

Case Report

Use of a fully-resorbable, biomimetic composite hydroxyapatite as bone graft substitute for posterolateral spine fusion: a case report

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Abstract: Introduction: A successful spinal fusion is the result of the proper integration between the fixation device, used to stabilize and correct the column posture, and the bone graft applied to replace or integrate the bone components. Background: In the recent past, the use of bone graft substitutes has been widely employed in spinal stabilization surgery, with the aim of improving the amount of bone graft material available, as well as to avoid the use of autograft and allograft bone, with related drawbacks and side-effects. However, since standardized non-invasive techniques (X-rays, CT scan images) are not sufficiently accurate in predicting whether bony fusion occurred, currently the only option to evaluate the bone graft osteointegration is through a revision surgery, due to the need of correcting the previous surgical procedure. Here, we present the osteointegrative properties of a third-generation hydroxyapatite bone graft substitute applied on a 65-year-old patient, who underwent a spinal stabilization surgery and, one year later, a revision surgery due to the rupture of a metallic bar. Materials and Methods: Bony fusion was evaluated by histological and immunohistochemical analysis performed on a biopsy sample one year after surgery. For this purpose, histological and immunohistochemical analysis were performed. Results: Histological analysis clearly evidenced the complete osteointegration of the device, together with new bone formation. Discussion and Conclusions: Third-generation bone graft substitutes allow bone ingrowth and tissue remodelling by providing three-dimensional structural support, thus resulting as ideal scaffolds for bone replacement and osteointegration.

Keywords: Posterolateral spine fusion, spinal stabilization, arthrodesis, bone grafts, hydroxyapatite, osteointegration

Introduction

A successful spinal fusion (or arthrodesis) mainly depends on the proper integration between fixation devices (metal implants, screws with rods or plates, cages), used to stabilize and correct the spine column, and bone grafts applied to replace or integrate the bone components [1, 2].

Currently, autograft and allograft materials are considered the “gold standard” options to achieve spinal fusion. Autologous bone, usually harvested from non-essential bones (spinous processes) or from the iliac crest (pelvis), has osteoinductive, osteoconductive and osteogenic properties, no concerns for diseases transmission and no risks of immunogenicity. However, side effects (such as donor-side mor-

bidity, post-operative chronic pain and the risk of relatively limited quantity) can reduce its use [3]. As well as autograft, allograft material shows osteoinductive and osteoconductive properties and, being harvested from cadaveric tissue donors, it shows reduced patients-related side-effects. Nonetheless, limitations (e.g. risks of disease transfer and poor osteogenic properties) restrict its applicability [3].

To circumvent all these issues, the use of bone graft substitutes has been extensively investigated for surgical applications [1, 4]. These materials can be artificially created from ceramics (or other naturally occurring and biocompatible substances) and hold mechanical properties similar to the bone component. Their immediate availability and unlimited quantity makes these products of relevant interest for surgical

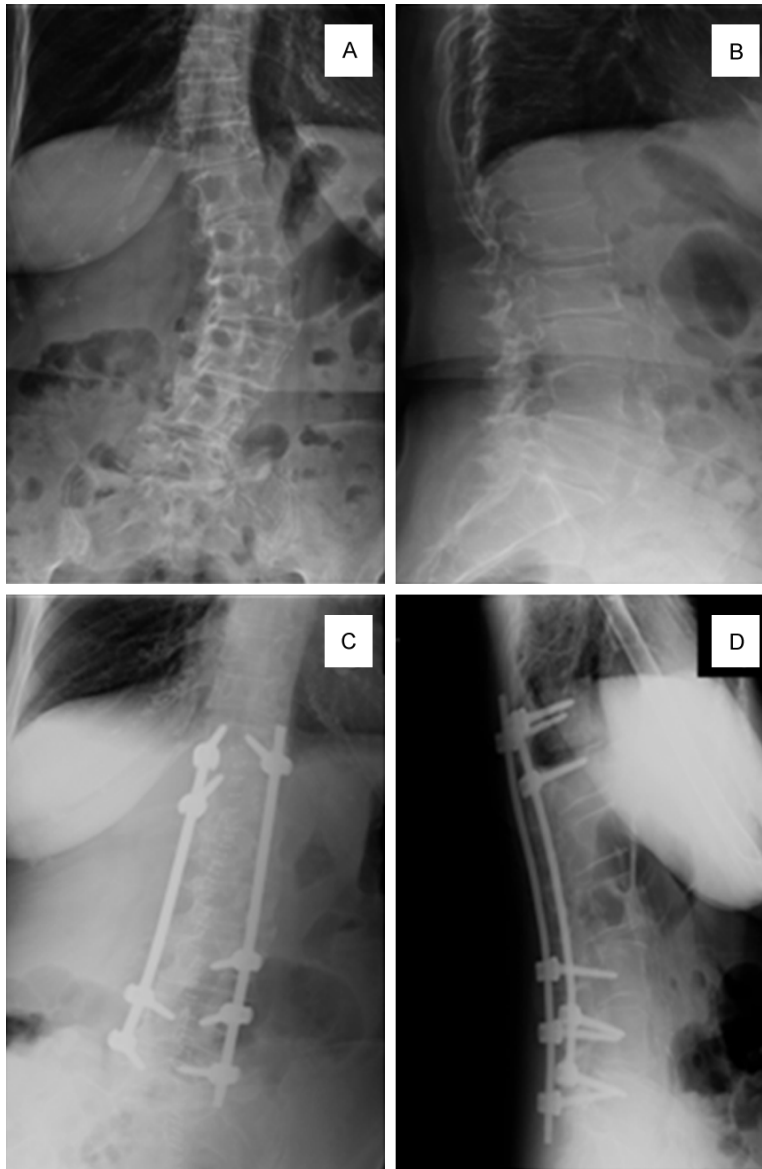


Figure 1. (A) Antero-posterior and (B) lateral view of pre-operative radiograph showing lumbar spine scoliosis. (C) Antero-posterior and (D) lateral view of post-operative radiograph showing lumbar spine scoliosis correction.

applications requiring a large amount of bone graft, therefore representing an immediate and ready-to-use alternative to autograft and allograft bone.

Among these, hydroxyapatite bone substitutes have been used as graft extenders to foster bone regeneration. Several experiments on animal models [5] and clinical studies on humans [6] have demonstrated that these biomaterials possess a chemico-physical structure which supports cell migration and scaffold colonization, sustaining new tissue formation and bone

regeneration, and therefore supporting their usability also in the spinal field. However, as standardized noninvasive evaluations (X-rays, CT scan images) are not 100% accurate in predicting whether a bony fusion has occurred [2, 7], only secondary surgical procedures (e.g. revision surgery for spinal stabilization) can provide information about successful joint ossifications.

RegenOss (provided by FinCeramica Faenza S.p.A., Faenza, Italy) is a fully-biomimetic and resorbable third-generation hydroxyapatite bone graft substitute, which resembles the process occurring during biological neo-ossification, through the patented process of nucleation of the Mg-Ha nanocrystals into type I Collagen fibers [4]. These features allow the product to serve as scaffold to guide effective bone regeneration, fostering cell attachment and proliferation and promoting a reduction of the osteointegration time periods [4, 8, 9].

Here we report osteointegration evidences of the Mg-enriched HA bone graft substitute RegenOss, ascertained after revision surgery for spinal stabilization.

Case report

A smoking-free, 64-year-old woman presented with a chronic low back pain in March 2012. The patient was diagnosed on 2011 with idiopathic lumbar spine scoliosis (**Figure 1A, 1B**), which worsened during the last year, rising to a left sciatic irritating pain. VAS (Visual Analog Scale for pain) score was 9. Oswestry Low Back Pain Disability Index was 50. The patient underwent spinal stabilization surgery through posterior approach performed by the use of rods stabilization system and pedicle screws, which were inserted bilaterally on L4-L5 levels, on L3 (left side), on D11 and D12 (right side) and on

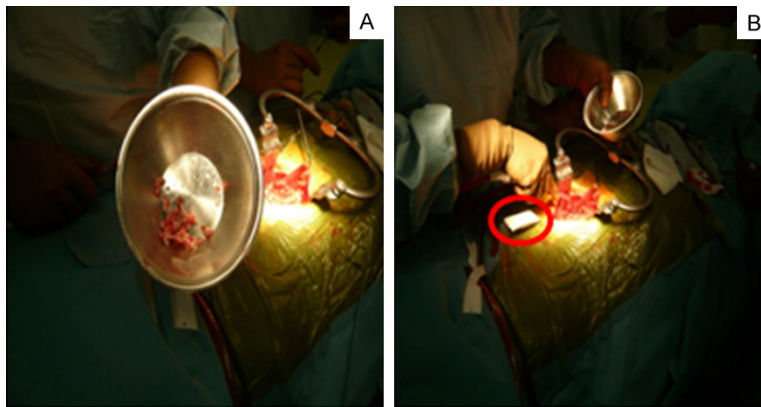


Figure 2. Images from a spinal stabilization surgery theatre. A. Autologous bone harvested from the laminar processes of the vertebrae and trimmed for spinal fusion. B. During spinal fusion, the composite bone substitute RegenOss (red circle) will be mixed with autologous bone and applied along the rods and the pedicle screws to improve spinal stabilization.

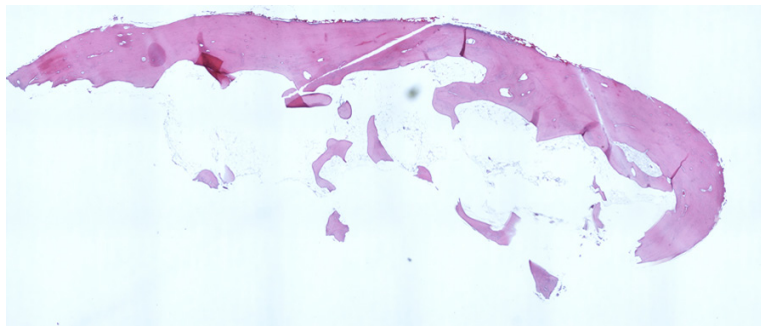


Figure 3. Histological evaluation of the biopsy sample by Haematoxylin/Eosin staining (Magnification 4X).

D10 (left side), followed by neurological left decompression and scoliosis curve correction (**Figure 1C, 1D**).

The screw-based system was integrated with the apposition of autologous bone (60%) plus a synthetic bone graft substitute (40%) (RegenOss, provided by Fin-Ceramica Faenza S.p.A., Faenza, Italy) along the rods and the articular processes on the right side (**Figure 2A, 2B**) in order to achieve bony fusion and stabilize the spine column. Patient was discharged from the hospital after routine postoperative period.

After one and a half years (August 2013) without any symptoms, the patient went back to the hospital with dorsalgia due to rupture of the left rod. We therefore proceeded for a spinal stabilization revision surgery, removing the D10 screw (left side) and positioning another pedicle screw in D11 (left side). During surgery,

arthrodesis was evaluated by a clinical point of view, providing a good outcome in all the vertebral positions.

In that occasion, we evaluated the bone graft substitute fusion progression. Therefore, a biopsy fragment was harvested for histological and immunohistochemical investigations. To this end, sample was placed in 10% neutral buffered formalin and decalcified for three weeks at Room Temperature (RT). Specimen was paraffin embedded and serial sections were cut at up to 5 μ m thickness and stained with Haematoxylin/Eosin (**Figure 3**) to evaluate general morphology, which evidenced a lamellar bony-like tissue morphology with osteocyte component and presence of bone marrow at the site of bone substitute application.

These results underline bone in growth and tissue remodeling. This was confirmed by Mallory's trichrome staining which showed the presence of various new bone formation

areas within mature bone (**Figure 4**). Immunohistochemical evaluation confirmed the good quality of the bone tissue as shown by a positive staining for typical osteogenic markers such as type I Collagen and Osteocalcin. In particular, we noticed a strong positivity for type I Collagen at both cellular and extracellular levels in mature and new bone areas (**Figure 5**). Similar results have been observed also for osteocalcin, but in this case the positivity was limited to the cells (**Figure 6**).

Discussion

Arthrodesis is a surgical procedure employed in a large number of traumatic, degenerative and oncological spinal diseases, in order to permanently fuse together two or more vertebrae and stabilize the spine column [1]. The need of metal implants to be integrated with vertebral bones of the spine has always represented a

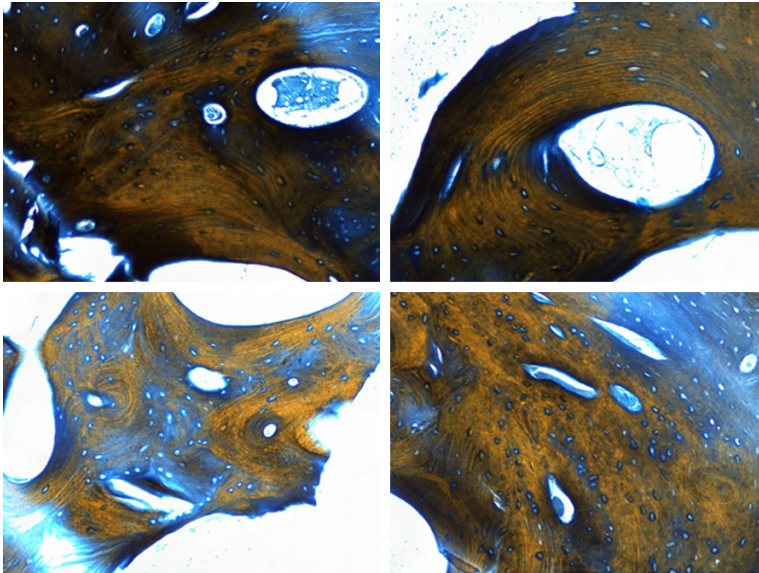


Figure 4. Histological evaluation of some representative areas of the biopsy sample by Mallory's trichrome staining. Light brown staining indicates new bone formation; Blue staining indicates mature bone (Magnification 10X).

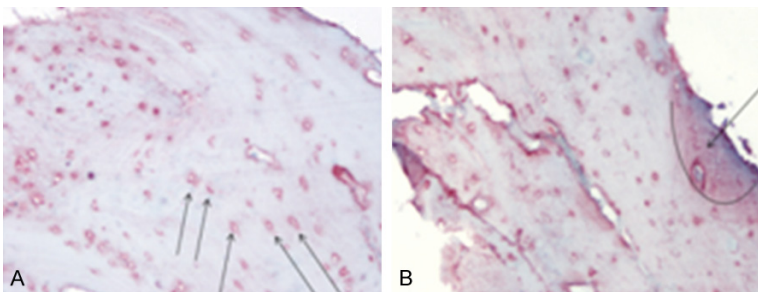


Figure 5. Immunohistochemical evaluation of type I Collagen in two different areas of the biopsy sample. A. Positivity to type I Collagen is present at cellular level as indicated by arrows; B. Positivity to type I Collagen is evident also in the extracellular matrix as indicated by arrow (Magnification 10X).

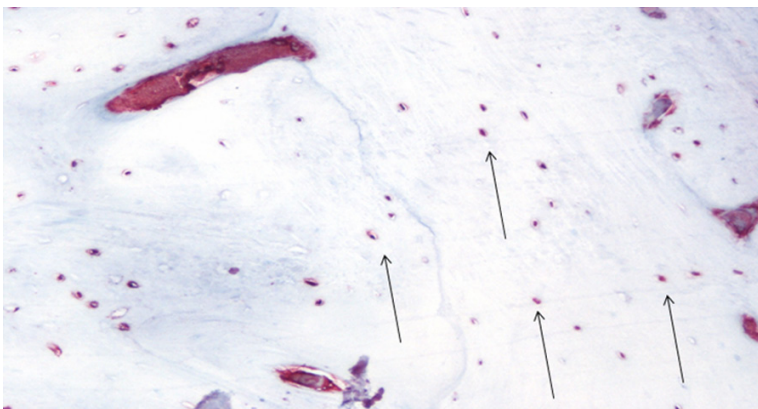


Figure 6. Immunohistochemical evaluation of Osteocalcin in some representative areas of the biopsy sample. Positivity is evident at cellular level as indicated by arrows (Magnification 10X).

challenge for orthopaedics as well as neurosurgeons, and different types of bone grafts have been extensively investigated to find out the perfect combination (metal implants + bone grafts) to achieve a solid bony fusion [1-3]. Even though autograft and allograft still represent the “gold standard” solutions, side effects can restrict their applicability [3]. For these reasons, in the last decades, bone substitutes have been widely investigated for either orthopaedic and spinal applications [1, 4]. Among these, hydroxyapatite bone substitutes have been developed and used as graft extenders, showing chemico-physical features which led to new tissue formation and bone regeneration [5, 6].

In this report, we showed the osteointegrative properties of a third-generation bone graft substitute (RegenOss) which has been used for a spinal fusion stabilization on a 64-year-old female patient suffering of dorsolumbar idiopathic scoliosis, who subsequently underwent a secondary revision surgery due to the breakage of one of the inserted metallic rods after 14 months. This event allowed us to investigate the efficacy of bony fusion performed by the use of this new bone substitute. Histological analysis clearly evidenced the complete osteointegration of the device and no residuals have been detected in the biopsy fragment. Histological evaluation indicated a good bone tissue remodeling, due to ongoing osteogenic processes of the bone substitute, as clearly evidenced by Mallory's trichrome staining. The positivity to type I Collagen and

Osteocalcin markers confirmed this process. Our results suggest how the fully-biomimetic and resorbable third-generation hydroxyapatite bone substitute RegenOss could be easily adapted as filling material during spinal fusion procedure from either biomechanical and histological perspectives.

Disclosure of conflict of interest

None.

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