Percutaneous vertebroplasty in sheep: testing a novel mesoporous bioactive glass/calcium sulphate cement

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ABSTRACT

Polymethylmethacrylate (PMMA) based cements are widely used for vertebroplasty. However, PMMA has disadvantages. The purpose of the present work was to test in vivo a new resorbable injectable composite cement – Spine-Ghost. The paste was percutaneously injected in bone defects manually drilled in L4 vertebral bodies of eight mature Merino sheep (Group B). A control group of eight sheep was injected with a known commercial calcium sulphate-based biphasic cement (Group A). After the 6-month implantation period the samples were assessed by micro-CT and histological studies. All sheep completed the 6-month implantation period. Cement resorption and new bone formation were observed in all samples with no signs of infection or inflammation.

Keywords: resorbable cement; percutaneous vertebroplasty; *in vivo* study; sheep.

INTRODUCTION

Synthetic composite biomaterials are widely accepted as valid bone graft alternatives. Presently, most of the cements used in percutaneous bone interventions are based on a polymeric matrix – polymethylmethacrylate (PMMA) –, providing immediate effect and safety. However, PMMA cements present several disadvantages [1]. Calcium sulphate-based injectable ceramic cements, like Cerament™ are effective, well documented bone substitutes since they are biocompatible, resorbable, and osteoconductive, displaying mechanical properties similar to those of cancellous bone, with reduced Young's Modulus [2].

Sheep are considered an appropriate large animal model for biomedical research because of their anatomical similarities to human bones. To date, only a small number of percutaneous vertebroplasty (PVP) preclinical studies have been performed in large animals, with several drawbacks, including cement leakage into the vertebral foramen, incomplete defect filling and lack of information on postoperative evolution.

With the goal of reducing long-term post vertebroplasty complications while ensuring immediate pain relief and mechanical stability, a new bioactive injectable cement for percutaneous vertebroplasty was developed – Spine-Ghost [3].

In the present work, the *in vivo* results of Spine-Ghost implantation in a sheep vertebral defect model are reported. The performance was compared to a commercial biphasic cement – Cerament™.

EXPERIMENTAL

Spine-Ghost is composed of type III α-calcium sulphate hemihydrate combined with mesoporous particles of a bioactive glass, and a radiopaque glass-ceramic phase. Prior to the *in vivo* study, the cement went through bioactivity and resorbability, *ex vivo* injection, mechanical and *in vitro* testing [3]. All the tests were carried out using a commercial reference as control.

Procedures were conducted according to European Community guidelines. 16 mature Merino sheep were randomly allocated into 2 groups: control group A, injected with Cerament™; and experimental group B, injected with Spine-Ghost. All underwent PVP under general anaesthesia. Vertebral body defects were created in the cranial hemivertebrae, through modified parapedicular approach developed by the authors [4]. Cements were injected under fluoroscopic guidance using a bone-filler system device (Medtronic Spine LLC, Portugal) and set for 2 hours in the anaesthetized sheep. Post-surgery care was spent in a pen of the veterinary hospital of the University of Évora. Fluorochromes were injected two weeks after surgery and two weeks before sacrifice. During the 6-month implantation period the sheep remained free ranging in the pasture. At the end of the implantation period, the animals were sacrificed, and the vertebrae explanted. Biological response and material integration were assessed by micro-CT and histological studies.

RESULTS AND DISCUSSION

Prior to the *in vivo* study, the cement went through bioactivity, resorbability, *ex vivo* injection, mechanical, and *in vitro* testing, all of which with favorable results. The experimental cement could be easily injected without interruption, and it showed a satisfactory radiopacity. Finally, Spine-Ghost exhibited a much higher compressive strength than the commercial reference. More results are shown in table 1.

Table 1. Comparison between the cements' *in vitro* and *ex vivo* properties - review

	Spine-Ghost	Cerament™
Cement characterization	70% CaS:20% SCNZgc: 10% W-SC Moderate radiopacity: conferred by the glass-ceramic phase (SCNZgc) Liquid phase: water	60% α-CaS: 40% HA High radiopacity: conferred by the iohexol Liquid phase: iohexol
	Highly bioactive Resorbable: 83% in 28 days Easy to handle; adequate injectability Working/ hardening time ≈ 8-20 minutes Setting time ≈ 1 hour Adequate stiffness and strength Compressive strength: 14±0.7 and 18.1±0.8 MPa (wet and dry conditions, respectively)	Bioactive Resorbable: 100% in 28 days Easy to handle; adequate injectability Working/ hardening time ≈ 7 minutes Setting time ≈ 1 hour Adequate stiffness and strength Compressive strength: 8.2±0.7 and 7.3±0.6 MPa (wet and dry conditions, respectively)

No cement leakage was observed into the vertebral foramina, with just one of the 16 animals presenting transient postsurgical mild neurologic deficits. A 100% survival rate was obtained.
After the first macroscopic evaluation, micro-CT scanning of the intact vertebrae was performed, for qualitative and quantitative analysis (Figure 1).

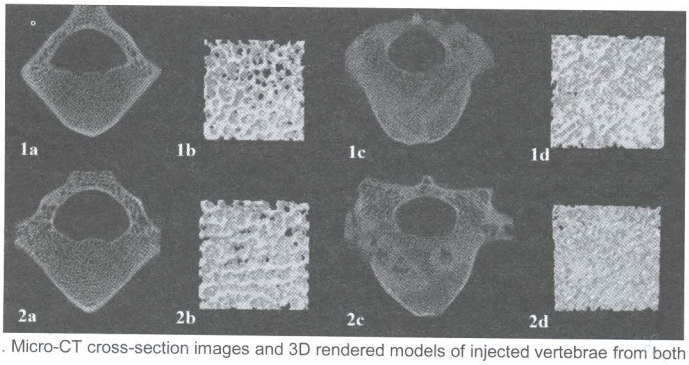

Figure 1. Micro-CT cross-section images and 3D rendered models of injected vertebrae from both groups.

Histology showed cement resorption and new bone formation; histomorphometric results showed no statistically significant differences between the two groups.

CONCLUSIONS

Spine-Ghost elicited a biological response identical in most aspects, with a higher measured BMD and BV/TV. In both groups new bone formation was observed, with concurrent cement resorption and integration into the new trabecular bone, as evidenced by the histological results presented.

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