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# Histological Assessment of New Bone Formation with Biomimetic Scaffold in Posterolateral Lumbar Spine Fusion

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## ABSTRACT

### Background context

Spinal fusion procedures often require the use of bone grafts (autograft or allograft) to help bone healing and to increase stability. However, the application of autografts is frequently limited by donor site morbidity. In recent years, different synthetic bone substitutes have been introduced in the clinical practice to overcome these limitations.

### Purpose

The purpose of this paper is to report a case where a biomimetic, synthetic and osteoconductive bone graft substitute was successfully implanted in a patient during lumbar spine arthrodesis.

### Study design

The case of a 58-year-old female subjected to lumbar spine arthrodesis with bone augmentation is described.

### Methods

The bone graft substitute RegenOss® (Finceramica, Faenza, Italy) was implanted during spinal arthrodesis. The successful bone integration was evaluated by X-rays. After 11 months, the patient underwent a second surgery due to spine imbalance; the debris of the bone graft was therefore collected and analyzed by macroscopic evaluation and by histology.

### Results

The bone substitute was successfully implanted during a spinal arthrodesis procedure. Histologic evaluation of the removed bone graft debris showed the

complete resorption of the implant and the formation of new bone, which was well integrated with the host bone.

**Conclusions**

This bone substitute may represent a safe and effective alternative to autologous bone grafts, avoiding adverse events related to donor-site morbidity.

**KEYWORDS**

Bone formation, posterolateral spinal fusion, biomimetic scaffold, bone graft substitute, histology, arthrodesis

## INTRODUCTION

Lumbar spinal arthrodesis may require the use of bone graft to augment bone mass, achieve healing and to provide stability. Different bone graft substitutes are available: autologous cancellous bone graft from the iliac crest is nowadays considered the gold standard as it possesses osteoconductive, osteoinductive, and osteogenic properties; in addition, the risk of infections or rejection is negligible (1-3). Thus, many authors reported the bone harvesting from the iliac crest as a safe and effective bone graft procedure (4). However, associated donor site morbidity and complications, such as pain or neurological lesions, occur in a significant number of cases, as widely reported (5-7).

Therefore, over the last 10 years, the use of growth factors such as rhBMP-2 was introduced as an effective alternative to the use of iliac crest grafts (8-11); however, papers and reviews have reported severe adverse effects related to the use of this osteoinductive bone graft in spinal fusion procedures (12,13). Synthetic osteoconductive carriers are also valid substitutes to bone autografts and they do not necessarily require the use of growth factors.

In this paper, we describe the successful implantation of a novel synthetic bone graft in a spinal fusion procedure. This implant perfectly integrated with the native bone and it was also completely replaced by new bone after 1 year.

## METHODS

The synthetic bone substitute RegenOss® (Finceramica, Faenza, Italy) was implanted during a spinal fusion procedure.

Bone integration was evaluated by X-rays and by histology. Histologic evaluation was performed on bone fragments removed from the site of arthrodesis one year later due the need of a second surgery to correct spine imbalance. The specimens were fixed in formalin solution, processed and paraffin-embedded. The samples were then cut along the transverse plane and stained with hematoxylin-eosin.

## RESULTS

A 58-year-old female was first admitted for symptomatic rigid thoracolumbar kyphoscoliosis. X-rays executed before surgery showed thoracolumbar scoliosis with kyphosis on the sagittal plane (Figure 1, a). Hence, arthrodesis from the fifth thoracic vertebra (T5) to the fifth lumbar vertebra (L5) with pedicle screw fixation was performed. Moreover, a Smith Petersen Osteotomy was completed from the second lumbar vertebra (L2) to the fourth lumbar vertebra (L4), and the area was covered with the synthetic bone graft to promote bone fusion. Post-operative course was regular, with no complications. However, a progressive spine imbalance with pelvic retroversion was recorded 11 months after the previous surgery (Figure 1, b). Therefore, the patient was readmitted for surgical revision one year after the first surgical procedure. A Pedicle Subtraction Osteotomy (PSO) of L2 and a transforaminal lumbar interbody fusion between L4 and L5 (TLIF) were performed to correct the fixed sagittal plane deformity. The outcome of the surgical revision was satisfactory and the restoration of lumbar lordosis was obtained (Figure 2).

During the surgical revision, the area where the bone graft had been previously applied, was removed to properly complete the PSO. Thus, an extensive macroscopic

and histological analysis was assessed on the bone fragments derived from the bone graft.

At macroscopic evaluation, no remnants of the implanted biomaterial were visible, and the quality of the newly formed bone was apparently normal with a dense bony mass formation.

The histological findings did not show any presence of fibrous tissue at the interface with host bone. At the site of the bone graft, histology also displayed the presence of newly formed bone, which had a well-organized trabecular structure resembling healthy bone (Figures 3 and 4). Thus, the bone substitute was successfully implanted and completely osteointegrated with the native bone.

## DISCUSSION

Nowadays, autograft or allograft bone substitutes are available for spinal arthrodesis together with over 60 synthetic biomaterials. However, the clinical outcome of those scaffolds is still uncertain and their benefit-cost ratio remains controversial. Autologous bone graft is limited due to site morbidity; thus, synthetic osteoconductive grafts, which can be associated with osteoinductive growth factors, may represent a valid alternative (14).

In the present report, we described the successful implantation of a bone graft during a spinal arthrodesis. In particular, the bony substitute was a biomimetic synthetic scaffold obtained by co-precipitation of magnesium-enriched hydroxyapatite nano-crystals into type I collagen fibers through a self-assembling process, mimicking natural bio-mineralization processes. The chemical composition of this bioceramic graft is very similar to human bone and the scaffold indeed shows

good biocompatibility. Moreover, it presents biodegradable characteristics even with regard to the mineral component (the magnesium-enriched hydroxyapatite); it is resorbed either by a cellular or enzymatic pathway allowing the formation of new bone tissue.

In this report, the bone graft was easily implanted during surgery, and it was well tolerated by the patient. At 1-year follow-up, X-rays showed bony fusion between the implant and the native bone. In addition, during the revision surgery a complete integration of the bone graft was observed and a bone consolidation forming a dense mass melted with the host bone was noted. Further histological evaluation confirmed the bony nature of the newly formed tissue. All analyses were completed after 1 year from the implantation; as shown in literature, this timing is considered a sufficient follow-up to evaluate the maturity of new ossification (2).

The particular features of the graft may have contributed to its complete resorption. In fact, this bone substitute is known to be usually resorbed by enzymes and cellular action over a period of 6-12 months.

This report demonstrates the potential application of a novel synthetic bone graft substitute with biomimetic properties in spinal fusion procedures. Based on the observation of this case report, the graft may represent a safe and effective alternative to the use of autologous bone grafts, avoiding adverse events related to donor-site morbidity.

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**Conflict of interest:** The authors Giuseppe Gioia, Marco Agnoletto, Alessia Di Giancamillo, Marco Domenicucci, Laura Mangiavini, Michele DM Lombardo and Giuseppe M. Peretti have no conflict of interest related to the subject of the present work.

## FIGURE LEGENDS

**Figure 1**: X-ray imaging before surgical instrumented D5-L5 arthrodesis (a) and after the surgical procedure at 1-year follow-up (b) in anteroposterior view.

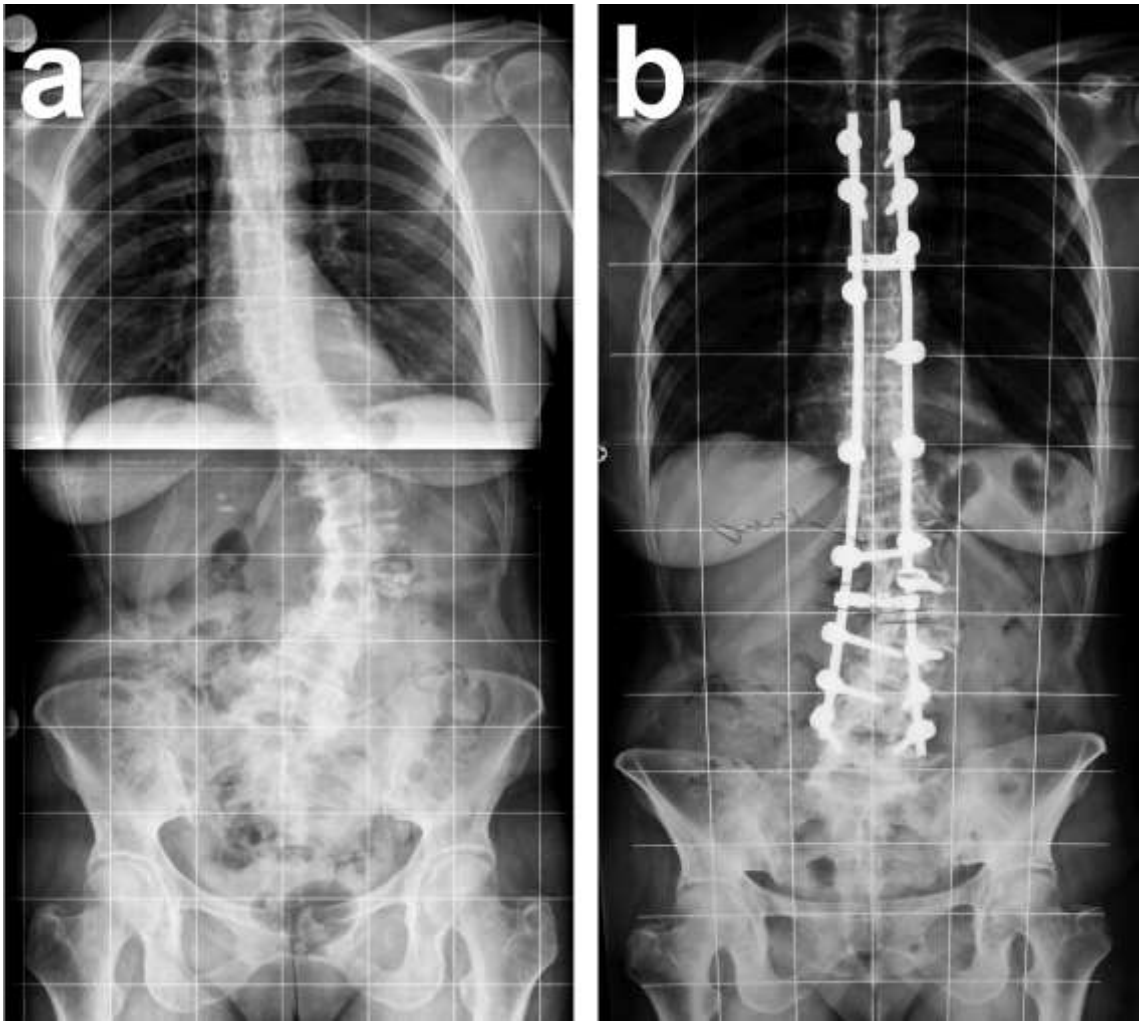

**Figure 2**: X-ray imaging in anteroposterior (a) and lateral view (b) after surgical revision at 1-year follow-up.

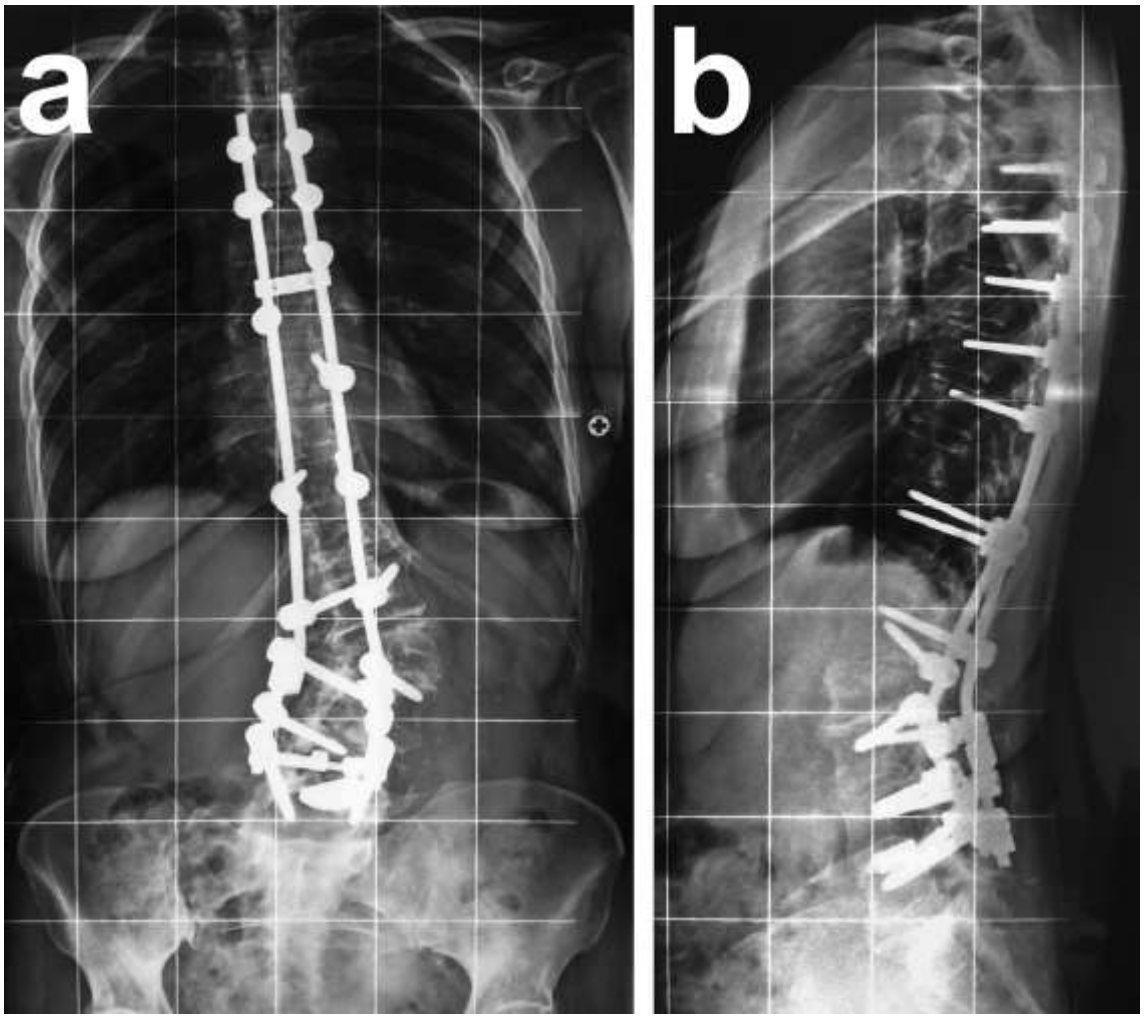


**Figure 3**: Hematoxylin-eosin staining of harvested bone at 1-year follow-up. Normal histological features of trabecular bone. Lamellae and osteocytes are clearly visible within the trabeculae. Normal structure of the bone marrow is also visible with abundant fat deposits. No remnants of the biomaterial were found at this stage in all histological specimens. Scale bar = 200 µm.

**Figure 4**: Hematoxylin-eosin staining of harvested bone at 1-year follow-up, which shows normal parallel lamellae in the trabecular bone on the right (black arrow). High concentration of red blood cells is visible within the bone marrow (white arrows), probably due to the technique of tissue harvesting, which implies the use a Stille-Luer bone rongeur and concentrates the blood cells at the moment of grabbing the tissue. Scale bar = 200 μm.