Case Report

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First-in-Patient Case Study of a Novel Nanosynthetic Bone Graft Substitute: OssDsign Catalyst™

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ABSTRACT

This case study describes the first use of a novel nanosynthetic bone graft, OssDsign™ Catalyst, in a Spinal fusion patient. This new bone graft consists of nanoscale calcium phosphate containing silicate substitution (5.8wt% silicon) which has been shown to be capable of regenerating bone via the endochondral ossification route in challenging animal models [1,2], resulting in high fusion rates at very early timepoints comparable to existing synthetic bone grafts as well as robust osteoconductive bone formation local to the graft. The first patient was a 40-year-old female, suffering from degenerative disc disease, who underwent a one level Transforaminal Lumbar Interbody Fusion. At 6 months post-operative follow up, CT scans show complete fusion both interbody and in the posterolateral gutters.

Keywords: Synthetic Bone Graft; Silicate; Calcium Phosphate; TLIF; Interbody Fusion

Abbreviations: CT: Computed Tomography Scan; ICBG: Iliac Crest Bone Graft; ODI: Oswestry Disability Index; PLF: Posterolateral Lumbar Fusion; TLIF: Transforaminal Lumbar Interbody Fusion; SF-36: Short-Form Health Survey; VAS: Visual Analogue Score for Pain

Introduction

Transforaminal Lumbar Interbody Fusion (TLIF) is one of the most popular and successful surgical techniques to treat various spinal disorders [3-6]. It has been used since the 1980's due to its biomechanical advantage of achieving circumferential fusion through a single posterolateral approach [5]. OssDsign Catalyst™ contains nanoscale, silicate-substituted calcium phosphate granules suspended in a resorbable gel carrier. The level of substituted silicate (5.8% wt% silicon) is the highest level achieved in any bone graft. Also, the high surface area of the nanoscale, porous granules promotes consistent and rapid bone ingrowth, remodeling, and cell-mediated resorption during the bone healing process [1,2] OssDsign Catalyst™ is osteoinductive, osteoconductive, resorbable, porous and is 100% synthetic without the need for adding any biological materials or natural proteins. This novel bone graft contains nanoscale silicate-substituted calcium phosphate granules suspended in a resorbable gel carrier, which enables direct implantation from the packaging without any further preparation time. OssDsign Catalyst™ can be used as a standalone bone graft or combined with autograft for use as a bone graft extender. The high surface area of the nanoscale granules has been designed to deliver consistent and rapid bone ingrowth, remodeling and cell-mediated resorption during the bone healing process, as shown in clinically relevant animal studies [1,2].

These studies showed that OssDsign Catalyst™ achieve fusion success rates comparable to iliac crest bone graft (ICBG) (the traditional 'gold standard'), as well as Actifuse ABX and MASTER-

GRAFT® Putty, two well-established synthetic bone grafts. The case history presented here details the first use of this novel bone graft in a patient as part of an initial first-in-human single center, prospective clinical study to determine the safety and performance of OssDsign Catalyst™.

Method

This patient was the first enrolled in a single center prospective study in which 17 patients have been recruited with the goal of having 15 evaluable patients after a 2-year post-op follow up. The follow-up visits include pre-operative (baseline) data with post-op assessments at 6 weeks, 3 months, 6 months, 12 months and 24 months. This clinical study is being conducted in accordance with the Declaration of Helsinki and ISO 14155, plus appropriate country-specific regulations for Hungary where the study is being performed. This case study describes the results of the first patient to reach 6 months follow up. The procedure involved a one-level TLIF (L5-S1) with posterior instrumentation. OssDsign Catalyst™ nanosynthetic bone graft was used as a standalone graft anterior to (2ml), and within (1ml) the interbody PEEK cage (Respace™) and was also placed bilaterally (4ml per side) in the posterolateral fusion (PLF) portion of the construct, stabilized with Expedium titanium internal fixation (2 rods and 4 pedicle screws). OssDsign Catalyst was mixed in a 1:1 ratio with morselized autologous bone harvested from the one-sided partial facetectomy performed during the TLIF procedure, for specific use in the interbody space posterior to the cage only (total volume 4.5ml). The following information was obtained at each patient visit: medications related to pain control; adverse events, neurological status; x-rays and CT scans, and quality of life patient reported outcome measures (i.e., Oswestry Disability Index (ODI), [7] back and/or radicular leg pain visual analog numerical scores (VAS), and SF-36™Health Survey).

Neurological status was determined by assessing motor function, sensory function, muscle strength, and reflexes, and was considered successful with maintenance or improvement in all assessments. Fusion success was defined by evidence of bridging bone (continuous bony connection) from the superior vertebral body to the inferior vertebral body, in the posterolateral gutters, and for interbody fusion within the interbody cage. All CT scans were reviewed blinded, by two experienced, independent radiologists, plus a third if the initial two disagreed. This radiographic fusion assessment was performed by Medical Metrics Ltd.

Results

This first OssDsign Catalyst™ bone graft patient was a 40-year-old non-smoking female diagnosed primarily with low back pain, secondary to degenerative disk disease at L5-S1 with mild radicular symptoms. She presented with a BMI of 26.5, and normal DEXA scan results (0.5 T-score, 0.2 Z-score). She was unresponsive to at least six months of non-operative treatment prior to clinical study enrollment (e.g., bed rest, physical therapy, bracing, traction, drug therapy). (Table 1) shows the fusion assessment results at 3 and 6 month post-op follow-up. (Figure 1) shows the CT images of fusion at 6 months. The results of the clinical assessments are shown in (Table 2) and (Figures 2-4) for time points up to the 6 month post-op follow up. (Table 1) shows the fusion assessment of partial interbody and posterolateral fusion at 3 months (Grade 2) and solid interbody and posterolateral fusion (Grade 3) at 6 months. (Figure 1) shows CT images of the fusion seen at 6 months. (Figure 2) shows VAS low back pain scores (0-10) improved from moderate (3.5/10) pain to almost complete resolution at each timepoint (0.4, 0.0, 0.9, at 6 weeks, 3 months, and 6 months respectively, this is supported by the discontinuation of the need for pain medication post-operatively (Table 2). (Figure 3) shows functional outcomes as demonstrated by ODI scores which improved from preoperative severe disability (44/100) to moderate disability at each follow-up time point. (Figure 3).

Table 1: Fusion assessment.

Follow up visit	Interbody bridging bone (through cage)	Left posterolateral bridging	Right posterolateral bridging
3 months ± 14 days	Grade 2	Grade 2	Grade 2
6 months ± 30 days	Grade 3	Grade 3	Grade 3

Note: (Grade 1=no fusion, Grade 2=partial fusion, Grade 3=fused (evidence of bridging bone)).

Table 2: Pain Medication.

Assessment Type	Pre-Operative (baseline)	6 weeks post-operative	3 months post-operative	6 months post-operative
Pain medication	Analgesics (Panadol 2-3x 500 mg, per day Algopyrin 2-3 tablets, per day)	None	None	None

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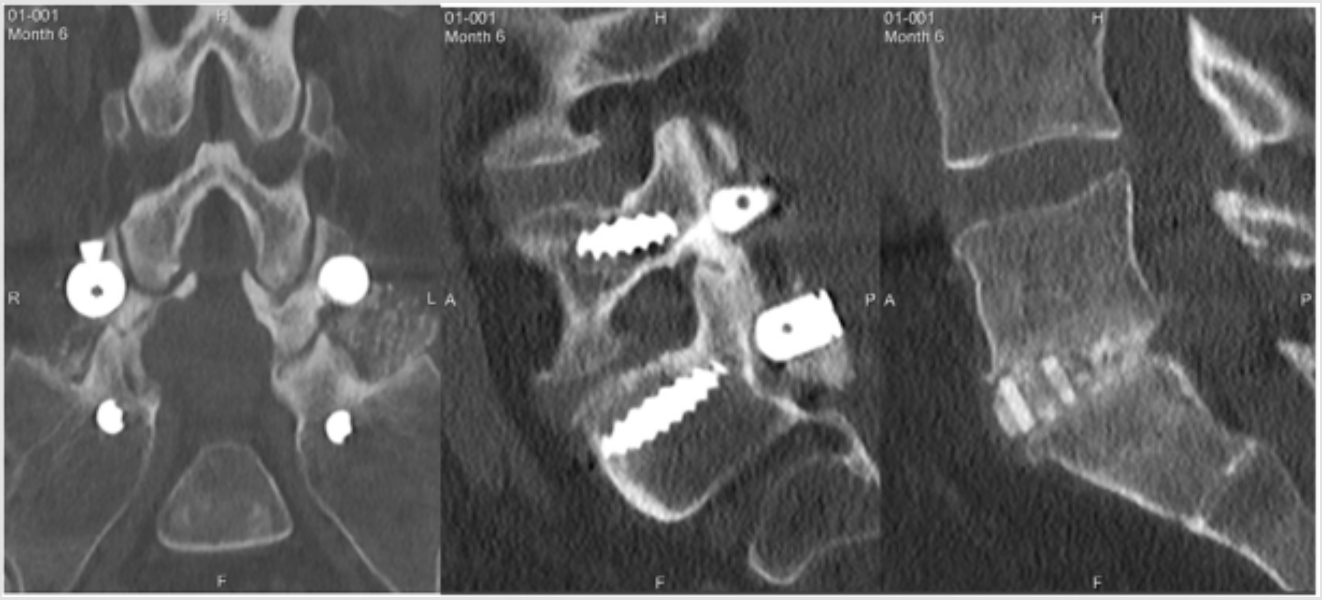

Figure 1: CT scans at 6 months Post-op.

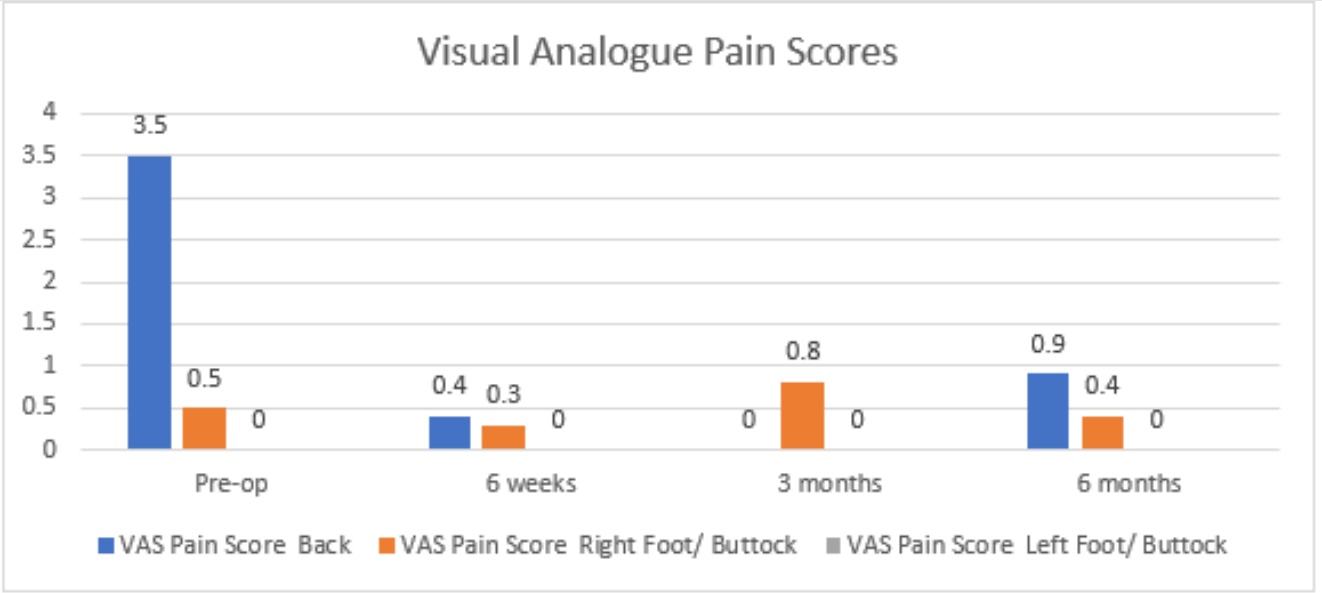

Figure 2: Visual Analog Scores (VAS).

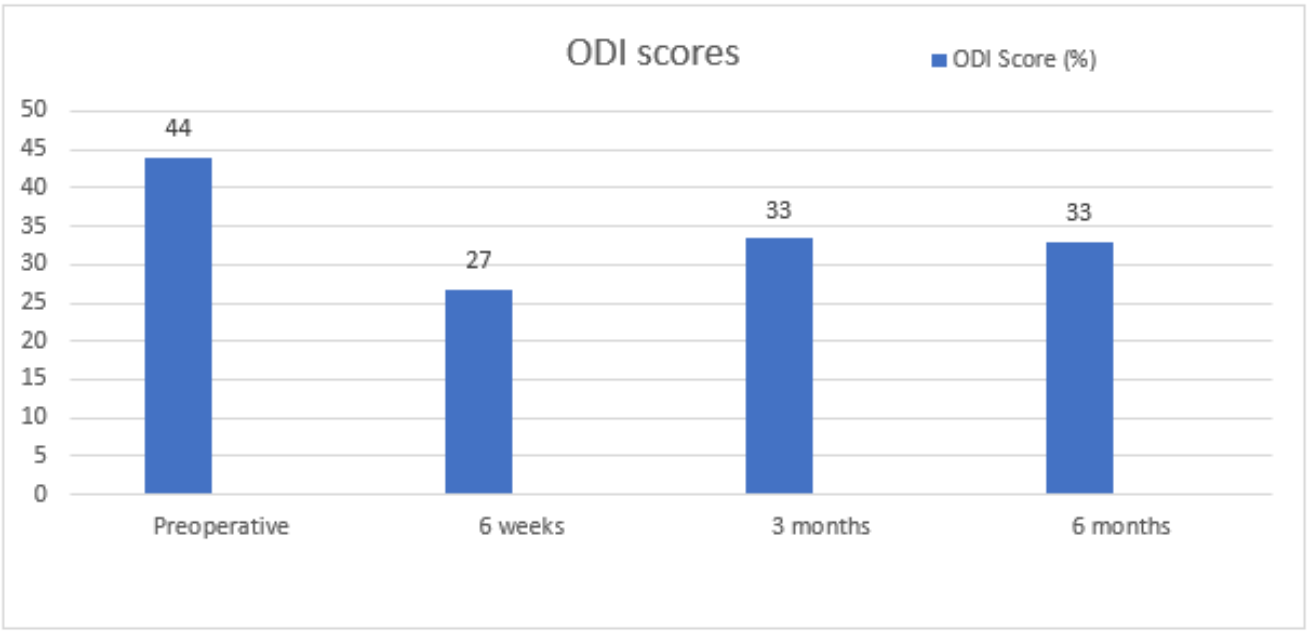

Figure 3: Oswestry Disability Index (ODI).

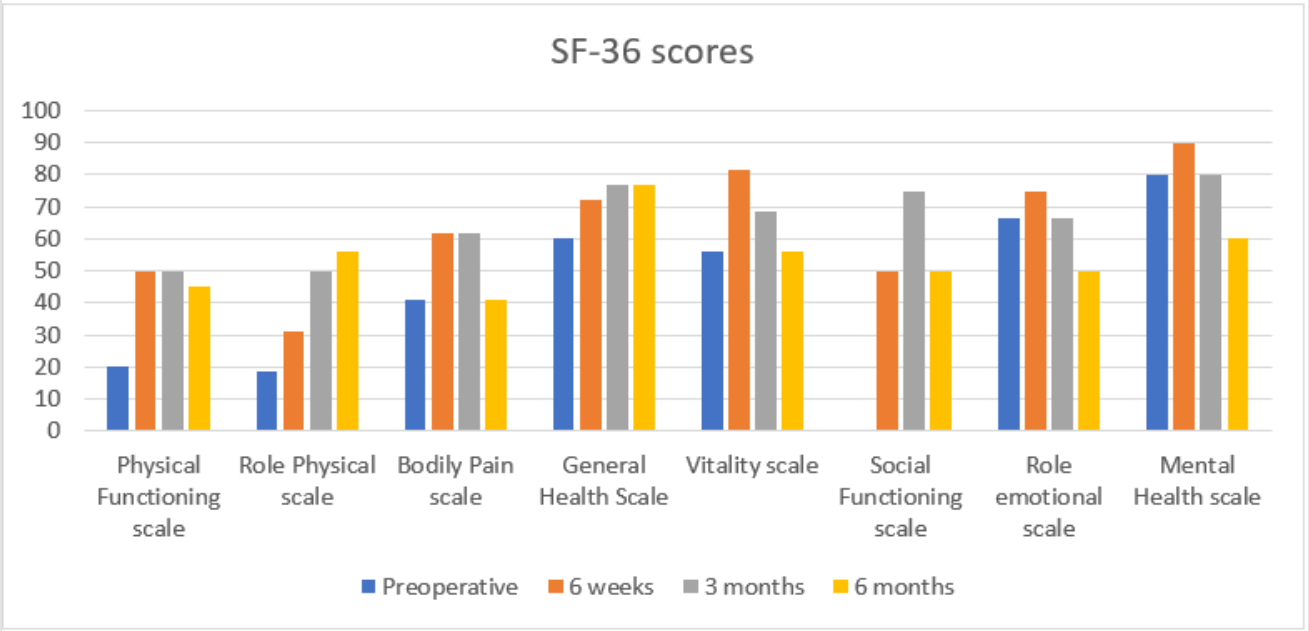

Figure 4: SF-36 Health Survey results.

(Figure 4) shows that the patient experienced rapid improvement in Physical Functioning, Role Physical, and General Health, with maintenance in other physical categories which correlate well with the positive clinical and radiographic outcomes seen up to 6 months. There were no intraoperative or post-operative device-related adverse events through the 6-month follow-up visit. The patient presented with a gallstone on their fourth post-operative day and was treated with diet and other supportive treatment until released from the hospital without symptoms.

Discussion

The results indicate that this first patient showed evidence of

progressing bone growth and healing at 3 months post-op and was evaluated to have achieved both interbody and posterolateral spine fusion at 6 months. These results are very encouraging, however, the results must be considered preliminary as this was a single case and bone healing rates can be variable depending on the individual patient's general health and risk factors. As evidenced by the encouragingly positive pre-clinical studies with this bone graft substitute [1,2], if OssDsign Catalyst is also shown to be osteoinductive in humans, it would be interesting to assess its potential for use in metabolically challenged patients (e.g., osteoporotic, immobilization, nutritional deficiencies, diabetic or heavy smokers), which are known to be slower healers and difficult to fuse with lower expectations of a good clinical outcome [8] The surgeon in this case was pleased with the handling characteristics of this synthetic bone graft and indicated its ease of use in placement in the various areas of the surgical construct (within the interbody cage, along the posterolateral gutters). The risk of graft migration and heterotopic bone formation are minimized by suspending the OssDsign Catalyst granules in a gel carrier to create a malleable putty formulation.

Conclusion

The first-in-patient use of OssDsign Catalyst bone graft was successful in achieving rapid bone healing and spinal fusion with corresponding improvement of pain and function, with no neurological degradation or device-related adverse events through the six-month follow-up.

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