Evaluation of an Increased Strut Porosity Silicate-Substituted Calcium Phosphate, SiCaP EP, as a Synthetic Bone Graft Substitute in Spinal Fusion Surgery: A Prospective, Open-Label Study

In a prospective, open-label, multicenter comparative study in 102 patients with degenerative spinal disorders requiring posterolateral fusion (PLF), INDUCTIGRAFT Osteoinductive Bone Graft Substitute provided high spinal fusion success rates and improved clinical outcomes related to baseline.[1]

Key Points

- The high microporosity of INDUCTIGRAFT Osteoinductive Bone Graft Substitute may further encourage natural bone growth and increase the likelihood of successful fusion.
- Successful fusion was achieved in 90.6% of patients at month 24.
- The fusion rate of 86.3% at month 12 with INDUCTIGRAFT Osteoinductive Bone Graft Substitute is an improvement in rates of 52–80%, observed with traditional autologous iliac crest and allograft material in PLF surgery.

Overview

Posterolateral fusion (PLF) surgery coupled with stabilizing rigid instrumentation is a reliable spinal fusion technique.[2] Iliac crest has been used as a bone graft material,[3] but it may be associated with complications at the donor site including hematoma, scarring and infection.[4,5]

INDUCTIGRAFT Osteoinductive Bone Graft Substitute is a silicate-substituted calcium phosphate (SiCaP EP) synthetic bone graft with enhanced porosity that was developed to further increase bone formation by mimicking the microporous osteocyte lacunae network presented in physiological bone.[1,6] In vitro studies demonstrate that INDUCTRIGRAFT supports greater cell proliferation and early osteoblastic differentation than earlier formulations, and Bioglass 45S5, in the absence of external osteogenic factors.[7]

An open-label, Phase IV, prospective, multicenter study was conducted in 15 research sites (UK, Germany, Spain, Hungary and the Republic of Ireland).[1] Patients underwent PLF surgery with INDUCTIGRAFT as the sole graft material which contains phase-pure, porous SiCap granules (1–2 mm; 80–85% total porosity, 31–47% micro (or strut) porosity and 0.8% Si by weight). Approximately 20 mL was placed in the posterolateral gutters.

The primary endpoint was evaluated in the per protocol population (N=102) as solid fusion at postoperative month 12 assessed using computed tomography (CT) scans, with motion assessed using flexion-extension radiographs.

Fusion was measured using CT scans performed at a central core laboratory. Successful fusion was defined as solid unilateral fusion (Grade 4) or solid bilateral fusion (Grade 5) detected by the presence of bone bridging adjacent vertebral bodies through or around the implants. Successful fusion was also defined by the absence of motion between the fused vertebral bodies for all treated vertebral levels ($\leq$ 3 mm difference in transitional motion and $<$ 5° difference in angular motion). For patients who received PLF surgery at two vertebral levels, fusion was considered successful if both levels fused. If fusion was absent at month 12, patients were re-assessed at 24 months.

Clinical outcomes included the Oswestry Disability Index (ODI), 36-Item Short-Form Health Survey for quality of life, visual analogue scale (VAS) for pain scores and neurological assessments. Adverse events were recorded.

Results

Patients had a mean age of 51.9 years and mean weight of 78.0 kg; body mass index (BMI) was 27.25 kg/m^2.[1] The proportion of males (n=59 [45.7%]) and females (n=70 [54.3%]) was similar and the prevalence of smokers was 27.6%. Most patients had a diagnosis of degenerative disc disease (n=79 [61.2%])(**Table 1**).

Table 1. Primary Diagnoses

Diagnosis	Number [Percentage]
Degenerative Disc Disease	n=79 [61.2%]
Spinal Stenosis	n=21 [16.3%]
Spondylolisthesis	n=27 [20.9%]
Degen. Spondylolisthesis	n=21 [16.3%]
Isthmic Spondylolisthesis	n=6 [4.7%]

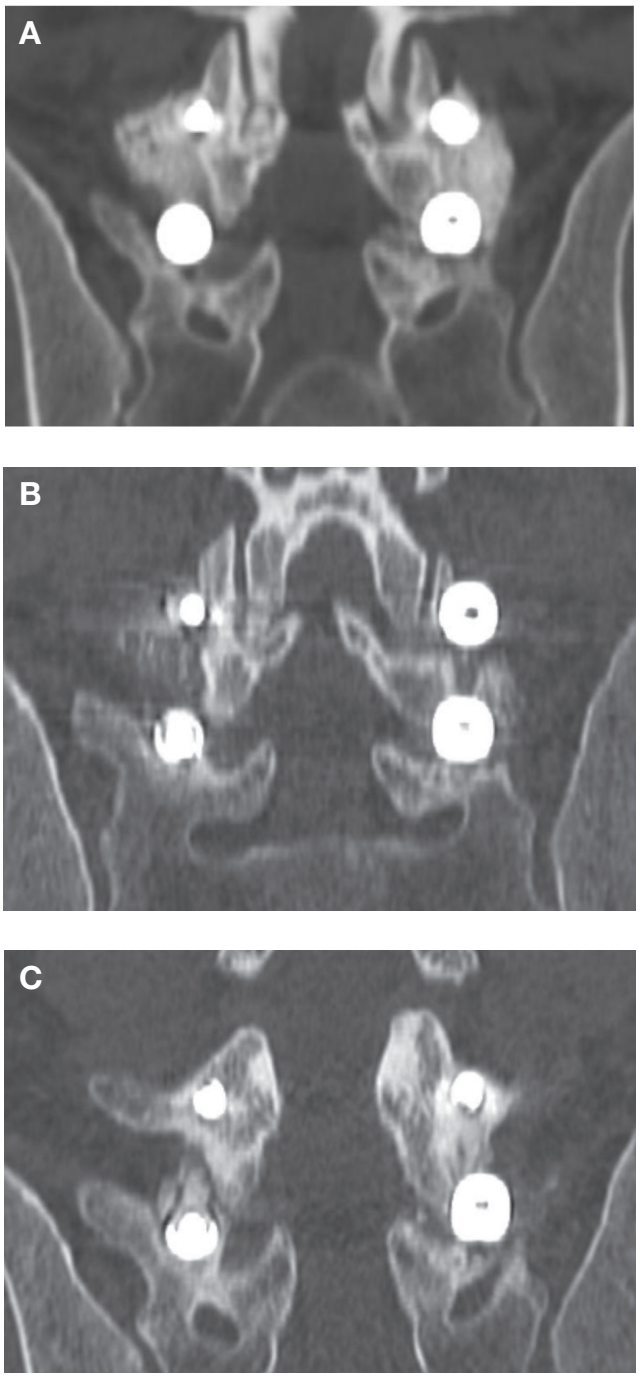
Successful fusion was achieved in 59/89 (66.3%) patients at month 6, 88/102 patients (86.3%) at month 12 (primary endpoint) and in 87/96 (90.6%) patients at month 24 (**Table 2**)(**Figure 1**- see next page).[1]

Table 2. Spinal Fusion Success

Visit	Fusion Success (n/N)	Rate %	95% CI
6 months	59/89	66.3%	55.5-76.0
12 months	88/102	86.3%	78.0-92.3
24 months	87/96	90.6%	82.9-95.6

Mean change from baseline ODI scores crossed the defined threshold of 15% for improvement from

Figure 1. Representative CT scans to illustrate development of fusion. At 6 months (A), patient displays Grade 3 Glassman fusion. Signs of partial bridging with graft material are present. At 12 months (B) and 24 months (C) a complete bridge is visible bringing the patient to Grade 4. The bridge was faint at 12 months, but more pronounced at 24 months.



baseline. At months 6, 12 and 24, mean change in ODI scores were –20.6 (n=87), –22.4 (n=97) and –19.7 (n=14), respectively (**Table 3**). VAS scores demonstrated patients had reduced pain levels for the majority of measured pain domains at month 6 and month 12. Quality-of-life improved and neurological function was maintained postoperatively.[1]

Table 3. Oswestry Disability Index (ODI) Scores

VISIT	Mean Score	Mean Change [P]
Baseline	46.6 (n=99)	---
6 months	26.2 (n=88)	-20.6 (n=87)[<0.0001]
12 months	24.4 (n=100)	-22.4 (n=97)[<0.0001]
24 months	33.4 (n=17)	-19.7 (n=14)[0.0105]

Forty-three (33.3%) of the 129 patients experienced adverse events. Back pain was the most frequent event (9 patients/7%); serious adverse events judged related to device and procedure were experienced in 9 patients (7%).[1] Despite complications arising from adverse events, the rates were well within the range expected, and it is known that these events frequently occur during follow-up periods.[8]

Discussion and Conclusions

This was the first prospective evaluation of efficacy and safety of INDUCTIGRAFT in patients with degenerative disc disease, spondylolisthesis and spinal stenosis undergoing instrumented PLF procedures. The primary endpoint of solid fusion at month 12 was achieved in 86.3% of patients, accompanied by clinically significant decreases in disability at all follow-up visits. Patients also reported reductions in pain and an improved quality-of-life post-surgery. Motor, sensory functions, reflexes, straight leg raise and femoral stretches were either maintained or improved in over half of patients. The study design did not include a comparator treatment, so no direct comparison can be made. However, the fusion rate of 86.3% at month 12 with INDUCTIGRAFT is an improvement in rates of 52–80%, observed with traditional autologous iliac crest and allograft material in PLF surgery.[1,9,10]

Instrumented PLF is a reliable technique leading to lasting improvement,[2] however, care should be taken when comparing fusion rates as these vary according to surgery type. Previous studies have used SiCaP with strut porosities of 20–25% in a range of surgical procedures. In a retrospective study of 42 patients who underwent PLF with SiCaP as the bone graft material, fusion rates of 76% were observed.[11] In retrospective studies, 108 patients who underwent spinal fusion procedures, including PLF with SiCaP, fusion rates of 90% were demonstrated at a follow-up of 12±4.7 months.[8] The fusion rate of 86.3% achieved in the current study falls within the range of previous SiCaP studies.

In summary, the current study satisfies the hypothesis by demonstrating fusion success in PLF surgery using INDUCTIGRAFT with a higher strut porosity of up to 47%. The high microporosity allows for bone implant contact which may further encourage natural bone growth and increase the likelihood of successful fusion. The results of this study indicate the potential use of INDUCTIGRAFT in instrumented PLF surgery.[1] Further studies are warranted to investigate the long-term effects and quality of natural bone formation.

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