Animal model for bone implant in swine

https://doi.org/10.56238/uniknowindevolp-136

Marco Antonio Schueda
Professor of the Faculty of Medicine of the University of Contestado
E-mail: schueda.sc@gmail.com

Thiago Fuchs
Professor of the Faculty of Veterinary Medicine of the University of Contestado
E-mail: thiago.fuchs@professor.unc.br

Welington Martins Belo
Graduating from the 8th phase of the Faculty of Medicine of the University of Contestado
E-mail: welington.belo@aluno.unc.br

Lara Thaís Marcon
Graduating student of the 6th phase of the Faculty of Medicine of the University of Contestado
E-mail: lara.marcon@aluno.unc.br

Leide Daiana Bay
Graduating student of the 6th phase of the Faculty of Veterinary Medicine of the University of Contestado
E-mail: leide.bay@aluno.unc.br

Fernanda Heidemann
Graduating student of the 6th phase of the Faculty of Veterinary Medicine of the University of Contestado
E-mail: fernanda.heidemann@aluno.unc.br

ABSTRACT
Objective: The main purpose of this study was to develop an Animal Model that could accommodate evaluation experiments for cortico-spongy implants in the areas of orthopedics, dentistry, and neurology. Methodology: On the anteromedial surface of the proximal third of the tibia of pigs, we have a cortico-spongy area that is basically subcutaneous. This region proved to be ideal for this purpose. Results and discussions: The pig is already a well-known animal for testing biomaterials in bones because its bone regeneration rate (1.2 and 1.5 mm/d) is comparable to that of humans (1.0 and 1.5 mm/d) Conclusion: The Animal Model was formatted, which proved to be simple and reproducible.

Keywords: Porcine Animal Model, Cortical Spongy Bone, Proximal Tibia.

1 INTRODUCTION

With the evolution of science and technology, especially in the field of medicine, the use of Animal Models for the evolution of techniques and treatments have become of paramount importance. Galen (129-210 A.D.), forerunner of experimental medical research with the use of animals inspired adherents to this plan of study, but it was Claude Bernard in 1865 who launched the principles of its use in the work "Introduction to the Study of Experimental Medicine" establishing the rules and principles for such. Since then, the significance of the use of animal models has gained greater attention and relevance1.

In orthopedics, an anatomy with greater proximity to the human is necessary, in addition to the similar pathophysiological and histological composition to be able to present relevant results2.

Several animal test models, such as rats/mice3,4,5, rabbits3,6,7, dogs3,8,9, sheep3,10,11, goats3,12,13 and pigs3,14,15, were developed to simulate environment and physical conditions by testing the biocompatibility of substitute biomaterials for human bones "in vivo". In order to simulate various orthopedic situations, many sites of defects were explored, such as calvary3,16,17, femur/tibia3,18,19 and ulna3,20,21,22.

Factors should be considered when selecting a specific animal species as a test model. First, the animal model chosen must clearly demonstrate significant physiological and pathophysiological analogies compared to humans. Secondly, it should evaluate whether it is possible to operate and observe a multiplicity of study objects after surgery over a period of time23. Other selection criteria include acquisition and care costs, availability of the animal, acceptability by society, tolerance to captivity and ease of housing24. According to the international standard, we should also consider the size of the implant test specimens, number of implants per animal, intended duration of the test and possible differences between species when correlated with biological responses25.

In the present study, pigs were preferred to be used as anatomical models. This choice was initially due to the greater morphological/anatomical similarity with man, in addition to the ease of releasing them for in vivo study. Followed by the choice of pigs as an animal model, the need for anatomical regions whose histology presented cortico-spongy regions was specified. Such histology is present in metaphyses of long bones, such as the femur and tibia. We limited the study to the tibia because it has a triangular shape and in the anteromedial region of its proximal third is basically subcutaneous, thus facilitating its approach.

It will be presented in this work a new procedure that will facilitate the evaluation of biocompatibility and recovery after cortico-spongy implants in Medicine and Veterinary Medicine in the specialties of Orthopedics, Traumatology, Dentistry and Neurology.

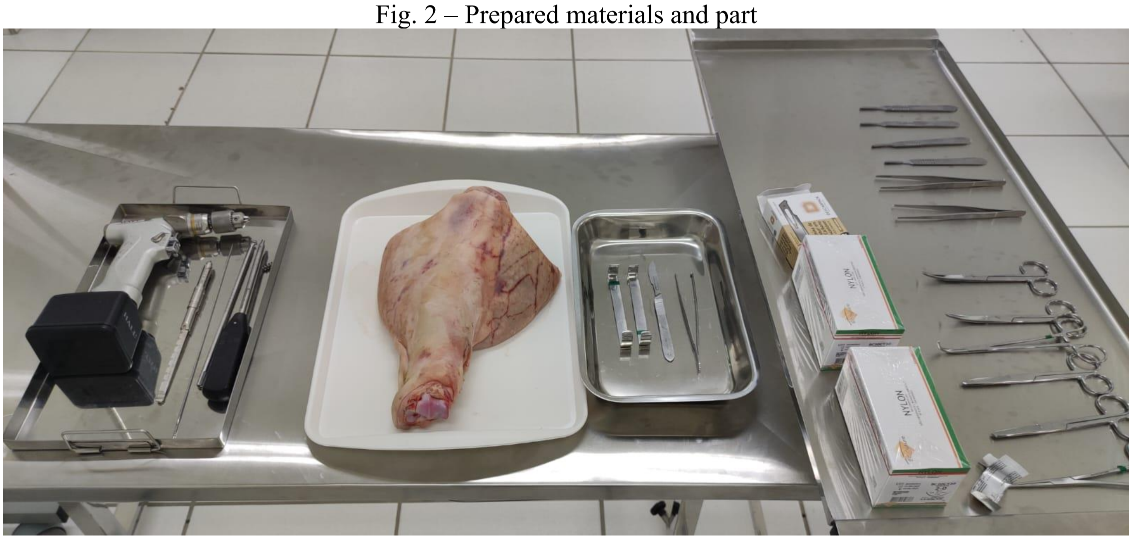
2 MATERIAL AND METHODS

Study carried out at the Veterinary Surgical Center of the Mafra Campus of UNC – Fundação Universidade do Contestado (Figures 1 A and 1 B)

Fig. 1 A – UNC Veterinary Surgical Center (Campus Mafra - SC)
Fig. 1 B – Procedure Room with specific lighting, instrumentation and anesthesia equipment.

Preparation and arrangement of materials and surgical specimen (Figure 2)

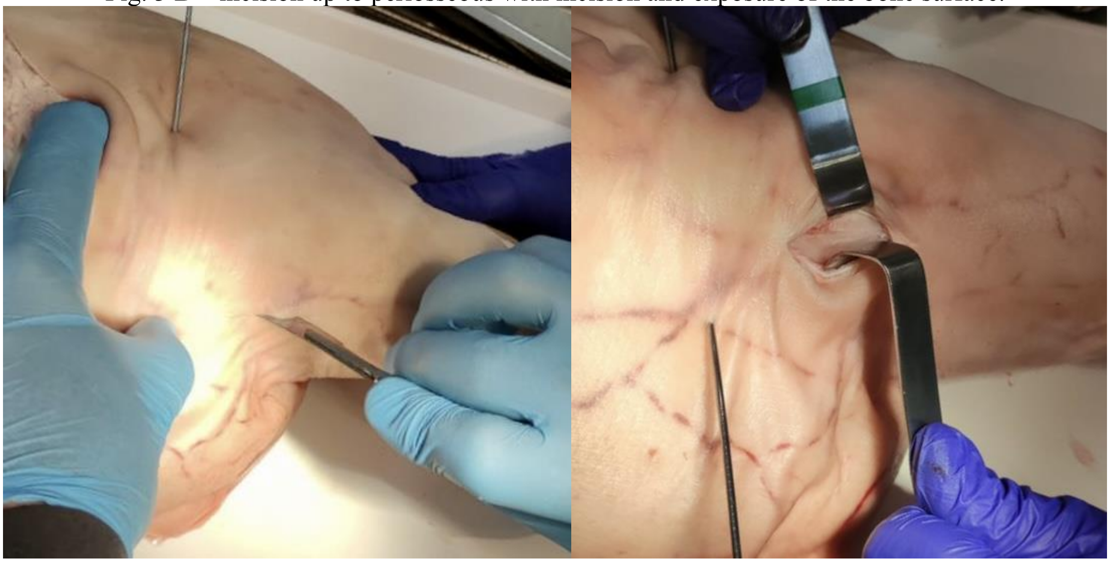
Fig. 2 – Prepared materials and part



After localization of the knee joint with Kirschner 2.0 thread, the anteromedial surface of the proximal tibia is accessed with a 3.5 cm incision with lamina number 23 up to the periosseous. (Figures 3 A and 3 B)

Fig. 3 A – After passage of the Kirschner Wire in the knee joint, an incision is made on the anteromedial surface of the proximal third of the tibia with 3.5 cm.

Fig. 3 B – incision up to periosseous with incision and exposure of the bone surface.



As a guide we used Kirschner wire 1.5 and then drilled with cannulated drill of 7 mm. (Figures 4 A and 4 B)

Fig. 4 A – Kirschner 2.0 guidewire perforation on the anteromedial tibial surface

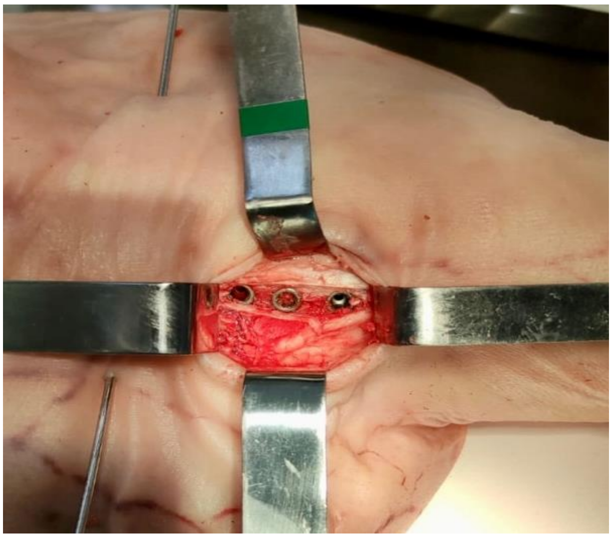
Fig. 4 B – Following the guide wire, drill 20 mm deep with 6 mm drill.

Following the guide wire, the bone screw of 7 mm x 20 mm is inserted, turning until it aligns with the cortical surface of the tibia. (Figures 5 A and 5 B)

Fig. 5 A – 70X20 mm implant is screwed following guide wire
Fig. 5 B – Until it aligns with the cortical surface of the Tibia

The procedure is repeated at 25 mm from the center of the first wire and at 50 mm by fixing two more screws. (Figures 6)

Fig. 6 – Fixation of the three bone interference screws on the anteromedial surface of the proximal third of the tibia.

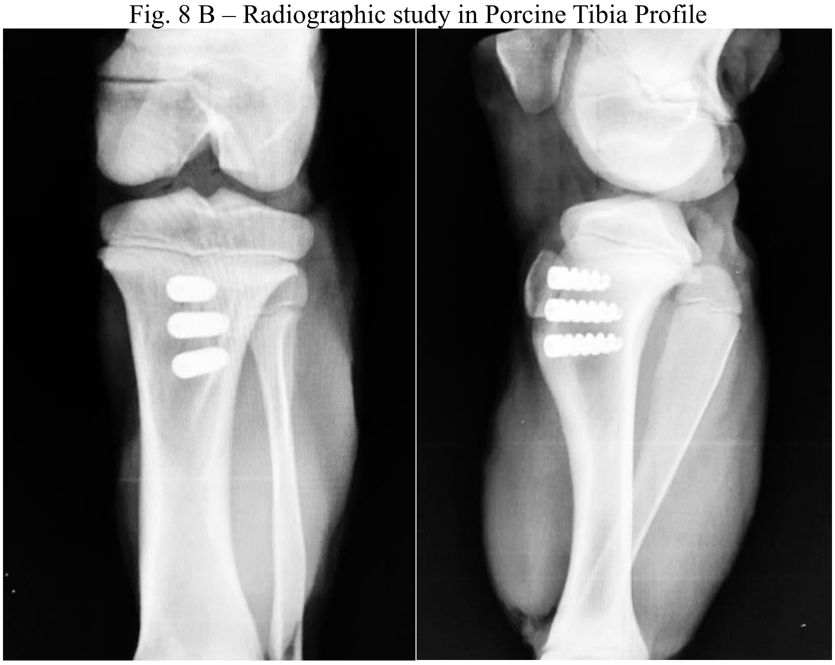


After fixation of the screws, the periosteum is sutured, the intra-articular thread and skin suture are removed. (Figures 7 A and 7 B)

Fig. 7 A – Periosteum suture
Fig. 7 B – Skin suture

A post-procedure radiographic study was performed to visualize the positioning of the implants. (Figures 8 A in Antero Posterior and 8 B in Profile)

Fig. 8 A – Radiographic study in AP (Antero Posterior) of the swine tibia
Fig. 8 B – Radiographic study in Porcine Tibia Profile



3 RESULTS, DISCUSSIONS AND THEORETICAL FRAMEWORK

Pigs are considered close representative models about bone anatomy, morphology, healing capacity, remodeling, mineral density and concentration26,27. Similarities were found in the diameter of the cross-section of the femur and in the area between humans and pigs28. Pigs have a lamellar bone structure like that of humans29. However, pigs have a denser trabecular network, considered intricate. They are difficult to handle, noisy and aggressive; therefore, pigs are often neglected in favor of more receptive species, such as sheep and goats30,31. In addition, the length of the tibias and femurs in pigs is relatively small, which cannot meet the special needs of human implants. The pig was the animal chosen for critical size defect models to test bone substitute biomaterials because its bone regeneration rate (1.2 and 1.5 mm/d) is comparable to that of humans (1.0 and 1.5 mm/d)22.

Commercial pigs are generally considered undesirable for orthopedic research because of their high growth rates and body weight. It should be noted that, the development of mini-pigs and micropigs has overcome this problem to some extent. However, in our region, it is easy to obtain and manage these animals, when compared to the others, making the application of this Animal Model much easier.

4 CONCLUSION

It was possible to format the Animal Model in pigs for spongy cortico implants of simple and reproducible execution.

REFERENCES

Rebollo R. A.; O legado hipocrático e sua fortuna no período greco-romano: de Cós a Galeno. Scientiae Studia [online]. 2006, v. 4, n. 1 [Acessado 26 Novembro 2022] , pp. 45-81.

Fagundes D.J. e Taha M. O.: Modelo animal de doença: critérios de escolha e espécies de animais de uso corrente. Acta Cirúrgica Brasileira [online]. 2004, v. 19, n. 1.

Ye L., Shu-Kui C., Long L., Ling Q., Xin-Luan W., Yu-Xiao L.; Bone defect animal models for testing efficacy of bone substitute biomaterials. review article Journal of Orthopaedic Translation (2015) 3, 95e104

Zwingenberger S, Niederlohmann E, Vater C, Rammelt S, Matthys R, Bernhardt R, et al. Establishment of a femoral critical-size bone defect model in immunodeficient mice. J Surg Res 2013;181:e7e14.

Bateman JP, Safadi FF, Susin C, Wikesjo UM. Exploratory study on the effect of osteoactivin on bone formation in the rat critical-size calvarial defect model. J Periodontal Res 2012;47:243e7.

Zhang X, Cai Q, Liu H, Heng BC, Peng H, Song Y, et al. Osteoconductive effectiveness of bone graft derived from antler cancellous bone: an experimental study in the rabbit mandible defect model. Int J Oral Maxillofac Surg 2012;41: 1330e7.

Schneider G, Blechschmidt K, Linde D, Litschko P, Korbs T, Beleites E. Bone regeneration with glass ceramic implants and calcium phosphate cements in a rabbit cranial defect model. J Mater Sci Mater Med 2010;21:2853e9.

Yano K, Namikawa T, Uemura T, Hoshino M, Wakitani S, Takaoka K, et al. Regenerative repair of bone defects with osteoinductive hydroxyapatite fabricated to match the defect and implanted with combined use of computer-aided design, computer-aided manufacturing, and computer- assisted surgery systems: a feasibility study in a canine model. J Orthop Sci 2012;17:484e9.

Takigami H, Kumagai K, Latson L, Togawa D, Bauer T, Powell K, et al. Bone formation following OP-1 implanta- tion is improved by addition of autogenous bone marrow cells in a canine femur defect model. J Orthop Res 2007; 25:1333e42.

Yang HL, Zhu XS, Chen L, Chen CM, Mangham DC, Coulton LA, et al. Bone healing response to a synthetic calcium sulfate/beta-tricalcium phosphate graft material in a sheep vertebral body defect model. J Biomed Mater Res B Appl Biomater 2012;100:1911e21.

Reichert JC, Epari DR, Wullschleger ME, Saifzadeh S, Steck R, Lienau J, et al. Establishment of a preclinical ovine model for tibial segmental bone defect repair by applying bone tissue engineering strategies. Tissue Eng Part B Rev 2010;16: 93e104.

Lippens E, Vertenten G, Girones J, Declercq H, Saunders J, Luyten J, et al. Evaluation of bone regeneration with an injectable, in situ polymerizable Pluronic F127 hydrogel derivative combined with autologous mesenchymal stem cells in a goat tibia defect model. Tissue Eng Part A 2010;16: 617e27.

Yu D, Li Q, Mu X, Chang T, Xiong Z. Bone regeneration of critical calvarial defect in goat model by PLGA/TCP/rhBMP-2 scaffolds prepared by low-temperature rapid-prototyping technology. Int J Oral MaxillofacSurg 2008;37:929e34.

Wehrhan F, Amann K, Molenberg A, Lutz R, Neukam FW, Schlegel KA. PEG matrix enables cell-mediated local BMP-2 gene delivery and increased bone formation in a porcine critical size defect model of craniofacial bone regeneration. Clin Oral Implants Res 2012;23:805e13.

Springer IN, Acil Y, Kuchenbecker S, Bolte H, Warnke PH, Abboud M, et al. Bone graft versus BMP-7 in a critical size defectdcranioplasty in a growing infant model. Bone 2005; 37:563e9.

Rahman CV, Ben-David D, Dhillon A, Kuhn G, Gould TW, Muller R, et al. Controlled release of BMP-2 from a sintered polymer scaffold enhances bone repair in a mouse calvarial defect model. J Tissue Eng Regen Med 2014;8:59e66.

Das A, Tanner S, Barker DA, Green D, Botchwey EA. Delivery of S1P receptor-targeted drugs via biodegradable polymer scaffolds enhances bone regeneration in a critical size cra- nial defect. J Biomed Mater Res A 2014;102:1210e8.

Li R, Nauth A, Li C, Qamirani E, Atesok K, Schemitsch EH. Expression of VEGF gene isoforms in a rat segmental bone defect model treated with EPCs. J Orthop Trauma 2012;26:689e92.

Cheng C, Alt V, Dimitrakopoulou-Strauss A, Pan L, Thormann U, Schnettler R, et al. Evaluation of new bone formation in normal and osteoporotic rats with a 3-mm femur defect: functional assessment with dynamic PET-CT (dPET- CT) using 2-deoxy-2-[(18)F]fluoro-D-glucose ((18)F-FDG) and (18)F-fluoride. Mol Imaging Biol 2013;15:336e44.

Mohan BG, Shenoy SJ, Babu SS, Varma HK, John A. Strontium calcium phosphate for the repair of leporine (Oryctolagus cuniculus) ulna segmental defect. J Biomed Mater Res A 2013;101:261e71.

Kim A, Kim DH, Song HR, Kang WH, Kim HJ, Lim HC, et al. Repair of rabbit ulna segmental bone defect using freshly isolated adipose-derived stromal vascular fraction. Cyto- therapy 2012;14:296e305.

Schlegel KA, Lang FJ, Donath K, Kulow JT, Wiltfang J. The monocortical critical size bone defect as an alternative experimental model in testing bone substitute materials. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:7e13.

Liebschner MA. Biomechanical considerations of animal models used in tissue engineering of bone. Biomaterials 2004;25:1697e714.

Pearce AI, Richards RG, Milz S, Schneider E, Pearce SG. An- imal models for implant biomaterial research in bone: a re- view. Eur Cell Mater 2007;13:1e10.

Upman PJ. ISO 10993-6: test for local effects after implan- tation. BONEZone 2006;5:50e2.

Thorwarth M, Schultze-Mosgau S, Kessler P, Wiltfang J, Schlegel KA. Bone regeneration in osseous defects using a resorbable nanoparticular hydroxyapatite. J Oral Maxillofac Surg 2005;63:1626e33.

Aerssens J, Boonen S, Lowet G, Dequeker J. Interspecies differences in bone composition, density, and quality: po- tential implications for in vivobone research. Endocrinology 1998;139:663e70.

Raab DM, Crenshaw TD, Kimmel DB, Smith EL. A histo- morphometric study of cortical bone activity during increased weight-bearing exercise. J Bone Min Res 1991;6: 741e9.

Mosekilde L, Kragstrup J, Richards A. Compressive strength, ash weight, and volume of vertebral trabecular bone in experi- mental fluorosis in pigs. Calcif Tissue Int 1987;40:318e22.

Mosekilde L, Weisbrode SE, Safron JA, Stills HF, Jankowsky ML, Ebert DC, et al. Calcium-restricted ovariec- tomized Sinclair S-1 minipigs: an animal model of osteopenia and trabecular plate perforation. Bone 1993;14:379e82.

Swindle MM, Smith AC, Hepburn BJ. Swine as models in experimental surgery. J Invest Surg 1988;1:65e79.