there was an increase in the availability of owners to invest in the treatment of their animals. Besides the sentimental value of certain animals, it is not to be despised the growth of the economic valuation of certain types of animals.

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3.1. The use of synthetic bone grafts in small animal clinical cases

Some isolated case reports in small animals using ceramic-based bone graft substitutes have been published in the last decades.

The application of β-tricalcium phosphate (TCP) has already stepped out of preliminary preclinical assays to veterinary patients' applications. Izumisawa et al. successfully solved *pes varus* in two miniature Dachshunds using a wedge of synthetic β-TCP to fill the gaps created by tibial corrective open osteotomies. According to the authors, 2 months after the surgery, the edge of osteotomies was integrated with the bone. The bone plates and screws were removed after 4 months, and, by then, the TCP wedges were completely resorbed and the osteotomy bone was remodelled. In both cases the use of synthetic bone graft TCP avoided the need of a second surgery to harvest autologous cancellous bone graft. In both cases, the postoperative angles were corrected and maintained during the follow-up period, and, morphologically, the body of the tibia in the affected hind limb nearly equalled that found in healthy limbs. Dogs were able to walk a few days postoperatively, and the authors concluded that the corrective transverse-opening osteotomy together with synthetic bone graft substitute β-TCP and veterinary T plate fixation is an effective method for the treatment of *pes varus* in small-breed dogs [35]. A single case of tarsal joint fusion with β-TCP and platelet-rich plasma (PRP) was reported by Hauschild et al., and ACBG, and hence the need of additional surgery to harvest the bone graft, was successfully avoided. The healing process was uneventful and was complete at 4 months after surgery, at which time the dog presented no signs of lameness [36].

Another report on the clinical use of β-TCP as synthetic cancellous bone graft in veterinary orthopaedics was presented by Franch et al. They retrospectively studied 13 clinical cases, where granules of β-TCP, with an irregular form and interconnected porous structure (without dead ends, mean porosity of 60% and mean pore size of 250 μm), were mixed with fresh blood and used as void filler in subcritical-sized bone defects in long bones. The β-TCP used in these clinical series was commercially available in sterile vials containing 2 g of granules with 99% of pure phase. The clinical cases are summarized in **Table 1**. All but one case achieved complete bone union, and radiographic bone ingrowth was at 100% in 10 cases, 90% in 1 case and 75% in another case. The publication reported excellent clinical results confirming the biocompatibility and usefulness of β-TCP as a synthetic bone graft for moderate to large subcritical bone defects with initially expected good biological conditions (blood supply, cellular activity, etc.), on which the main problem is to provide a structural scaffold to allow bone and capillary ingrowth and the healing of the defect [37]. The same author described the treatment of a distal radius atrophic non-union in a 1-year-old male Yorkshire terrier using a 3D-printed β-TCP scaffold with rhBMP-2 (TruScient®) to create a scaffold with the same shape as the defect. After the removal of the bone plate (10 months), load started to transmit along the bone axis, reducing the potential risk of stress protection. Eighteen months after surgery, the scaffold was no longer visible, and complete corticalization of the regenerated bone area was observed on computed tomography (CT) scan evaluation. Given the results, the author suggests that the 3D-printed β-TCP scaffold with rhBMP-2 is an excellent bone substitute, due to good osteoinductive properties given by rhBMP-2 complemented with good osteoconductive potential provided by the open-interconnected macroporosity from the β-TCP scaffold [38].

Type of treatment	Author	Type of macroporous ceramic	No. of cases	Species	Breed	Sex-age-weight	Problem	Reduction device	Bone defect grading	Results			Removal of the implant	Ref.
										Consolidation time (weeks)	Percentage new bone formation	Functional recovery		
β-TCP	Izumisawa et al. 2005	β-TCP wedge shaped	1	Canine	Dachshund	♂-10m	Pes varus and grade 3 lateral patellar luxation	Open-wedge osteotomy in the distal tibia and veterinary 1.5/2.0 T plate	NCSD	About 6	100	Excellent	4 months	[35]
			2	Canine	Dachshund	♂-9m	Pes varus and grade 3 lateral patellar luxation	Open-wedge osteotomy in the distal tibia and veterinary 1.5/2.0 T plate	NCSD	About 6	100	Excellent	4 months	
	Franch et al. 2006	Irregular interconnected granules of β-TCP (60% porosity)	3	Canine	Shiba Inu	♀-7 y-12kg	Traumatic carpal hyperextension	Pancarpal arthrodesis with 2.7 DCP plate	NCSD	12	100	Excellent		[37]
			4	Canine	Shiba Inu	♀-7y-12kg	Traumatic carpal hyperextension	Pancarpal arthrodesis with 2.7 DCP plate	NCSD	10	100	Excellent		
			5	Canine	Crossbreed	♂-12y-10kg	Fractures of the distal radius (cranial bone loss), ulna, III–IV–V metacarpal bones and I phalanx and comminuted carpal bone fracture-luxation	Pancarpal arthrodesis, radial and III metacarpal fractures treated together with 2.7 DCP plate	NCSD	8 (radius) 12 (carpus)	100	Excellent		
			6	Canine	German Shepherd	♂-2y-38kg	Comminuted mid-shaft femoral fracture	Interlocking nail with four cerclage wires	NCSD	9	90	Excellent		
			7	Canine	German Shepherd crossbreed	♂-7y-37kg	Tibial fracture	3.5 DCP plate	NCSD	10	100	Good		
			8	Canine	Belgium Shepherd	♀-8y-34kg	Distal radius fracture	3.5 DCP plate	NCSD	10	100	Excellent		
			9	Canine	English Bulldog	♂-10y-11kg	Tarsometatarsal luxation	Cross pinning tarsometatarsal arthrodesis	NCSD	12	75	Good		

Type of treatment	Author	Type of macroporous ceramic	No. of cases	Species	Breed	Sex-age-weight	Problem	Reduction device	Bone defect grading	Results			Removal of the implant	Ref.
										Consolidation time (weeks)	Percentage new bone formation	Functional recovery		
			10	Canine	Golden Retriever crossbreed	♂-3y-35kg	Radius and ulna comminuted fracture	3.5 DCP plate	NCSD	8	100	Excellent		
			9	Canine	Mastiff crossbreed	♂-2y-48kg	Hypertrophic femoral non-union. Osteopenic bone at surgery due to disuse	Interlocking nail with 4 screws	NCSD	12	100	Excellent		
			11	Canine	Chihuahua	♂-2y-3.5kg	Tibiotarsal fracture/luxation	Cross pinning tibiotarsal arthrodesis + temporary transarticular external fixator	NCSD	12	100	Good		
			12	Canine	Yorkshire Terrier	♀-7y-3.4kg	II, III, IV and V metacarpal atrophic non-union	Intramedullary pins	CSD	/	0	Poor, the patient needs a permanent splint		
			13	Canine	German Shepherd	♀-5y-44kg	Traumatic carpal hyperextension	Carpal arthrodesis stepped plate	NCSD	8	100	Excellent		
			14	Feline	European crossbreed cat	♀-2y-3.8kg	Highly comminuted distal femoral fracture	2.7 DCP distal femoral prebent plate	NCSD	11	100	Excellent		
β-TCP + PRP 300mg + blood + 0.6 ml PRP	Hauschild et al. 2005		15	Canine	Beagle	♀-10m-?kg	3 weeks old traumatic luxation of the right intertarsal joint and compressive fracture of the fourth tarsal bone	Partial tarsal arthrodesis with lateral 2.0 DCP plate and a K wire plus coaptation bandage for 4 weeks	NCSD	16	100	Excellent, no sign of lameness	7 months later and leaved the K wire in place	[36]
Collagen-TCP sponges + rhBMP-2 + monocortical fenestrated rib	Boudrieau et al. 2004	Collagen-TCP sponges	16	Canine	Golden Retriever	♀-14 month-23.6kg	Mandibular reconstruction after partial mandibulectomy for tumour resection	2.0 miniplate and 2.4 mandibular reconstruction plate in the right side and 2.0 miniplate and 2.4 unilockin plate	2 CSBD (1.5 cm × 1 cm × 2 cm) and (7 cm × 1 cm × 2 cm)	12		Excellent	One exposed plate 1 year later	[47]

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Type of treatment	Author	Type of macroporous ceramic	No. of cases	Species	Breed	Sex-age-weight	Problem	Reduction device	Bone defect grading	Results			Removal of the implant	Ref.
										Consolidation time (weeks)	Percentage new bone formation	Functional recovery		
β-TCP +ACBG (1:1) and a titanium mesh cage	Segal and Shani 2010	β-TCP	17	Canine	Crossbreed	♂-7y-25kg	Highly comminuted fractures (femur, radius and ulna) that fail to previous fixation	IM pin through the cage and a locking plate	2 CSBD 71mm segmental femoral bone defect and 27mm segmental radial defect	22–63	70% of femoral cage at 22 weeks and 100% at 63 weeks	Successful long-term clinical outcome	No due to the associated costs	[41]
Contralateral bone widening and transfer and silicate calcium phosphate	Petazzoni 2016	Silicate calcium phosphate	18	Feline	Maine Coon	♀-5y-5kg	Non-union and bone loss	2.5 mm locking plate	CSBD 60mm corresponding to 48% of mechanical axis on the sagittal plane	At 13 satisfactory healing. 22 weeks non-union. 20 weeks post revision surgery with ACBG healing of non-union.		Excellent long-term follow-up	6 weeks–18 weeks good; at 22 weeks implant fails and revision surgery was done; the plate was removed 20 weeks later	[43]
CRM + rhBMP-2	Massie et al. 2017	CRM	19	Canine	Italian Greyhound	3Y-3kg	Non-union of left and right radius/ulna	2.0 mm 14-hole LCP	R 65 mm L 2.5 mm	R 9 and L 10				[46]
			20	Canine	Rat Terrier	1y-7.1kg	Atrophic-oligotrophic non-union of R tibia	2.0 mm 13-hole LCP	32 mm	10				
			21	Canine	Golden Retriever	12y - 24.3kg	Dystrophic non-union of the L tibia	3.5 mm 10-hole LCP	16 mm	10				
			22	Canine	English Pointer	11y - 29.7kg	Atrophic-oligotrophic non-union of R lateral humeral condyle	5.5 mm cortical lag screw + 2.4 mm 8-hole LCP	1 mm	16				
			23	Canine	Schipperke	2y - 7.1kg	Atrophic-oligotrophic non-union of R radius/ ulna	2.4 mm 10-hole LCP	5 mm	6				
			24	Canine	Border Collie	9y - 16kg	Atrophic-oligotrophic non-union of L tibia	ESF hybrid	10 mm	10				
			25	Canine	Cocker Spaniel	10y - 12kg	Atrophic-oligotrophic non-union of L lateral humeral condyle	3.5 mm cortical screw and washer + 2.4 mm 4-hole LCP	1 mm	20				
			26	Canine	Miniature Poodle	2y - 3kg	Dystrophic non-union of R an L radius/ulna	R 7-hole LC-DCP and L 8-hole LC-DCP	2 mm	8				

Type of treatment	Author	Type of macroporous ceramic	No. of cases	Species	Breed	Sex-age-weight	Problem	Reduction device	Bone defect grading	Results			Removal of the implant	Ref.
										Consolidation time (weeks)	Percentage new bone formation	Functional recovery		
			27	Canine	Mixed breed	4y - 12kg	Dystrophic non-union of R radius/ulna	2.4 mm 10-hole LCP	10 mm	7				
	Arzi et al. 2015	CRM (collagen sponge with embedded granules of HA and TCP)	28–32	Canine	–	8–9y (mean 8.8Y), 25-37kg (mean 29kg)	Reconstruction of the bone defects after segmental mandibulectomy for tumour resection	Titanium 3.0 mm locking plates	CSD 42–60 mm (mean, 50.5 mm)	8	100	Excellent function, occlusion and quality of life		[49]
	Verstraete et al. 2015	CRM (collagen sponge with embedded granules of HA and TCP)	32–38	Canine	Small-breed dogs	2–11 y (mean, 7.3y), 3.4–6kg (mean, 4.8kg)	Non-union mandibular fractures	2.0 locking titanium miniplate	CSD 5–18 mm (mean, 9.2 mm)	4 to 12		Excellent long-term follow-up		[48]

CRM, compression-resistant matrix; CSD, critical-sized bone defects; DCP, dynamic compression plate; LCP, locking compression plate; LC-DCP, limited contact dynamic compression plate; ESF, external skeletal fixation; L, left; NCSD, noncritical-sized bone defects; R, right.

Table 1. Description of reported clinical cases using ceramic-based bone substitutes in small animals, based on available literature.

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Treatment of long bones affected with large segmental defects is challenging in human and veterinary medicine [39]. Different surgical approaches have been developed, but most of these techniques present major complications. Cortical allografts are prone to infection and are rarely fully incorporated [11, 39]. Distraction osteogenesis should only be used in docile animals and cooperative owners because it needs a lot of adjustments and cleaning of the fixator besides having to be kept in place for prolonged periods that could lead to loss of stability and discomfort [40]. Osteoconductive materials and osteoinductive substances, such as canine-demineralized bone matrix, canine autogenous bone grafts and bone morphogenetic proteins, have been used for the treatment of bone defects and comminuted fractures, alone or in combinations with bioceramics [6, 12]. Another alternative treatment that has been used with success is the clinical application of titanium mesh cages [41], nevertheless with extreme variable outcomes [42].

One case report in a dog with large segmental femoral and radial bone defects that failed in the first attempt of surgical stabilization and finally treated with a combined approach with titanium mesh, β-TCP, ACBG into the defects and fractures was stabilized with locking plates. Titanium mesh allowed maintaining bone fragments and grafts within the defect being further, between 22 and 63 weeks, surrounded by a bony bridge. Clinical outcome was successful without visible lameness in pace, but it was visible, while running and reduction in range of motion with crepitation were noticed on the stifle joint. Those limitations could be associated with original trauma or complications of fixation methods. Long-term follow-up (greater than 1 year) shows a satisfactory active mobilization of the limb. In this case, the technique has been simple and should be an alternative for treatment of long segmental bone defects. However, further systematic clinical studies are needed in order to evaluate the efficacy, complications and spectrum of the clinical use of this method [41].

A case report of successful reconstruction of a long segmental tibial defect in a 5-year-old 5 kg-spayed female Maine Coon cat were transverse distraction osteogenesis in the contralateral tibia was used to create free autograft for filling the defect. After fixation of the bone fragments with a locking plate, the autograft was transferred to the defect in the contralateral tibia, and the remnant space was filled with silicate calcium phosphate bone graft substitute. By 27 months, both tibias were healed; implants had been removed with an excellent functional outcome [43].

Combination of BMPs for augmentation of bone regeneration associated with bioceramics in the treatment of non-union fractures of long bones was mentioned in a review as a single case of non-union of the distal radius in a Pomeranian [44] and in a distal radius atrophic non-union in a 1-year old male Yorkshire terrier by Franch [45]. A recent prospective longitudinal cohort study of the use of compression-resistant matrix (CRM) immersed in rhBMP-2 in the treatment of 11 non-union long bone fractures in 9 dogs was evaluated, and treatment was successful with healing time from 7 to 20 weeks (median 10 weeks) and return to full or acceptable function in all dogs [46].

Non-weight-bearing bone lesions can also greatly benefit from the application of synthetic bone substitutes, such as those resulting from dental procedures. Boudrieau et al. published in 2004

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one case report of treatment of severe mandibular malocclusion after partial mandibulectomy in a 14-month-old golden retriever using fenestrated, monocortical rib grafts with rhBMP-2 in a collagen-TCP sponge that showed new bone formation after 3 months with reconstruction of the defect. One year later, the bone was collected, and the new bone was robust with evidence of continued remodelling. No major complications were noticed, and bony remodelling was evident at 4-year follow-up [47].

According to the authors' knowledge, those are the first reports of the use of rhBMP-2 delivered via adsorption into a CRM for regenerating bone in chronic defect non-union fractures in dogs. Its radiographic appearance seems to have a normal bone density and was integrated to native bone. The combined surgical and regenerative strategies reported achieved predictable, timely reconstruction of defect non-union fractures in small-breed, older dogs. The use of rhBMP-2 should be done with caution due to its very potent effect that is very versatile and with a wide range of functions and dose dependent. Finally, the incorporation of a regenerative strategy into the surgical resolution of non-union fracture defects avoided the morbidity associated with autologous bone grafting and provides fast return to normal function [48].

CRM is made of a collagen sponge with implanted granules of hydroxyapatite and tricalcium phosphate generating a semi-rigid framework that can resist to compressive forces in vivo, and it has been successfully used to fill bone defect in several studies [46, 48, 49]. In a prospective case series published by Arzi et al., CRM was used with rhBMP-2 in immediate reconstruction of segmental mandibulectomies (mandibular defects ≥5 cm) in four dogs for treatment of benign or malignant tumours. After tumour recession, the critical-sized bone defects were stabilized with titanium locking plates, and CRM, soaked with 0.5 mg/ml rhBMP-2 15 min before implantation at a volume equivalent to half of the calculated volume of CRM (with a half to three quarters of the mandibular height and a length 2 mm greater than the defect), was tightly implanted. Radiographic evaluations were made postoperatively at weeks 2, 4, 8 and 12 after surgery. In two clinical cases, a CT scan of the mandible was acquired 3 months after surgery. All dogs had proper occlusion after surgery and in the follow-up evaluation and returned to normal activity. After 2 weeks the entire defect site was covered with gingiva, and at 4 weeks, it was completely solid. There was no recurrence of the tumour or fractures during the controls at 2 and 3 months after surgery, and all owners reported an excellent quality of the life of their dogs [49]. The radiodensity of regenerated mandible increases throughout radiographic controls from postoperative radiographs to 4 weeks after surgery. The CRM scaffold had evidence of new bone formation connecting the adjacent mandible and smooth margins at 4 weeks post-surgery. At 8 weeks the scaffold continued to increase its radiodensity, and a mineralized union with the mandible was noticed. New bone formation and complete integration of CRM material with native mandible tissue were evident on CT image evaluation. The authors concluded that this surgical and regenerative approach achieved a rapid return to normal activity, with normal anatomy and occlusion, bone regeneration and re-established biomechanical function [49].

Verstraete published another case series in six dogs where CRM and rhBMP-2 were used as a regenerative approach to fill non-union mandibular fracture defects stabilized with locking titanium miniplate. All dogs were adopted from a shelter, and, apart from two dogs, it was not

possible to know the duration of the non-union. In all cases the non-union defect was debrided and cleaned from fibrous and devitalized tissues and old implant materials. The volume of the defects was estimated with a CT with three-dimensional reconstruction, and an amount of CRM enough to fill a half to three quarters of the mandibular height with a length of 2 mm greater than the mandibular gap was prepared. The CRM was soaked with a volume of rhBMP-2 (0.5 mg/ml) corresponding to 50% of the CRM volume used to fill the defect. As an example, with a CRM piece of 2 cm length, 0.5 cm width and 1 cm height ($2 \times 0.5 \times 1$), the total CRM volume is 1 cm^3, corresponding to 0.5 ml of rhBMP-2 solution with 0.5 mg/ml concentration. An extra-oral approach was used to counter the plate in ventrodorsal position. The wedges of the non-union were debrided to remove sclerotic and devitalized bone and attached soft tissues, and the plate was then fixed to the bone with two to three locking titanium screws in each segment of the mandible and CRM was implanted. Radiograph follow-ups of the mandible were started immediately after surgery and 2, 4, 8 and 12 weeks after surgery. All dogs healed the soft tissues over the defects and with immediate to normal function and correct occlusion, and solid cortical bone formation was noticed within 3 months. There were no recurrence fractures on the follow-up period [48].

Synthetic bone graft (Bonelike®) is produced by the incorporation of P_2O_5–CaO glass-based system within a hydroxyapatite (HA) matrix. Bonelike® macroporous (BL® Poro) consists of polygonal granules with 2000–2800 and 4000–5600 μm of diameter with pore size range from 100 to 400 μm (**Figure 1**). Its osteoinductive and osteoconductive properties have been confirmed in experimental models of bone regeneration in sheep, have been used in clinical orthopaedic application and recently are being used in small animals [50–54].

We used Bonelike® in small granules and Bonelike® presenting macroporous structure (BL® Poro) in vivo in combination with ACBG (**Figure 2(A)**), PRP (**Figure 2(B)**) and rigid internal fixation with bone plates and screws to treat atrophic non-union of long bones in two adult dogs that were referred to the veterinary medicine teaching hospital, Vasco da Gama University, Coimbra, Portugal, for surgical correction of atrophic non-union that fails in at least one previous surgery. After clinical and orthopaedic examination, two orthogonal views of the affected and contralateral bone were obtained with a standard marker to calibrate magnification. Informed consent to use BL Poro® was obtained from all clients. Clinical cases were classified according to Weber-Cech terminology, as defect, dystrophic, necrotic or oligotrophic-atrophic non-union, and were labelled as infected if this was suspected due to either radiographic evaluation or appearance and tissue culture at surgery. For both clinical cases, autologous cancellous bone grafts were harvested from the uppermost proximal humerus as described by Innes [5]. One dog had a large femoral diaphyseal bone defect and is not able to apply loading to the affected pelvic limb. The second dog had an oligotrophic non-union in the proximal radius and two non-unions in the ulnar diaphysis caused by a gunshot trauma. Revision surgery was performed to remove all the failed implants, debridement, ischemic bone fragments and other avascular soft tissues. Sclerotic and atrophic bone ends of the biologically inactive non-unions were osteotomized with a bone. Rongeur until bleeding is seen to expose medullary cavity and improve vascularity in a bone defect. Prior to copious flushing, samples of the removed tissues and deep wound swabs were collected

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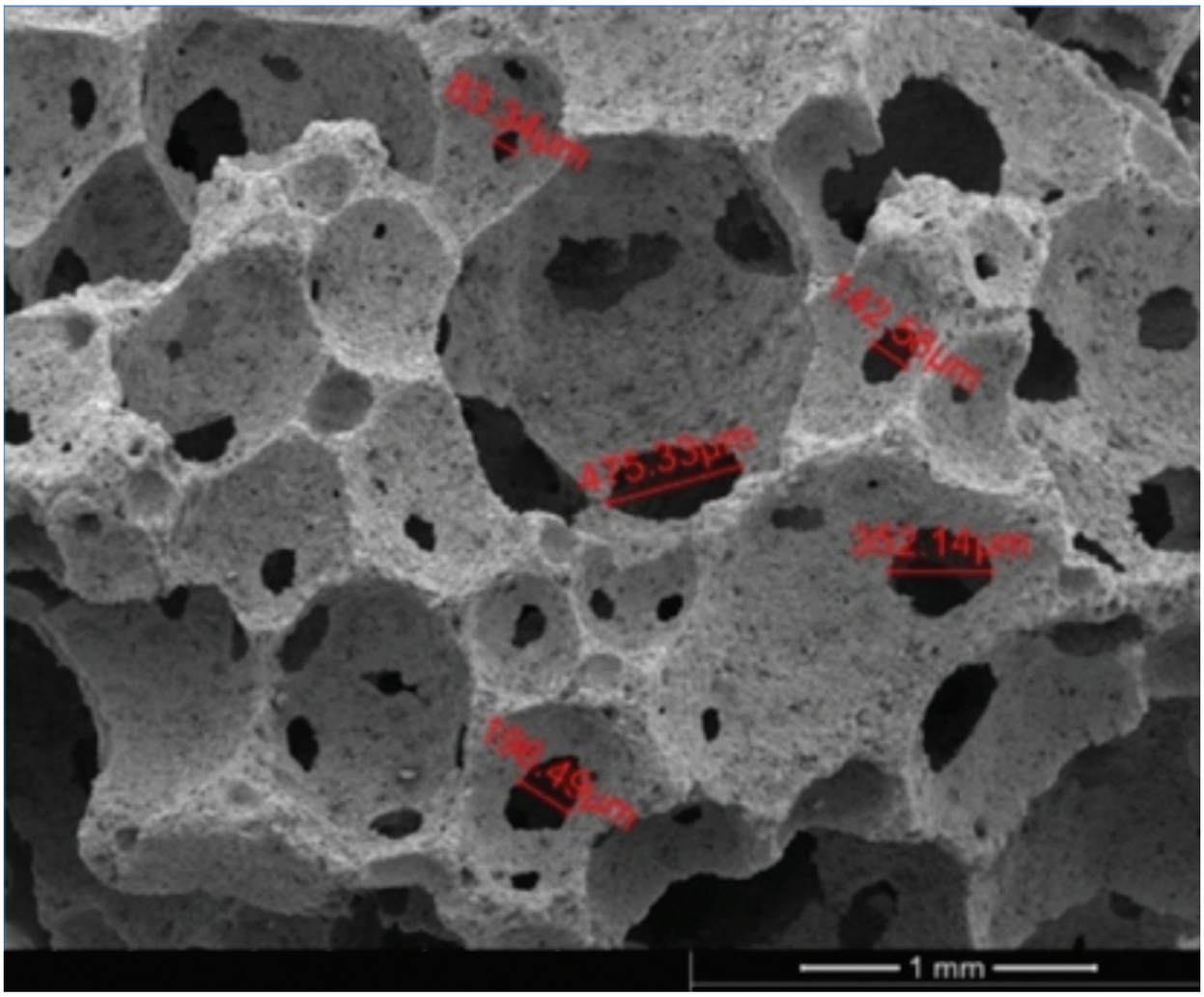

Figure 1. Scanning electron microscope image of a Bonelike® Poro granule showing the interconnected pore architecture with macropores and micropores.

for bacterial culture and sensitivity antibiogram. Joints are aligned, bone segments are pulled apart trying to restore original length of the bone and the fracture was stabilized with a bone plate and screws maintaining a rigid fixation for a prolonged time with minimal discomfort to the animal during postoperative period. The bone defect created after cleaning and the fracture fixation was filled with a homogenous mixture of ACBG and BL® Poro in 1:1 proportion in a PRP gel to maintain the aggregation of the components. The mixture was applied gently avoiding rupture and consequent collapse of the macroporous architecture of BL® Poro (**Figure 3**). Soft tissues were closed routinely and contribute to maintain the bone graft in situ with created soft tissue envelope. All the animals returned to acceptable or good function and decrease lameness grades. All cases achieved bone union between 2 and 8 months without major complications [54].

Our research group also has been using Bonelike® and a BL® Poro mixed with fresh blood to fill voids in noncritical-sized bone defects in dogs and cats with good clinical and radiographical outcomes without any adverse local nor systemic reaction (**Figures 4** and **5**). A

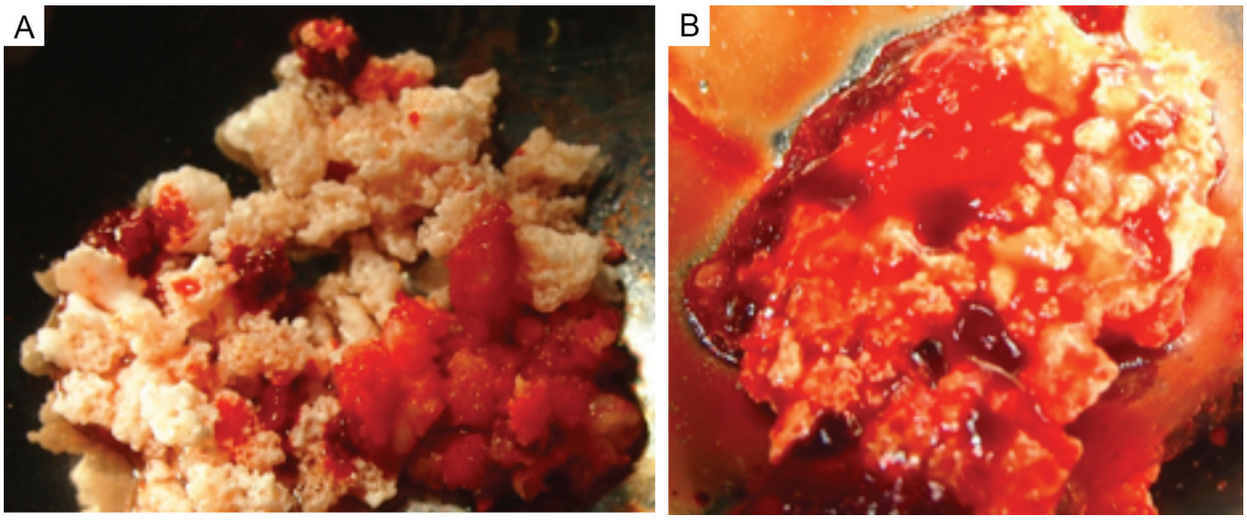

Figure 2. BL® Poro granules (white) mixed with autologous cancellous bone graft (red) (A). Mixture of BL® Poro granules with autologous cancellous bone graft and platelet-rich plasma, ready for implantation (B).

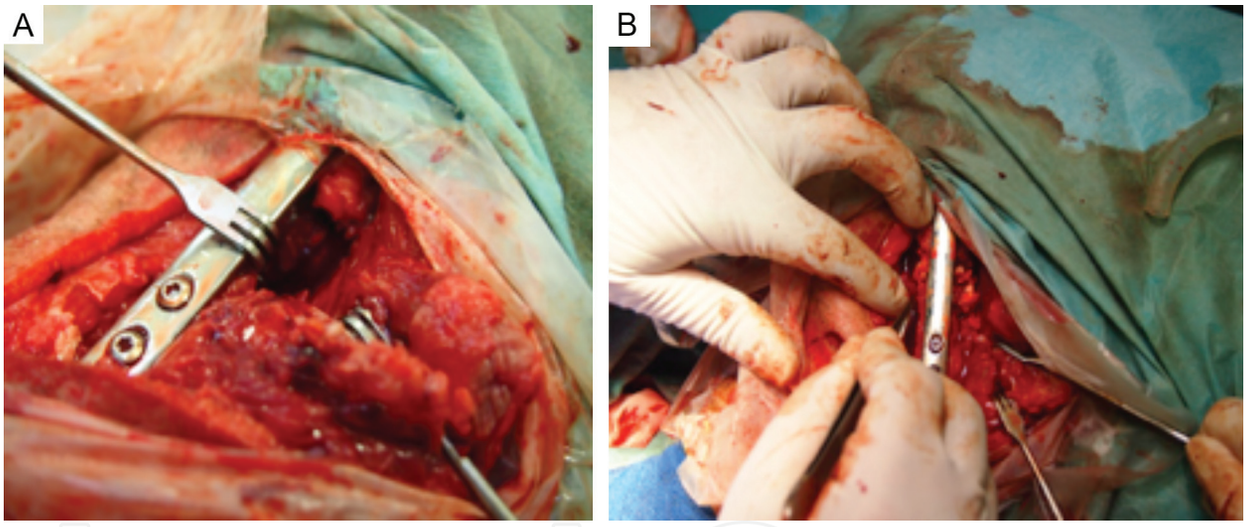

Figure 3. Femoral bone defect after fracture bridging plate fixation (A). Careful filling of defect to avoid the collapse of BL® Poro macroporous architecture (B).

clinical case of an 8-year-old, 21 kg, female Collie with a mandibular fracture along the root of canine teeth. The loose teeth exodontia and improved dental occlusion with an external skeletal fixator where fixation pins were placed along the aboral bone surface avoiding tooth roots were performed. The pins were bended and fixed together with a mouldable-stage application of methyl methacrylate. After hardening of the acrylic, the bone gap was approached directly from the oral mucosa and filled with mixture of Bonelike® (spherical granules of 250–500 μm) and blood. The soft tissues were surgically routinely closed and healed uneventfully. On radiographic evaluation 5 weeks post-surgery, the osteointegration of the biomaterial was visible, and fracture line was no longer visible. The fixator was removed 4 months later, and there was no story of mandible retraction or other types of complications (**Figure 6**) (unpublished data).

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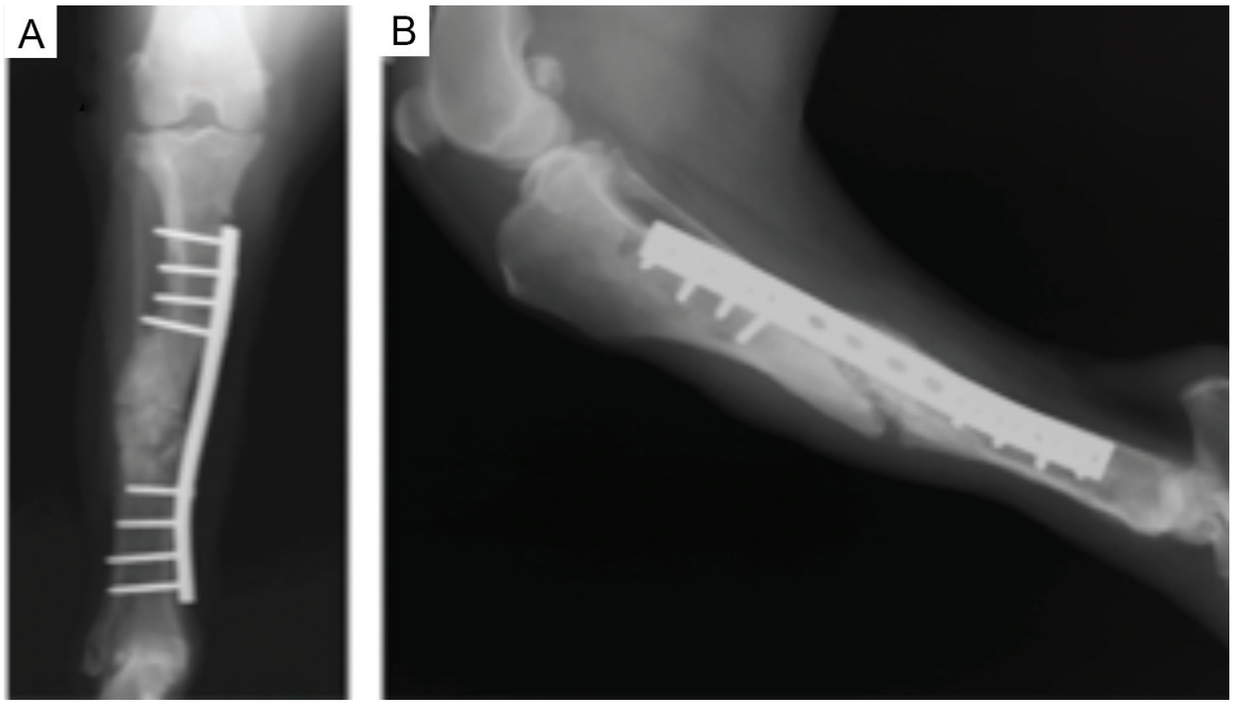

Figure 4. Immediate postoperative radiographs of the tibia of a 7-year-old 35 kg male german shepherd dog with a non-union fracture stabilized with a 3.5 mm 12-hole broad DCP plate. Bone defect was filled with Bonelike® 250–500 μm, autologous cancellous bone graft and platelet-rich plasma: cranio-caudal view (A) and mediolateral view (B). Radiolucent lines were visible within the graft and between the graft and the edges of the bone defect.

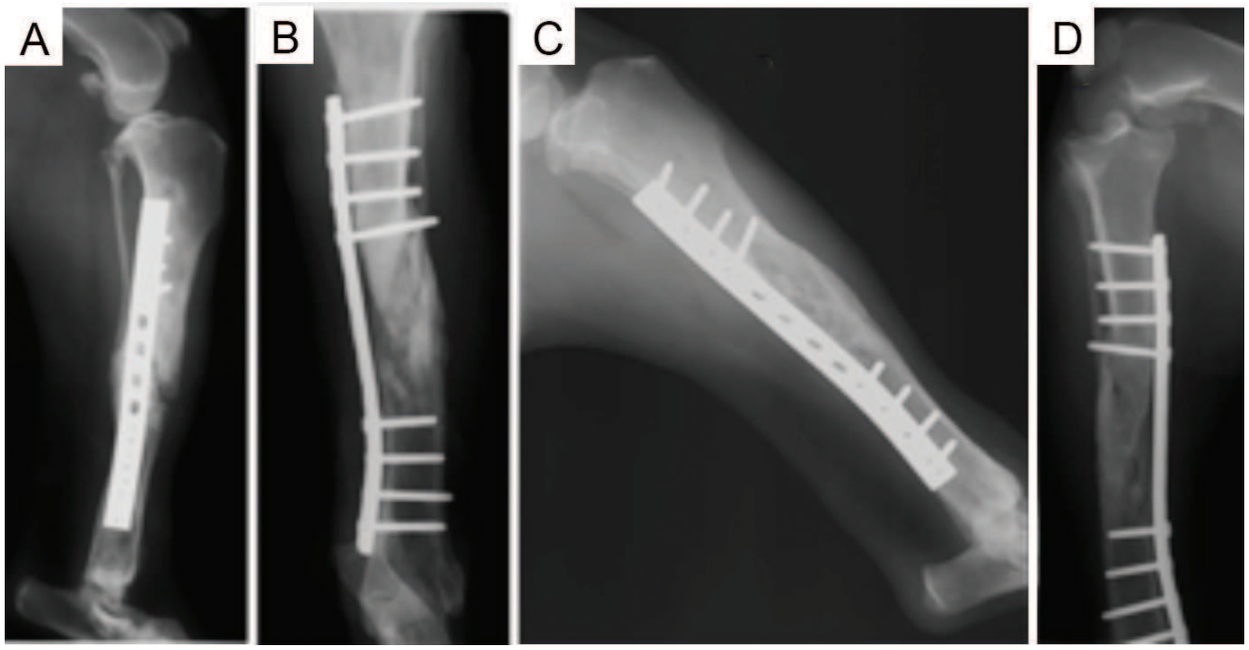

Figure 5. Postoperative radiographic evaluation. Mediolateral view at 2 months of control showing complete bone union on the caudal edge of the defect and not on the cranio-distal edge; here, a radiolucent line was noticed but with a grey colour compatible with new bone formation (A). Cranio-caudal view at 2 months of control, complete bone bridge was observed in lateral and medial cortices with irregular pattern within the bone defect (B). Mediolateral view at 8 months of control (C) and cranio-caudal view at 8 months of control. In both radiographs completed, bone union and remodellation were visible without radiolucent lines in the bone defects (D).

3.2. The use of synthetic bone grafts in equine clinical cases

Besides the majorly emotionally driven small animal clinics, other veterinary medicine fields are growing regarding the clinical application of the biomaterials, as economic implications are added to the scenario. For example, equines are the 'driving force' of an industry that moves enormous financial amounts, with competition prizes and price of some animals reaching astronomical values. With this set of constraints, the use of biomaterials in animals no longer restricts to preclinical trials carried out before their application in humans and is now part of the procedures available to veterinary clinicians. These techniques can be used in a number of clinical situations in veterinary medicine, where there is a bone defect, including fractures such as comminuted fractures, filling of bone cysts and arthrodesis [6, 55–59].

Equine patients are challenging in terms of orthopaedic pathologies and viable treatment options. While most of the small animal cases referred for orthopaedic treatment relate to fractures, and surgical reduction leads to expected full recovery, but even if this is not possible, they can survive with minimal complications with unsupported limb. Contrarily, in result of their weight, equine patients with unsupported limb have a high risk of developed severe secondary pathologies at contralateral limb, like laminitis. Other problems can surge in these equine patients; these animals cannot spend long periods lying down due to complications of myositis, nerve paralysis and decubital scars, so they weight injured limb for prolonged periods. For all those situations, fracture cases are seldom amenable of medical or surgical correction, often resulting in the decision of euthanasia. Other clinical situations are however indicated for grafting and/or biomaterial application, such as arthrodesis procedures.

Arthrodesis techniques were developed for treatment of debilitating osteoarthritis. These are also indicated for treatment of (stable) articular fractures, unstable joint injuries, septic arthritis and osteochondrosis. It is a surgical procedure used to promote the fusion between opposite bones in the joint, resulting in immobilization. Surgical arthrodesis involves the destruction of

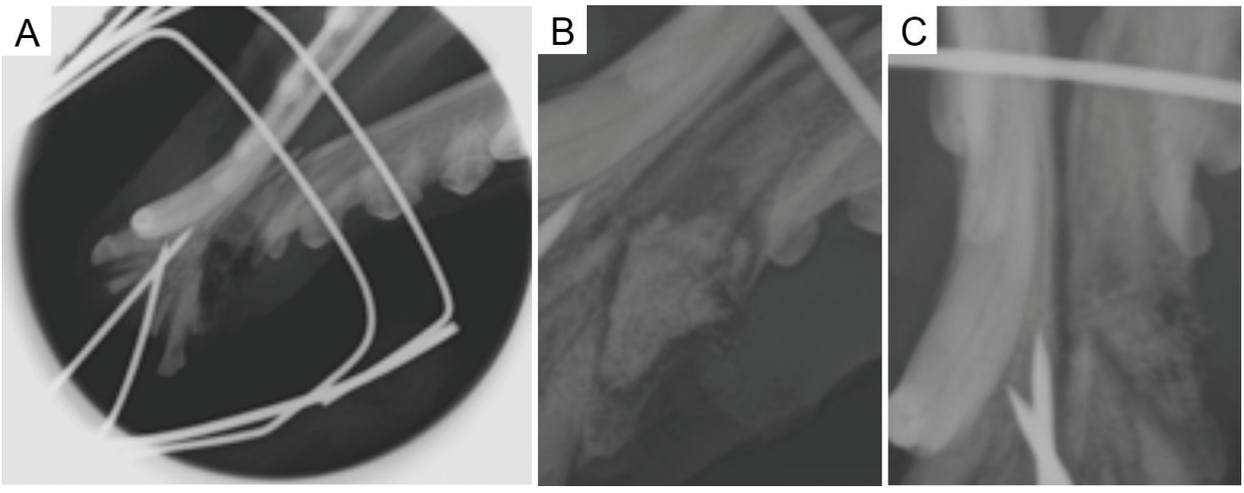

Figure 6. Bone defect resulting from canine teeth exodontia and mandibular fracture along the root of canine stabilized with a methyl methacrylate external skeletal fixator (A); immediate postoperative image of the defect filled with Bonelike® 250–500 and blood. The biomaterial was noticeable due to its multiple radiopaque spherical structures inside the bone defect. Radiolucent lines were visible within the spheres and between the graft and the edges of the bone defect. Fracture line was visible near by the fixation pin (B); 5 weeks of radiographic control, loss of radiopaque appearance of the biomaterial and radiopaque fracture lines was no longer visible due to new bone formation (C).

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the articular cartilage of the bones to promote a bone-to-bone contact and subsequent fusion. Then, the joint must be aligned and stabilized into a stable, weight-bearing position [60–63]. Synthetic bone grafts can be used in the arthrodesis technique as void filler, improving the bone contact, helping the joint stabilization and avoiding the autologous bone graft collection. Since synthetic bone grafts deliver important osteoconductive and osteoinductive proprieties, the healing process is improved and shortened [50, 52]. Surgical arthrodesis is used in clinical situations that it is not possible recover the joint. With this technique the joint is stabilized, relieving the pain and improving horse's quality of life. In this species, the proximal interphalangeal, the intertarsal and the tarsometatarsal joints are the joints where more arthrodeses are performed, due to these joints that only have little range of movements, and their permanent immobilization does not affect normal locomotion of the horse. In these cases, the goal of the surgical procedure is to return the horse to its activity. Although the permanent immobilization does not affect normal locomotion, this procedure can weaken the joint region, due to loss of shock absorption capacity of the joint, and fracture risk may be increased [64–66]. Arthrodesis technique is also used in joints that have important movements (like metacarpophalangeal joint), knowing that in these cases the horse will have a mechanical lameness. The use of this technique in these types of joints allows to decrease pain and to increase comfort and the use of the affected limb, thus preventing the appearance of lesions in the contralateral limb overhead [64–66].

As examples of the use of synthetic bone grafts, it will be described in three clinical cases, where Bonelike® was applied in the arthrodesis of metacarpophalangeal joint, in the proximal interphalangeal joint and in the distal intertarsal joint together with tarsometatarsal joint.

The first clinical case is a newborn donkey, born with a severe metacarpophalangeal joint flexural deformity. The flexural deformity is so severe that it is impossible to manipulate and move the metacarpophalangeal joint and the dorsal surface of the fetlock supported the animal's weight. Due to this situation, the dorsal aspect of the fetlock presented an ulceration that communicated with the joint (**Figure 7**). It was decided, as the first approach, the surgical treatment, to quickly as possible resolve the situation and prevent the worsening of the complications [67, 68]. In this type of surgery, to relieve flexor forces, the tightened tendons can be cut [67, 69, 70]. In this clinical case, both the superficial flexor tendon and the deep flexor tendon were involved in the contracture of the joint, as well as the extensor digital tendon, which was displaced caudally, working as a flexor, further forcing the joint to adopt the flexor position (**Figure 8(A)**). Tenotomy of the three involved tendons was undertaken, in order to reposition the joint into a physiological alignment (**Figure 8(B)**). With this aggressive approach, the metacarpophalangeal joint stayed without support; so, a surgical arthrodesis of metacarpophalangeal joint was also performed to stabilize the joint in a physiological position. To do the arthrodesis, first the joint cartilage was removed with a curette to promote a bone-to-bone contact between the metacarpal bone and the first phalange; after that the joint space was filled with Bonelike® spherical granules mixed with autologous blood. A plate with cortical screws was used to stabilize the joint in a physiological position (**Figure 8**(**C** and **D**)) [68]. Although arthrodesis is not commonly used on flexural limb deformities, it was decided to apply this technique in the described clinical case, considering the lack of structural support of the joint after the tenotomy of the three tightened tendons. This approach was previously described by [71] that performed arthrodesis in a llama, in a miniature horse and in a

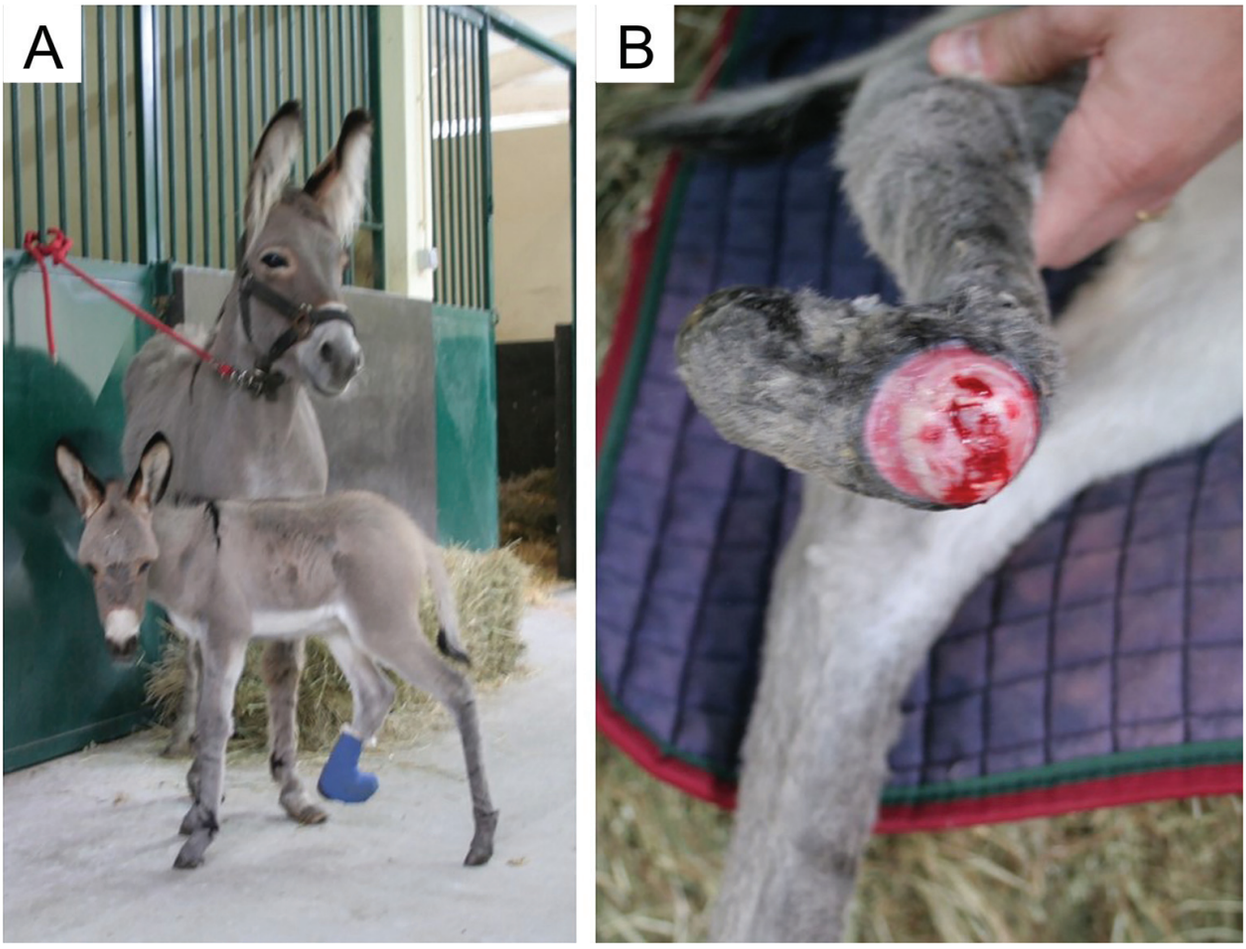

Figure 7. Newborn donkey with a severe metacarpophalangeal joint flexion deformity. The donkey supported the right hind limb with the dorsal aspect of fetlock (A). Large cutaneous ulcer on dorsal aspect of fetlock (B).

miniature donkey, with severe bilateral congenital flexural deformities of the metacarpophalangeal joint. The arthrodesis of the fetlock joint was not aimed at full recovery for future athletic activity but rather having in mind the animal's life quality [68].

The second clinical case was an adult horse that suffered an accident that resulted in the laceration of the medial aspect of the pastern. With this laceration, a medial ligament that causes instability to the pastern joint and consequently lameness was damaged. In clinical examination, a biomechanical instability of this joint was observed, and in X-ray examination, radiologic signs of subluxation and an increase in the medial joint space can be seen. Towards that it was decided to do the arthrodesis of proximal interphalangeal joint [68]. To approach the proximal interphalangeal joint, an I-shaped incision was performed in the skin over the dorsal aspect of the joint, and then a Z-incision was performed over the digital extensor tendon to expose the proximal interphalangeal joint. During the procedure, it was confirmed that this joint was not stable and there was an increased articular gap between the first and the second phalange on the medial aspect of the joint (**Figure 9(B)**). The cartilage from proximal interphalangeal was removed using a curette, and the joint space (**Figure 9(A)**) was filled with Bonelike® (**Figure 9(C)**). Three lag screws 3.2 mm were placed from the first to the second

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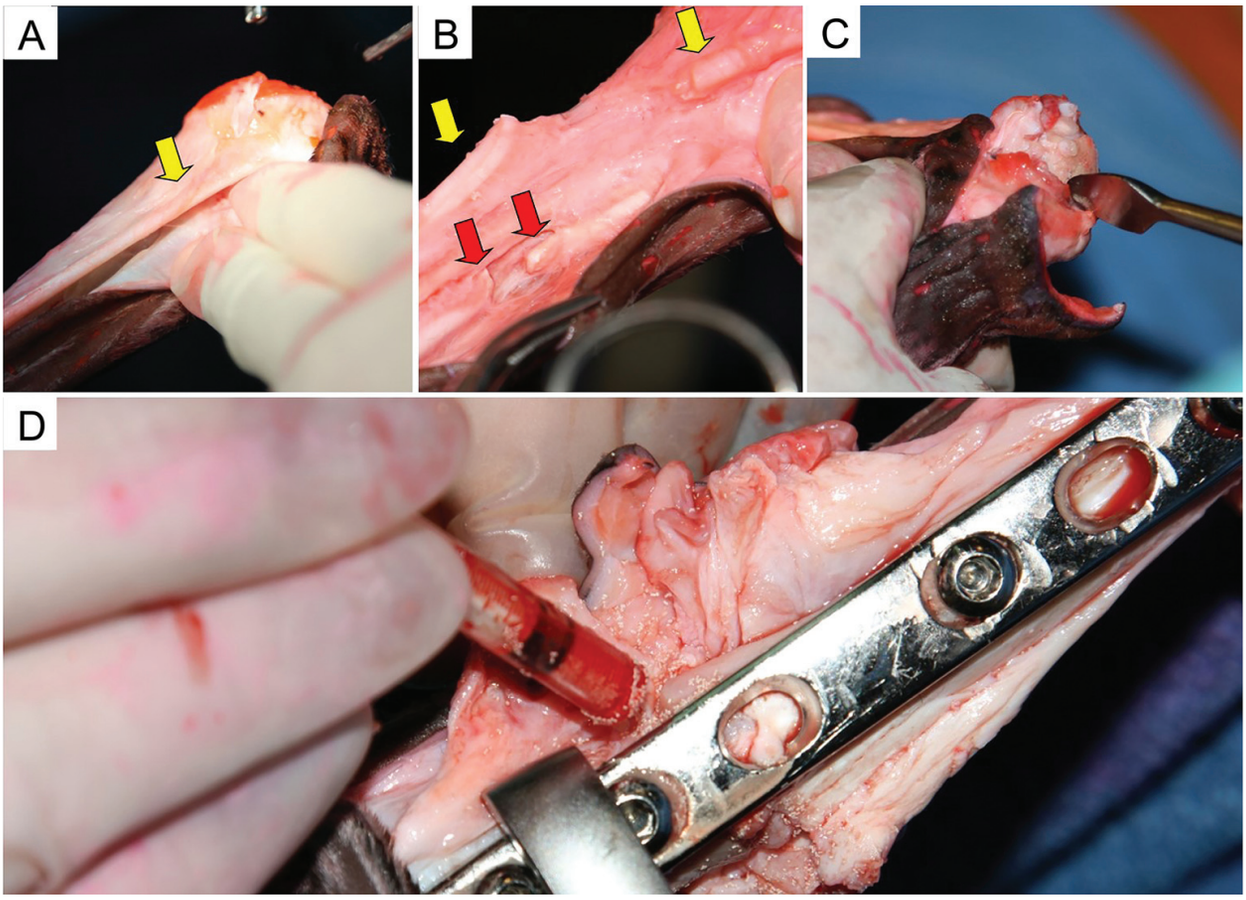

Figure 8. Metacarpophalangeal joint arthrodesis. Extensor digital tendon (yellow arrow) displaced caudally (A). Tenotomy of extensor digital tendon (yellow arrows) and flexor digital tendon (red arrows) (B). Removal of joint cartilage with a curette (C). A plate and screws to stabilize the joint and fill joint space, using a syringe, with Bonelike® spherical granules (D).

phalange crossing the joint space. The head screws stayed in a shelf made previously with an osteotome (**Figure 9(D)**). On the follow-up X-rays performed after the surgery, an important bone proliferation, with evidence of bone fusion and gradual reduction of the joint space, was noticed (**Figure 10**) [68].

The third clinical case was a report of a horse with chronic and intermittent lameness of the right hind limb, with a slight biomechanical instability of the tarsal region during walking, posing clinical and radiological signs of bone spavin. After the confirmation of joint pain by clinical examination with the positive nerve blocks, it was decided to do the distal intertarsal joint together with tarsometatarsal joint arthrodesis. The surgical approach to those joints was made by an incision over the medial aspect of the tarsus perpendicular to the cunean tendon. The cunean tendon was transected, and joints were identified with two needles (**Figure 11(A)** and **(B)**). A 3.2 drill bit was inserted into the joint space of each joint and forced in three different directions, using a single entry point (**Figure 11(C)** and **(D)**) [68]. Drilling paths were filled with Bonelike® (**Figure 11(E)** and **(F)**). The objective of drilling the joint space was to destroy the cartilage and to promote the contact between the bones and subsequent bone fusion. Due to the osteoconductive proprieties of Bonelike®, the application of this bone graft

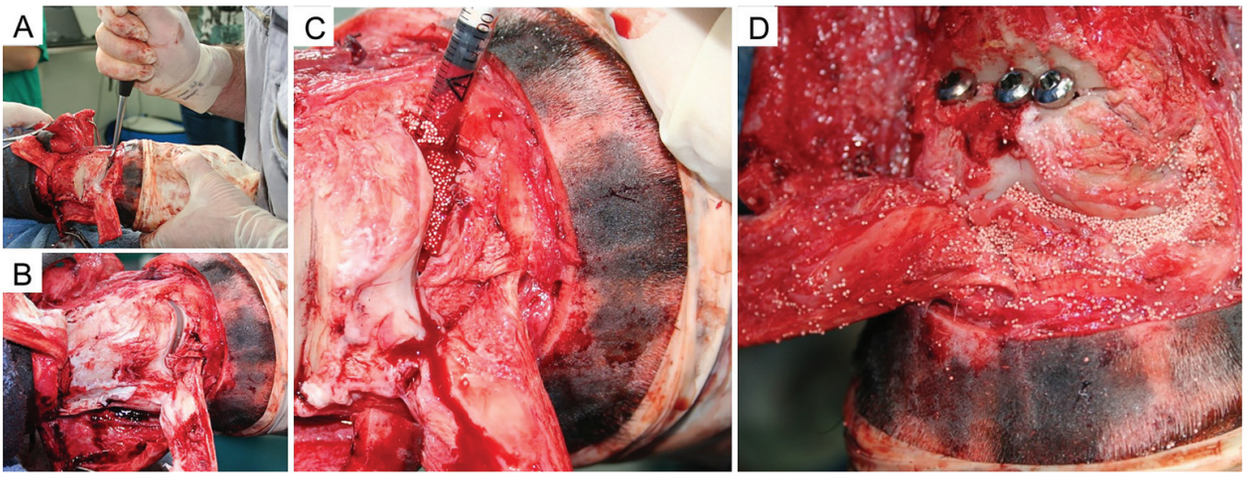

Figure 9. Proximal interphalangeal joint arthrodesis. Removing cartilage from proximal interphalangeal joint using a curette (A). A subluxation gap between the first and the second phalange at medial aspect of the joint (B). Applying with a syringe Bonelike® in proximal interphalangeal joint space (C). Three lag screws were placed from the first to the second phalange crossing the joint space (D).

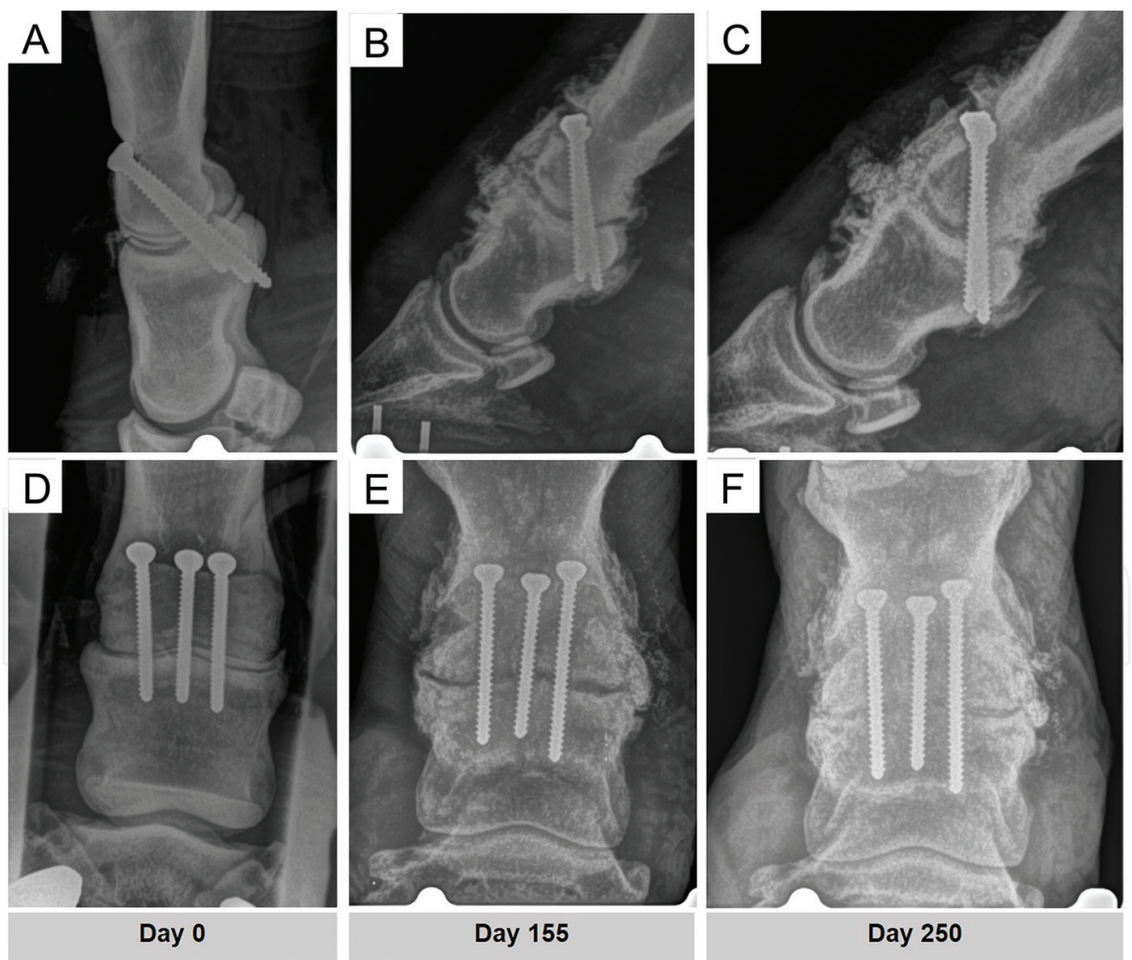

Figure 10. X-ray analysis follow-up of the proximal interphalangeal joint arthrodesis. The X-rays were taken at day 0 (pre-surgery), at day 155 and at day 250, with two projections. Lateral projection (A–C). Dorsoproximal projection (D–F).

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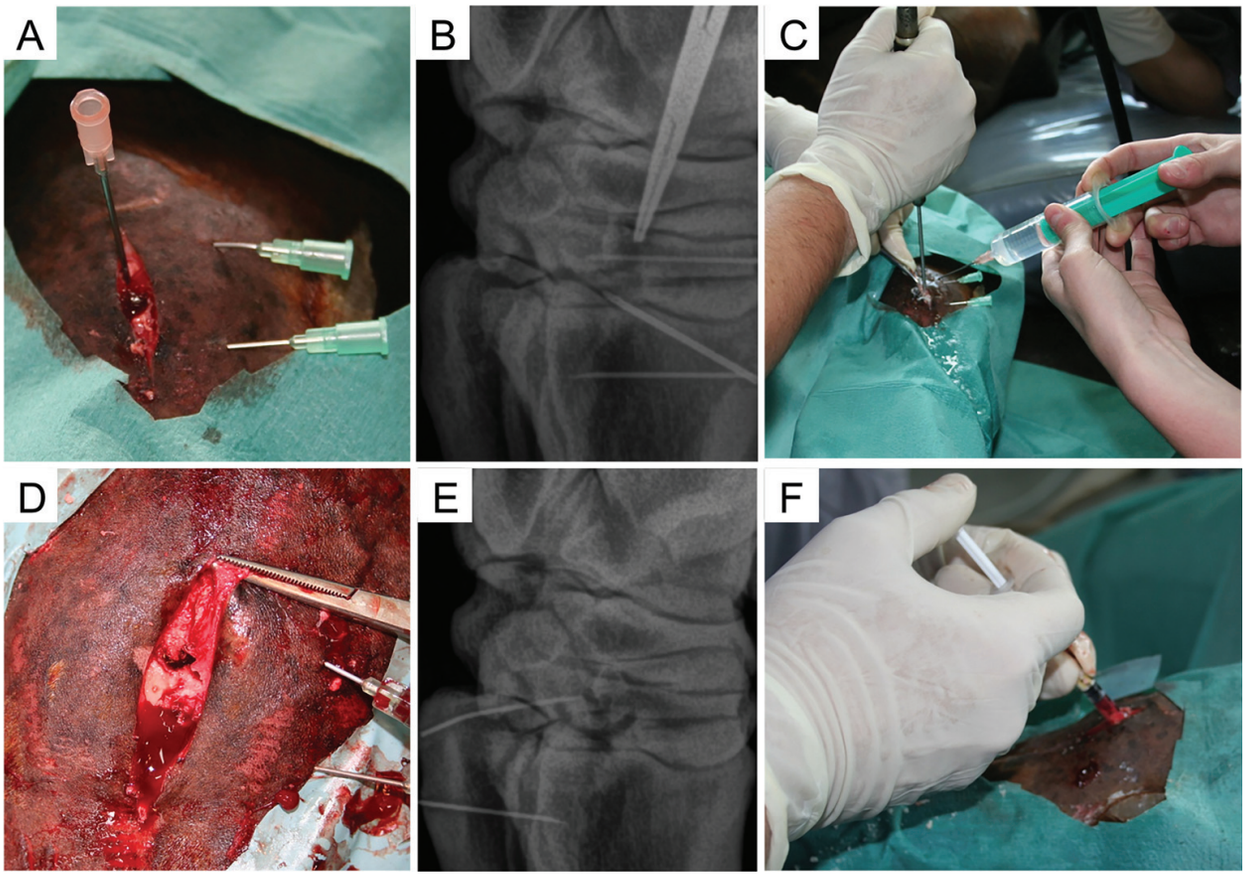

Figure 11. Arthrodesis of distal intertarsal joint together with tarsometatarsal joint. Needle is placed to identify the tarsometatarsal joint (A). Confirmation of correct position of the needle into joint space was made by X-ray (B). Create a hole with 3.2 drill bit in both joints, in three different directions using a single entry point, with a continuous flushing in order to minimize thermal damage (C) and remove any residual bone and cartilage (D). The hole created at the joint after drilling (E). Lateral X-ray of the tarsus showing the created hole (F). Hole filled with Bonelike®.

in the void space of the performed holes improved the biomechanical stability of the distal intertarsal and tarsometatarsal joint, and the bone bridging was accelerated, improving the joints' ankylosis. At the arthrodesis technique, it should be removed as much joint cartilage as possible to allow a greater bone-to-bone contact. But in this specific technique of the distal tarsal joint arthrodesis, as no additional surgical fixation is advised, the excessive drilling causes instability and severe pain [72]. It can be argued that the limited drilling of the distal tarsal joints involved in the three-drill-tract technique does not induce complete arthrodesis, but results in multiple focal areas of arthrodesis and the biomechanical stability of the distal tarsal joints are usually observed, and lameness is eliminated [73]. Using Bonelike® as a bone substitute that will fill the drilled paths, these focal areas of arthrodesis are improved and reinforced [68]. Arthrodesis using Bonelike® as a bone graft promotes bone fusion that permitted the horse to return to the athletic activity and improved the horse quality of life, decreasing the pain and increasing the joint stability. The Bonelike® application can enhance the bone production due to osteoinductive and osteoconductive proprieties, shortening the healing period after the arthrodesis and promoting the joint fusion in a shorter period [68, 74].

These three clinical cases were strongly evidenced that Bonelike® is an appropriate synthetic bone graft substitute with osteoconductive and osteoinductive properties to be used in surgical arthrodesis, as void space filler, associated or not with standard orthopaedic procedures of stabilization of the joints, in order to promote a faster bone fusion without any local or systemic adverse reaction. This procedure permits the horse to return to the athletic performance faster or, at minimum, improves the horse's quality of life, decreasing the pain and increasing the joint stability with positive clinical outcomes [68].

3.3. The use of synthetic bone grafts in ruminant clinical cases

Although the use of synthetic bone grafts in companion animals and horses is becoming a reality, its application in production animals is yet marginal.

Most of the surgery cases in large production animals (ruminants, mostly) are performed in the field settings, and the number of surgical cases referred to specialized veterinary centres is considerably small [75]. Constraints for orthopaedic surgery and bone grafts use in ruminants include the economic (cost of the treatment) and legal issues, the value of the individual in contrast to the group value and the size and weight of the animal [75, 76]. Nevertheless, the high genetic performance and value of some of these animals and the recent improvements in surgical management of production animals, concerning chemical restrain, pain management and surgical techniques, could be accompanied by the use of some biomaterials.

Fractures commonly occur in ruminants. Limbs, digits and skull fractures are often reported in bovine and small ruminants, often subsequent to trauma. The most common limb fractures occur especially in calves, as consequence to incorrect handling of dystocia or injuries due to falls on slippery floors in livestock facilities. Metacarpus and metatarsus fractures represent 50% of the limb fractures cases, tibia fractures represent 12% and radius and ulna almost 7%. Humerus fractures are rare and represent less than 5% of the cases. Still, fractures of the femur, of the pelvis and of the axial skeleton are more uncommon [75, 76].

The selection of the osteosynthesis procedure is influenced by the bone site of fracture, the degree and severity of soft tissue and neurovascular trauma of the status of the environment fractures (close or open), the patient temperament and the surgeon skills. The selected procedure must provide the patient the return to weight-bearing and normal mobility [75–77].

In many cases, it's advisable to do a prompt temporary fracture stabilization with external coaptation (splints or casts), avoiding additional trauma and clinical status worsening (preventing the closed fracture from becoming open or further fracture fragmentation and reducing eburnation of the fracture ends) prior to fracture fixation or during convalescence [75–77]. External coaptation is inadequate in oblique, spiral and comminuted fractures, and with extensive soft tissue trauma. In these cases, surgical procedures are advisable (internal or external fixation) [76].

In ruminants, the most common fractures' surgical procedures include external skeletal fixation (transfixation pin casts and external skeletal fixators) and internal fixation (intramedullary pinning, intramedullary interlocking nail and bone plates). The former procedure can be easily done in the field settings; it's less expensive and allows load bearing in the traumatized limb,

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and it's indicated in open fractures and wounds, but fracture reduction and reconstruction may fail and may not accomplish ideal fracture stabilization leading to non-union. The latter procedure, although more expensive as it requires specialized equipment and surgeon performance, allows more stability during the osteosynthesis process [76, 78, 79].

Autologous cancellous graft can be collected from the sternum, proximal tibia, proximal humerus and ilium. However, in cattle with chronic non-healing fractures, the lack of movement and the lack of alternating weight support, due to the strong lameness, lead to medullar atrophy, which limits the amount of cancellous bone graft that can be harvested from long bones. To perform the collection of a significant amount of cancellous bone graft from the sternum, general anaesthesia is advised, to avoid thorax trauma [78]. The use of synthetic bone grafts in ruminants' fractures with impaired bone repair mechanisms due to compromised vascular supply after severe trauma, with large long bone defect with septic non-union, infected open fractures, or in fixation failure, will promote and enhance bone healing process in order to restore the original bone structure and function.

The clinical case presented refers to a dwarf goat with sequence of a trauma event, resulting in a tibia open fracture, with soft tissue trauma (**Figure 12(A)** and **(B)**). The patient was 2 months into gestation, in risk of developing complications that could worsen the clinical situation. Surgical treatment, with internal fixation was considered as a first-choice treatment option. Also, it was of importance to restore normal weight-bearing function in a short period of time, as the gestation was close to the end. To stabilize the fracture, an intramedullary pin was applied, and the defect in the fracture ends was filled with Bonelike® spherical granules of 250–500 μm, mixed with autologous blood collected from the jugular vein during the surgery (**Figure 12(C)**).

On the follow-up, X-rays were performed at 2 (**Figure 13(A)**) and 4 (**Figure 13(B)**) weeks after the surgery; bone proliferation and bone fusion were noticed. The intramedullary pin was removed at 5 weeks after surgery (**Figure 13(C)**), presenting complete bone union and good ossification. The intramedullary pin was removed. The patient returned to its normal function. No local or systemic adverse reaction or rejection of the material during the healing process was observed.

Figure 12. The patient was attended for consultation. The X-ray image showed a spiral fracture in the distal third of tibial bone (A). After hair clipping an open wound was evident. An internal fixation was considered as a first-choice treatment option to avoid additional tissue trauma and further fracture stress (B). An intramedullary pin was applied, and the defect in the fracture ends was filled with Bonelike® spherical granules of 250–500 μm, mixed with autologous blood collected from the jugular vein (C).

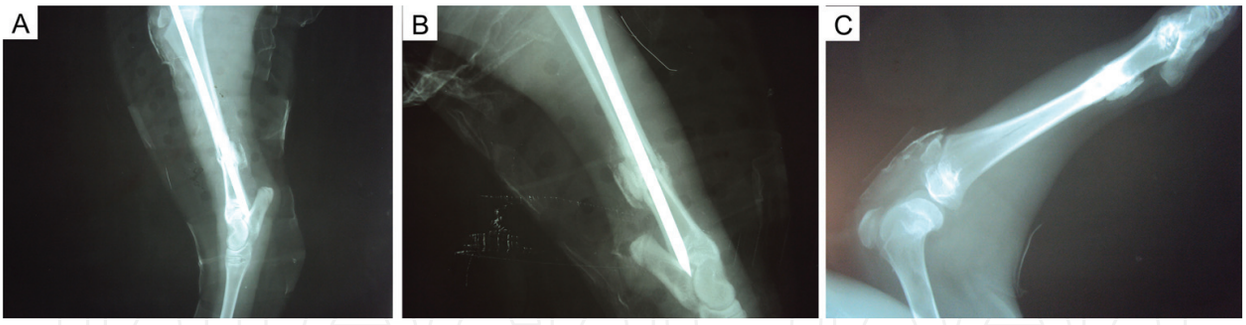

Figure 13. At 2 weeks after surgery, check-up and follow-up X-ray (A). At 4 weeks after surgery, a considerable callus was formed (B). At 5 weeks after surgery, the X-ray showed complete bone union and good ossification (C).

4. Conclusions

Although ceramic-based graft substitute materials and calcium phosphate ceramics such as hydroxyapatite, β-tricalcium phosphate and Bioglass® were used for a long time (since the 1970s in dentistry and 1980s in orthopaedics), its use alone or in combination with osteogenic or osteoinductive strategies still has a place in veterinary surgery. Macroporous granular forms with intrinsic osteoinductive properties could be a practical alternative to a customized 3D-printed scaffold or edges that allow filling of different shapes of bone defects as naturally occurs in the clinical cases. Another presentation of HA and TCP involved in a collagen membrane that resists to compression and could be cut with defects' size before the implantation is also available. Those synthetic bone substitutes offer an adequate alternative allowing the replacement of autologous cancellous bone grafts in management of fractures, vascular non-unions, noncritical-sized bone defects and arthrodesis. Nevertheless, basic surgical principals such as biomechanical stability, vascular preservation and infection control are still vital for providing an ideal environment for bone healing. However, when the local biology is compromised as previously mentioned, the bioceramics scaffold should be complemented with growth factors, cell-based therapies or a combination of those, in order to provide osteoinductive and osteogenic properties to increase the likelihood of bone healing. Experimental and clinical examinations are needed in veterinary surgery, as well as in human field to adequately compare the outcome of the novel treatment options and its combinations, establishing the most appropriate treatment protocols for each clinical presentation.

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References

[1] Griffon DJ. Fracture healing. In: Johnson AL, Houlton JEF, Vannini R, editors. AO Principles of Fracture Management in the dog and cat. New York: AO; 2005. pp. 72-97

[2] Brinker W, Piermattei D, Flo G. Fractures: Classification, Diagnosis and Treatment. Handbook of Small Animal Orthopedics & Fracture Repair; 4th Ed. St Louis, MO: Saunders - Elsevier. 2006. pp. 25-159

[3] Cross A. Fracture Biology and Biomechanics. Veterinary Surgery: Small Animal; 2012. pp. 565-571

[4] Perren S. Basic Aspects of Internal Fixation. Manual of Internal Fixation in Small Animals. editors. Brinker, W.O., Olmstead, M.L., Sumner-Smith, G., Prieur, W.D. (Eds.). Springer; 1998. pp. 1-94

[5] Innes J. Bone grafting in small animal orthopaedic surgery. In Practice. 2014;**36**(4):173-181

[6] Vertenten G, Gasthuys F, Cornelissen M, Schacht E, Vlaminck L. Enhancing bone healing and regeneration: Present and future perspectives in veterinary orthopaedics. Veterinary and Comparative Orthopaedics and Traumatology. 2010;**23**(3):153-162

[7] Ragetly G, Griffon D. The rationale behind novel bone grafting techniques in small animals. Veterinary and Comparative Orthopaedics and Traumatology. 2011;**24**(1):1-8

[8] Conway JD. Autograft and nonunions: Morbidity with intramedullary bone graft versus iliac crest bone graft. Orthopedic Clinics of North America. 2010;**41**(1):75-84; table of contents

[9] Blokhuis TJ, Termaat MF, den Boer FC, Patka P, Bakker FC, Haarman HJ. Properties of calcium phosphate ceramics in relation to their in vivo behavior. The Journal of Trauma. 2000;**48**(1):179-186

[10] Penwick RC, Mosier DA, Clark DM. Healing of canine autogenous cancellous bone graft donor sites. Veterinary Surgery. 1991;**20**(4):229-234

[11] Akagi H, Ochi H, Kannno N, Iwata M, Ichinohe T, Harada Y, et al. Clinical efficacy of autogenous cancellous bone and fibroblast growth factor 2 combined with frozen allografts in femoral nonunion fractures. Veterinary and Comparative Orthopaedics and Traumatology. 2013;**26**(2):123-129

[12] Hoffer MJ, Griffon DJ, Schaeffer DJ, Johnson AL, Thomas MW. Clinical applications of demineralized bone matrix: A retrospective and case-matched study of seventy-five dogs. Veterinary Surgery. 2008;**37**(7):639-647

[13] Southwood LL, Frisbie DD, Kawcak CE, McIlwraith CW. Delivery of growth factors using gene therapy to enhance bone healing. Veterinary Surgery. 2004;**33**(6):565-578

[14] García-Gareta E, Coathup MJ, Blunn GW. Osteoinduction of bone grafting materials for bone repair and regeneration. Bone. 2015;**81**:112-121

[15] Nandi S, Roy S, Mukherjee P, Kundu B, De D, Basu D. Orthopaedic applications of bone graft & graft substitutes: A review. Indian J Med Res. 2010 Jul;**132**:15-30

[16] Pearce AI, Richards RG, Milz S, Schneider E, Pearce SG. Animal models for implant biomaterial research in bone: A review. European Cells & Materials. 2007;**13**:1-10

[17] Martini L, Fini M, Giavaresi G, Giardino R. Sheep model in orthopedic research: A literature review. Comparative Medicine. 2001;**51**(4):292-299

[18] Nahid M, Bottenberg P. Importance of cell cultures in biocompatible dental materials research. Revue belge de medecine dentaire. 2003;**58**(3):189-196

[19] Lu J, Flautre B, Anselme K, Hardouin P, Gallur A, Descamps M, et al. Role of interconnections in porous bioceramics on bone recolonization in vitro and in vivo. Journal of Materials Science: Materials in Medicine. 1999;**10**(2):111-120

[20] Boyd D, Carroll G, Towler M, Freeman C, Farthing P, Brook I. Preliminary investigation of novel bone graft substitutes based on strontium–calcium–zinc–silicate glasses. Journal of Materials Science: Materials in Medicine. 2009;**20**(1):413-420

[21] Atayde LM, Cortez PP, Pereira T, Armada-da-Silva P, Afonso A, Lopes MA, et al. A new sheep model with computing automatized analysis to evaluate the in vivo biomaterial's

behavior on bone tissue regeneration. Journal of Materials Science: Materials in Medicine. 2014;**25**(8):1885-1901

[22] Schopper C, Ziya-Ghazvini F, Goriwoda W, Moser D, Wanschitz F, Spassova E, et al. HA/TCP compounding of a porous CaP biomaterial improves bone formation and scaffold degradation—A long-term histological study. Journal of Biomedical Materials Research Part B, Applied Biomaterials. 2005;**74**(1):458-467

[23] Anderson ML, Dhert WJ, de Bruijn JD, Dalmeijer RA, Leenders H, van Blitterswijk CA, Verbout AJ. Critical size defect in the goat's os ilium. A model to evaluate bone grafts and substitutes. Clinical Orthopaedics and Related Research. 1999;(364):231-239

[24] Salgado AJ, Coutinho OP, Reis RL. Bone tissue engineering: State of the art and future trends. Macromolecular Bioscience. 2004;**4**(8):743-765

[25] Lansdowne JL, Devine D, Eberli U, Emans P, Welting TJ, Odekerken JC, et al. Characterization of an ovine bilateral critical sized bone defect iliac wing model to examine treatment modalities based on bone tissue engineering. Biomed Research International. 2014;**2014**:250958

[26] Hollinger JO, Kleinschmidt JC. The critical size defect as an experimental model to test bone repair materials. Journal of Craniofacial Surgery. 1990;**1**(1):60-68

[27] Bosch C, Melsen B, Vargervik K. Importance of the critical-size bone defect in testing bone-regenerating materials. Journal of Craniofacial Surgery. 1998;**9**(4):310-316

[28] Lindsey RW, Gugala Z, Milne E, Sun M, Gannon FH, Latta LL. The efficacy of cylindrical titanium mesh cage for the reconstruction of a critical-size canine segmental femoral diaphyseal defect. Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society. 2006;**24**(7):1438-1453

[29] Le Guehennec L, Goyenvalle E, Aguado E, Houchmand-Cuny M, Enkel B, Pilet P, et al. Small, animal models for testing macroporous ceramic bone substitutes. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2005;**72**(1):69-78

[30] Reichert JC, Saifzadeh S, Wullschleger ME, Epari DR, Schutz MA, Duda GN, et al. The challenge of establishing preclinical models for segmental bone defect research. Biomaterials. 2009;**30**(12):2149-2163

[31] Schmitz JP, Hollinger JO. The critical size defect as an experimental model for craniomandibulofacial nonunions. Clinical Orthopaedics and Related Research. 1986;(205):299-308

[32] Li Y, Chen S-K, Li L, Qin L, Wang X-L, Lai Y-X. Bone defect animal models for testing efficacy of bone substitute biomaterials. Journal of Orthopaedic Translation. 2015;**3**(3):95-104

[33] Cheng L, Wang T, Zhu J, Cai P. Osteoinduction of calcium phosphate ceramics in four kinds of animals for 1 year: Dog, rabbit, rat, and mouse. Transplantation Proceedings. 2016;**48**(4):1309-1314

[34] Dorea H, McLaughlin R, Cantwell H, Read R, Armbrust L, Pool R, et al. Evaluation of healing in feline femoral defects filled with cancellous autograft, cancellous allograft or Bioglass. VCOT Archive. 2005;**18**(3):157-168

[35] Izumisawa Y, Reona A, Miyoshi K, Maehara S, Wakaiki S, Kushiro T, et al. Axial correction of pes varus by transverse-opening wedge osteotomy and T-plate fixation with beta-tricalcium phosphate (beta-TCP) transplantation in dachshunds. Journal of Veterinary Medical Science. 2005;**67**(4):437-440

[36] Hauschild G, Merten H-A, Bader A, Uhr G, Deivick A, Meyer-Lindenberg A, et al. Bioartificial bone grafting: Tarsal joint fusion in a dog using a bioartificial composite bone graft consisting of beta-tricalciumphosphate and platelet rich plasma—A case report. VCOT Archive. 2005;**18**(1):52-54

[37] Franch J, Diaz-Bertrana C, Lafuente P, Fontecha P, Durall I. Beta-tricalcium phosphate as a synthetic cancellous bone graft in veterinary orthopaedics: A retrospective study of 13 clinical cases. Veterinary and Comparative Orthopaedics and Traumatology. 2006;**19** (4):196-204

[38] Rabillard M, Grand J-G, Dalibert E, Fellah B, Gauthier O, Niebauer G. Effects of autologous platelet rich plasma gel and calcium phosphate biomaterials on bone healing in an ulnar ostectomy model in dogs. Veterinary and Comparative Orthopaedics and Traumatology. 2009;**22**(6):460-466

[39] Johnson KD, August A, Sciadini MF, Smith C. Evaluation of ground cortical autograft as a bone graft material in a new canine bilateral segmental long bone defect model. Journal of Orthopaedic Trauma. 1996;**10**(1):28-36

[40] Degna MT, Ehrhart N, Feretti A, Buracco P. Bone transport osteogenesis for limb salvage following resection of primary bone tumors: Experience with six cases (1991–1996). VCOT Archive. 2000;**13**(1):18-22

[41] Segal U, Shani J. Surgical management of large segmental femoral and radial bone defects in a dog. Veterinary and Comparative Orthopaedics and Traumatology. 2010;**23**(1):66-70

[42] Zoi S, Papadimitriou S, Galatos A, Prassinos N, Psalla D, Dalstra M, et al. Influence of a titanium mesh on the management of segmental long bone defects. Veterinary and Comparative Orthopaedics and Traumatology. 2015;**28**(6):417-424

[43] Petazzoni M. Contralateral bone widening and transfer for limb sparing in a cat. Veterinary and Comparative Orthopaedics and Traumatology. 2016;**29**(2):174-180

[44] Kirker-Head CA, Boudrieau RJ, Kraus KH. Use of bone morphogenetic proteins for augmentation of bone regeneration. Journal of the American Veterinary Medical Association. 2007;**231**(7):1039-1055

[45] Franch J. A preliminary clinical experience in combination with rhBMP-2 in a distal atrophic non-union. 18th ESVOT Congress. London; 2016. pp. 120-121

[46] Massie AM, Kapatkin AS, Fuller MC, Verstraete FJ, Arzi B. Outcome of nonunion fractures in dogs treated with fixation, compression resistant matrix, and recombinant human bone morphogenetic protein-2. Veterinary and Comparative Orthopaedics and Traumatology. 2017;**30**(2):153-159

[47] Boudrieau RJ, Mitchell SL, Seeherman H. Mandibular reconstruction of a partial hemimandibulectomy in a dog with severe malocclusion. Veterinary Surgery. 2004;**33**(2):119-130

[48] Verstraete FJM, Arzi B, Huey DJ, Cissell DD, Athanasiou KA. Regenerating mandibular bone using rhBMP-2: Part 2—Treatment of chronic, defect non-union fractures. Veterinary Surgery. 2015;**44**(4):410-416

[49] Arzi B, Verstraete FJM, Huey DJ, Cissell DD, Athanasiou KA. Regenerating mandibular bone using rhBMP-2: Part 1—Immediate reconstruction of segmental mandibulectomies. Veterinary Surgery. 2015;**44**(4):403-409

[50] Atayde LM, Cortez PP, Afonso A, Santos M, Mauricio AC, Santos JD. Morphology effect of bioglass-reinforced hydroxyapatite (Bonelike®) on osteoregeneration. Journal of Biomedical Materials Research Part B, Applied Biomaterials. 2015;**103**(2):292-304

[51] Gutierres M, Dias A, Lopes M, Hussain NS, Cabral A, Almeida L, et al. Opening wedge high tibial osteotomy using 3D biomodelling Bonelike® macroporous structures: Case report. Journal of Materials Science: Materials in Medicine. 2007;**18**(12):2377-2382

[52] Cortez PP, Silva MA, Santos M, Armada-da-Silva P, Afonso A, Lopes MA, et al. A glass-reinforced hydroxyapatite and surgical-grade calcium sulfate for bone regeneration: In vivo biological behavior in a sheep model. Journal of Biomaterials Applications. 2011(2):201-217

[53] Cortez PP, Atayde LM, Silva MA, Armada-da-Silva P, Fernandes MH, Afonso A, et al. Characterization and preliminary in vivo evaluation of a novel modified hydroxyapatite produced by extrusion and spheronization techniques. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2011;**99B**(1):170-179

[54] Pinto PO, Campos JM, Caseiro AR, Pereira T, Santos JD, Atayde LM, Maurício AC. Use of a Macroporous Glass-Reinforced Hydroxyapatite Synthetic Bone Substitute in Treatment of Long-Bone Atrophic Non-Union Fracture- Two Clinical Cases in Dogs. London: ESVOT; 2016. pp. 448-449

[55] Schwarz N, Schlag G, Thurnher M, Eschberger J, Dinges HP, Redl H. Fresh autogeneic, frozen allogeneic, and decalcified allogeneic bone grafts in dogs. The Journal of Bone and Joint Surgery British. 1991;**73**(5):787-790

[56] Dowdle S, Spotswood T, Lambrechts N, Duncan N. Aneurysmal bone cyst in the distal radius of a dog: Diagnostic imaging and surgical treatment. Veterinary and Comparative Orthopaedics and Traumatology. 2003;**16**(2):116-121

[57] Duval J, Chambers J, Newell S. Surgical treatment of an aneurysmal bone cyst in a dog. Veterinary and Comparative Orthopaedics and Traumatology: VCOT. 1995;**8**:213-217

[58] Kim CS, Choi SH, Cho KS, Chai JK, Wikesjö UM, Kim CK. Periodontal healing in one-wall intra-bony defects in dogs following implantation of autogenous bone or a coral-derived biomaterial. Journal of Clinical Periodontology. 2005;**32**(6):583-589

[59] Kerwin SC, Lewis DD, Elkins AD, Oliver J, Pechman R, Mccarthy RJ, et al. Deep-frozen allogeneic cancellous bone grafts in 10 dogs: A case series. Veterinary Surgery. 1996;**25** (1):18-28

[60] Lesser AS. Arthrodesis. In: Slatter D, editor. Text Book of Small Animal Surgery. Third ed. Saunders; 2002. pp. 2170-2190

[61] Zubrod CJ, Schneider RK. Arthrodesis techniques in horses. Veterinary Clinics of North America Equine Practice. 2005;**21**(3):691-711, vii

[62] Schoenhaus HD, Lam S, Treaster A, Troiano M. Use of a small bilateral external fixator for ankle fusion. Journal of Foot and Ankle Surgery. 2009;**48**(1):89-92

[63] Sorrel Langley-Hobbs MA, editor. Arthrodesis principles. 3 rd World Veterinary Orthopaedic Congress, ESVOT-VOS 15th ESVOT Congress. Bologna (Italy); 2010

[64] Caron J, Fretz P, Bailey J, Barber S. Proximal interphalangeal arthrodesis in the horse a retrospective study and a modified screw technique. Veterinary Surgery. 1990;**19**(3):196-202

[65] Knox P, Watkins J. Proximal interphalangeal joint arthrodesis using a combination plate-screw technique in 53 horses (1994–2003). Equine Veterinary Journal. 2006;**38**(6):538-542

[66] MacLellan KN, Crawford WH, MacDonald DG. Proximal interphalangeal joint arthrodesis in 34 horses using two parallel 5.5-mm cortical bone screws. Veterinary Surgery. 2001;**30**(5):454-459

[67] Kidd J, Barr A. Flexural deformities in foals. Equine Veterinary Education. 2002;**14**(6):311-321

[68] Atayde LM. Substitutos ósseos para regeneração do tecido ósseo: estudos in vivo e futuras aplicações clínicas e medicina veterinária; 2014

[69] Adams SB, Santschi EM, editors. Management of congenital and acquired flexural limb deformities. Proceedings of the American Association of Equine Practitioners. 2000;**46**: 117-125

[70] Auer JA. Diagnosis and treatment of flexural deformities in foals. Clinical Techniques in Equine Practice. 2006;**5**(4):282-295

[71] Whitehair KJ, Adams SB, Toombs JP, Parker JE, Prostredny JM, Whitehair JG, et al. Arthrodesis for congenital flexural deformity of the metacarpophalangeal and metatarsophalangeal joints. Veterinary Surgery. 1992;**21**(3):228-233

[72] Auer JA. Arthrodesis techniques. In: Stick Aa, editor. Equine Surgery. 1. 3rd ed. Philadelphia: Saunders; 2006. pp. 1073-1086

[73] Dechant JE, Baxter GM, Southwood LL, Crawford WH, Jackman BR, Stashak TS, et al. Use of a three-drill-tract technique for arthrodesis of the distal tarsal joints in horses with distal tarsal osteoarthritis: 54 cases (1990-1999). Journal of the American Veterinary Medical Association. 2003;**223**(12):1800-1805

[74] Lobato JV, Hussain NS, Botelho CM, Maurício AC, Afonso A, Ali N, et al. Assessment of Bonelike® graft with a resorbable matrix using an animal model. Thin Solid Films. 2006;**515**(1):362-367

[75] Anderson DE, Jean GS. Management of fractures in field settings. Veterinary Clinics of North America: Food Animal Practice. 2008;**24**(3):567-582

[76] Pentecost R, Niehaus AJ, Anderson DE. Surgical management of fractures and tendons. Veterinary Clinics of North America: Food Animal Practice. 2016;**32**(3):797-811

[77] Nuss K. Plates, pins, and interlocking nails. Veterinary Clinics of North America: Food Animal Practice. 2014;**30**(1):91-126

[78] Weaver AD, Jean GS, Steiner A. Bovine Surgery and Lameness. John Wiley & Sons; 2013

[79] Vogel SR, Anderson DE. External skeletal fixation of fractures in cattle. Veterinary Clinics of North America: Food Animal Practice. 2014;**30**(1):127-142

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