NEW ALOPLASTICS BIOMATERIALS FOR BONE REGENERATION: *IN VIVO* STUDY

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INTRODUCTION

The need to obtain bone substitutes capable of assisting in the regeneration of large defects drives research towards the development of new synthetic biomaterials [1, 2]

OBJECTIVE

Evaluate the biological behavior of two experimental bioceramics (AA; U) [3] in the regeneration of critical bone defects.

MATERIALS AND METHODS

Biomaterials AA and U are composed primarily by osteogenic compounds like monetite doped with zinc, hidroxyapatite and silica gel (SG), in different amounts (Table 1) with particles between 0.25 to 1.0 mm in size, were implanted in similar amounts in critical size defect (8.5 mm Ø) made in calvarias of *Rattus norvegicus* (1.1, 1.2, 1.3). In some animals, the defect remained empty as negative control (C-). Animals were sacrificed at 15 days. The calvarias were decalcified in EDTA and embedded in paraffin. Serial sections (4 µm) were stained with hematoxylin-eosin (HE), pycrosirius red (PR) and masson-goldner trichrome (MGT) stains. Histological analysis were conducted on images obtained in the light microscope. All procedures were approved by CEUA/UEFS/BA/BR Protocol nº 12/11

Table 1: Elemental analyses

Compounds	Monetite (Ca1-xMxHPO4) (wt, %)	Ionic Sust (100X, Mon)	Silica gel n(H2SiO3) (wt, %)	Hidroxyapatite Ca9(PO4)6-x(OH)x (wt, %)	Wollastonite $CaSiO_3$ (wt, %)
AA	78	3, Zn	7	15	-
U	20	3, Zn	27	46	7

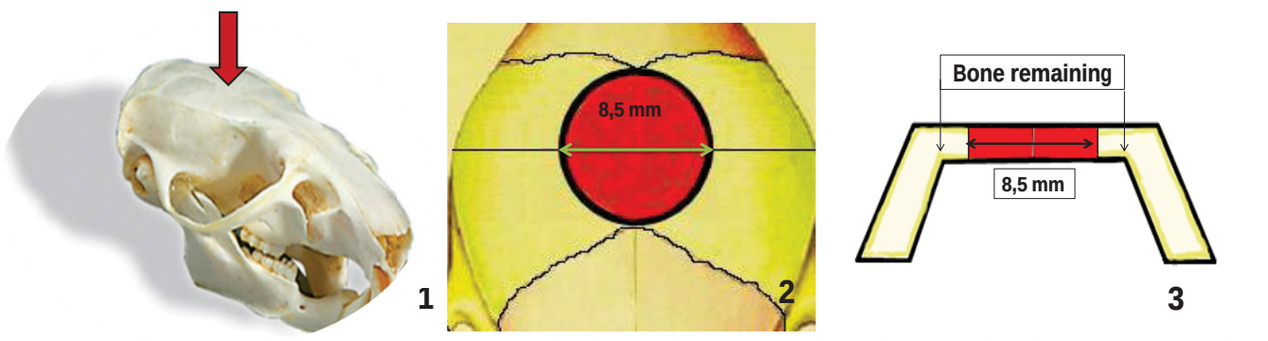

Fig. 1: (1) *Rattus norvegicus* calvaria (2) Schematic drawing of the bone defect (3) Schematic drawing of the bone defect to be analysed

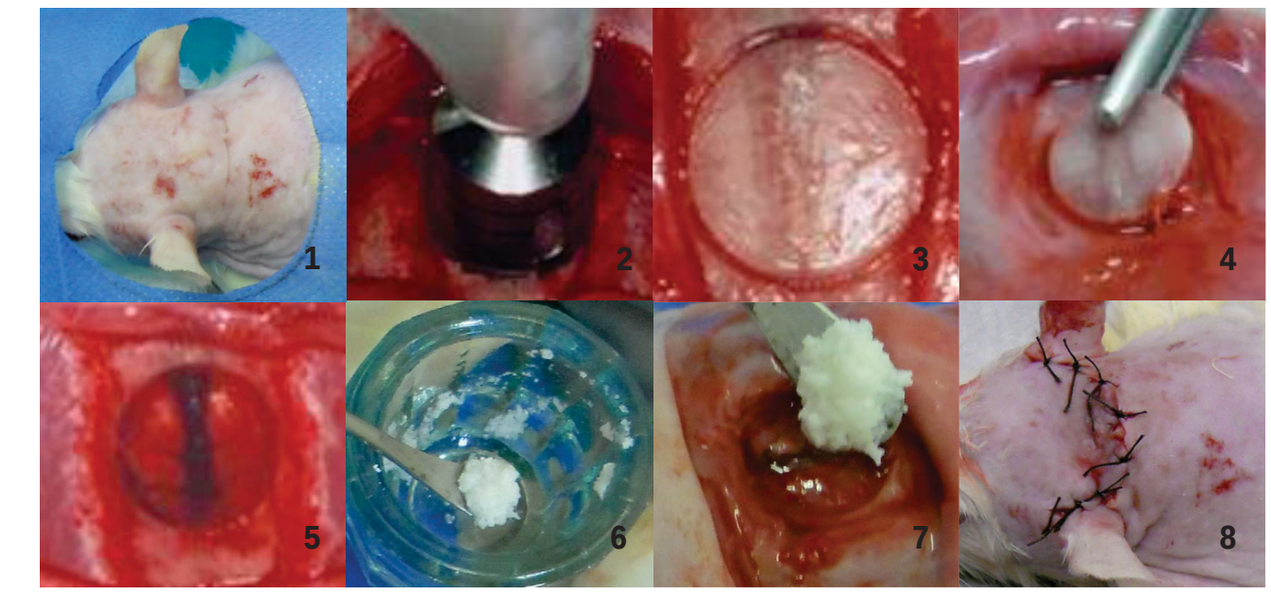

Fig. 2: Surgical sequence (1) Trichotomy and assepsy (2) Making the defect (3) Delineation of the defect (4) Removal of the fragment (5) Critical bone defect (6) Hydration of the biomaterials (7) Implantation of biomaterials (8) Suture

RESULTS AND DISCUSSION

All groups have shown mild inflammatory signs and reparative new bone formation at the borders (3.1, 3.2, 3.3). C- presented only fiber tissue in the defect area (3.1). Signs of biomaterial fragmentation were seen in both implanted groups (3.2, 3.3). Osteoid matrix, osteoblasts and newly vascularised bone forming were observed along the whole defect, including the inner part of biomaterial particles more frequently in AA (3.4) than in U, probably due to the wide availability of bioactive ions such as calcium, phosphate and zinc which were released because of the high solubility of monetite [3, 4, 5]. Collagen fibres were detected permeating AA particles (3.5) and encapsulating U particles (3.6) probably because of the higher hidroxyapatite content in this biomaterial, which is the less resorbable component. [6]

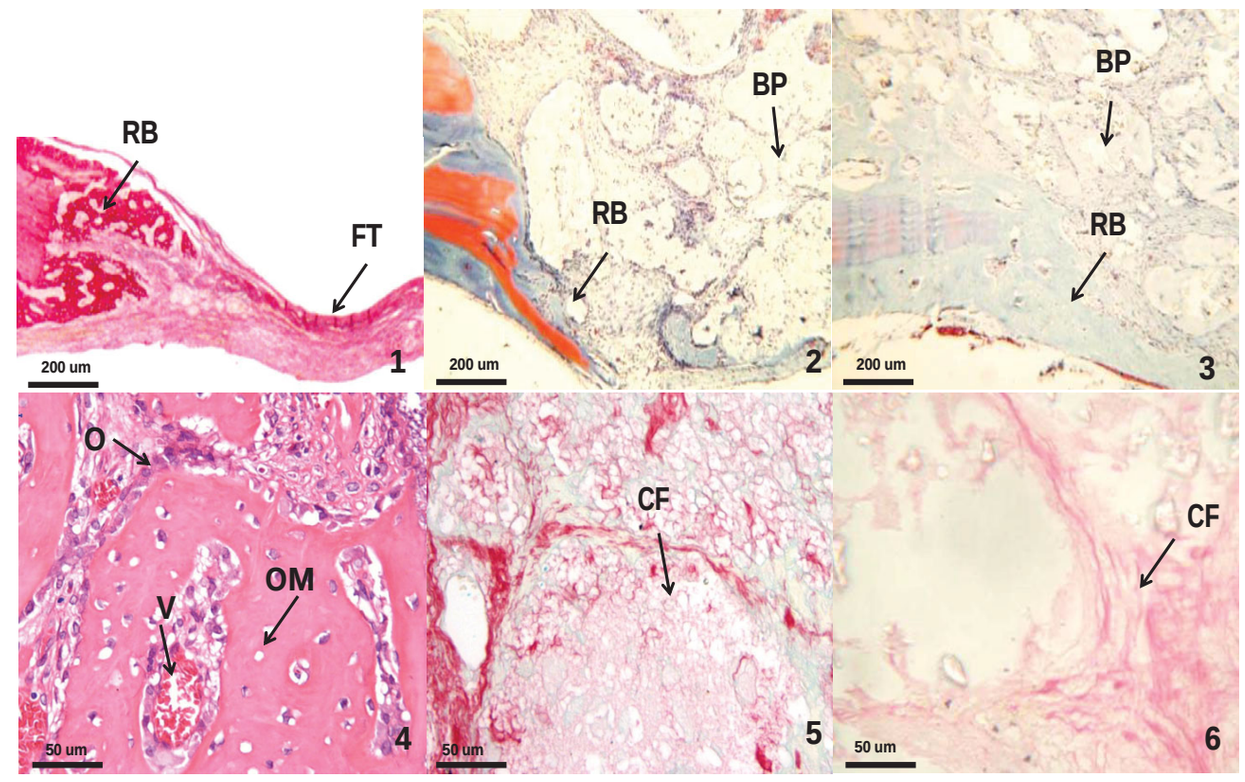

Fig. 3: Histological analisys C- (1), U (3, 6) and AA (2, 4, 5). Reactive bone (RB) at the borders and fiber tissue (FT) in defect area (1) PR 10x. Reactive bone at the borders and biomaterials particles (BP) in defect area (2) MGT 10x (3) MGT 10x. New osteoid matrix (OM), osteoblasts (O) and vessels (V) in AA (4) HE 20x. Collagen fibers (CF) permeating AA particles (5) PR 20x. Collagen fibers encapsulating U particles (6) PR 20x

CONCLUSION

It was concluded that both biomaterials are biocompatible but AA proved to be more pro-osteogenic than U, although more studies in other biological points are needed

CLINICAL IMPLICATIONS

These results are highly relevant for both orthopedics and dentistry with a decrease of morbidity by the development of a new resorbable biomaterial which accelerates bone regeneration

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REFERENCES

1 Tamimi F, Torres J, Kathan C, Baca R, et al. Bone regeneration in rabbit calvaria with novel monetite granules. J Biomed Mater Res A 2008;87A:980–5
2 Habibovic P, Gbureck U, Doillon CJ, Bassett DC, et al. Osteoconduction and osteoinduction of low-temperature 3D printed bioceramic implants. Biomaterials 2008;29 (7):944–53
3 García de Castro A, García Carrodeguas R, Padilla S, Acosta N. Osseous regeneration material from combinations of monetite with other bioactive calcium compounds. WO2010/092001 A1 (Patent) 2010
4 Yamaguchi M. Role of zinc in bone formation and bone resorption. J Trace Elem Exp Med 1998;11 (2-3):119-35
5 Kwun I-S, Cho Y-E, Lomeda R-AR, Shin H-I, et al. Zinc deficiency suppresses matrix mineralization and retards osteogenesis transiently with catch-up possibly through Runx 2 modulation. Bone 2010;46 (3):732-41
6 De Aza PN, Guitian F, Merlos A, Lora-Tamayo E, De Aza S. Bioceramics-simulated body fluid interfaces: pH and its influence on hydroxyapatite formation. J Mater Sci: Mater Med 1996;7:399-402