



# Ceramic bone graft substitute vs autograft in XLIF: a prospective randomized single-center evaluation of radiographic and clinical outcomes

Cristiano Magalhães Menezes<sup>1,2</sup> · Gabriel Carvalho Lacerda<sup>1,2</sup> · Germano Senna Oliveira do Valle<sup>1,2</sup> · André de Oliveira Arruda<sup>1</sup> · Erica Godinho Menezes<sup>1,3</sup>

Received: 10 September 2021 / Revised: 8 May 2022 / Accepted: 23 May 2022 / Published online: 20 June 2022  
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

## Abstract

**Purpose of the Study** The objective of this prospective, parallel, randomized, single-center study is to evaluate the clinical success of a commercial ceramic bone graft substitute (CBGS) for autograft in eXtreme Lateral Interbody Fusion (XLIF) procedures.

**Methods** Forty-five adult subjects were consecutively enrolled and randomized into a single-level XLIF procedure using either CBGS or iliac crest bone graft autograft (30 and 15 subjects, respectively). The primary outcome was fusion rate at 12, 18, and 24 months. Secondary outcomes were pain and disability measured by HRQOL questionnaires.

**Results** The fusion rates for both CBGS and autograft groups at the 24-month follow-up were 96.4% and 100%, respectively. For the CBGS group, mean ODI, mean back pain, and mean worst leg pain significantly improved at the 24-month follow-up by 76.7% (39.9–9.3), 77.6% (7.3–1.6), and 81.3% (5.1–1.0), respectively. For the autograft group, mean ODI, mean back pain, and mean worst leg pain significantly improved during the same time period by 77.1% (35.9–8.2), 75.6% (6.1–1.5), and 86.0% (6.6–0.9), respectively (all time points between groups,  $p < 0.05$ ).

**Conclusion** The results of this prospective, randomized study support the use of CBGS as a standalone bone graft substitute for autograft in single-level XLIF surgery. The clinical performance and safety outcomes reported here are consistent with published evidence on CBGS. Improvements in patient-reported back pain, leg pain, and disability outcomes were comparable between the CBGS and autograft groups.

**Keywords** XLIF · Ceramic bone graft · Biologics · Fusion · Spinal fusion · Randomized clinical trial

## Introduction

Extreme Lateral Interbody Fusion (XLIF) is a minimally invasive spine surgery technique developed to decrease surgical morbidity and increase the biomechanical stability of anterior column, promoting satisfactory indirect decompression [1, 2]. Most of the XLIF procedures are supplemented by percutaneous pedicle screw fixation in order to improve stability. This approach does not compromise posterior tension bands nor promote injury to the posterior musculature

attached to the spine. It requires, however, posterior fixation, which increases operative time in the procedure of changing operating room settings and patient positioning from lateral to prone. Single position lumbar fusion surgery (SPLS) has been developed as an alternative performed in lateral decubitus position [3].

Several studies were conducted to establish fusion rates in XLIF, but few of them compare different types of graft material [4–7]. Classically, autologous bone grafting (ABG) has been used to create large fusion masses [7]. Autologous iliac bone graft is the 'gold standard' due to its three desirable properties: osteogenicity, osteoinductivity, and osteoconductivity [8, 9]. Nevertheless, graft harvesting can implicate higher morbidity and complications such as chronic pain at the donor site [10–12]. Different kinds of materials have been developed in order to promote solid fusion at the same time that reduce morbidity. They act as osteoconductive

✉ Cristiano Magalhães Menezes  
cristiano@columnainstituto.com

<sup>1</sup> Columna Institute, Belo Horizonte, Brazil

<sup>2</sup> Vila da Serra/Ortopédico Hospital, Belo Horizonte, Brazil

<sup>3</sup> UniBH University, Belo Horizonte, Brazil

scaffolds, designed to insert osteogenic material [13]. Furthermore, synthetic bone grafts have emerged in an attempt to avoid or minimize complications of autograft harvest [11].

Bone Morphogenetic Proteins (BMPs) emerged in this context. The literature data show that BMPs are effective when compared to iliac crest bone graft, although its higher costs and some safety concerns due to reported complications [14–16]. Allogeneic demineralized bone matrix (DBM) is another type of bone graft material as an alternative to ABG. It has osteoinductive qualities and can serve as the three-dimensional scaffold to support new tissue growth [17]. Based on the available evidence, the use of DBM as an autograft bone extender in posterolateral lumbar spine fusion and lumbar interbody fusion shows a similar fusion rate compared to autograft alone [18–20]. Although the results of DBM in satisfactory fusion seemed solid, it has a high cost and its use is not universally approved.

A new generation of synthetic ceramic bone graft substitutes has gained popularity as they intimately resemble natural bone with intrinsic osteoinductive properties due to their specifically engineered surface microarchitecture, designed to induce cell differentiation and drive bone fusion [9, 10]. CBGS is a synthetic bone material composed of tricalcium phosphate (TCP) granules with a polymeric binder able to promote spinal fusions similar to autologous bone graft. Studies demonstrated non-inferior fusion results and support CBGS as a standalone bone graft substitute for autograft in instrumented thoracolumbar postero-lateral fusion [21, 22].

This is the first comparative interbody fusion study to evaluate the clinical success of CBGS as a bone graft substitute for autograft in XLIF procedures. It was conducted in the scenario of less morbid and less invasive surgery, looking for a cost-effective graft substitute in order to avoid bone harvesting.

## Materials and methods

A total of 45 adult subjects were consecutively enrolled and randomized to a single-level XLIF procedure using either the commercial CBGS Attrax Putty or iliac crest bone graft (ICBG) autograft with an allocation ratio of 2:1 (30 subjects in the CBGS group and 15 subjects in the ICBG group). A 1:1 treatment allocation was originally planned, but due to study delays and enrollment challenges, the treatment allocation was changed to 2:1 mid-study. For those patients who had given informed consent to participate, a random envelope containing a randomization number was drawn and the biologic used during the XLIF procedure was determined. Patient and surgeon were blinded to the biologic to be used until 48 h prior to surgery (or as required per surgical planning timelines), at which time the surgeon and staff were unblinded to accommodate scheduling and ordering

of appropriate equipment and operating room preparation. All subjects were diagnosed with degenerative conditions of the lumbar spine at one level and underwent XLIF with posterior supplemental fixation in single position. All surgical procedures were performed by the same senior spine surgeon (CMM), between 2015 and 2019, in a single tertiary center, in Brazil. The follow-up period was 24 months.

Exclusion criteria were: (1) prior fusion at the operative level; (2) prior failed fusion at any level; (3) concomitant diseases that significantly inhibit bone healing; (4) ongoing treatment with drugs interfering in calcium metabolism; and (5) fail to obtain informed written consent.

Radiographic surveillance consisted of standard radiographs at 15 days and 3 months; flexion and extension studies at 6, 12, 18, and 24 months; CT evaluation at 18 months to check fusion. Patients remained under clinical supervision, with scheduled visits in which they underwent physical examination and were invited to answer HRQOL questionnaires.

The primary outcome was fusion rate at 12, 18 and 24 months. Fusion grade was classified according to the criteria of Lenke and Bridwell [23] by a qualified, independent reviewer. Secondary outcomes were pain and disability, measured by Visual Analogue Scale (VAS)—patient-reported back pain, worst leg pain, and iliac crest harvest site pain—and scores of Oswestry Disability Index (ODI) and EuroQol 5D-3L (EQ-5D-3L).

Patient complications were identified and reported throughout the study. Pseudarthrosis and other situations that required intervention or simple/complex treatment, with or without long-term, temporary or prolonged adverse effects or death, were considered complications. They were classified as “XLIF procedure related” or not, both in the CBGS and autograft groups.

The statistical analysis was carried out using JMP Software from SAS (JMP®, version 15. SAS Institute Inc., Cary, NC, 1989–2021). All measures were compared using independent *t*-tests and Chi-squared analyses with significance set at  $p < 0.05$ . Minimum clinically important difference (MCID) values were adopted as 12.8 points for ODI, 1.2 for back pain, and 1.6 points for leg pain [24]. Substantial clinical benefit (SCB) thresholds for the ODI Index were an 18.8-point net improvement, a 36.8% improvement or a final raw score of  $< 31.3$  points. SCB thresholds for the back and leg pain numeric rating scales were a 2.5-point net improvement or a final raw score of  $< 3.5$  points [25].

## Results

From March 2015 to April 2019, a total of 45 subjects were included in the study. Patient baseline demographics and clinical characteristics are described in Table 1. The

**Table 1** Baseline patient demographics and clinical characteristics

Characteristic	Statistic
<i>Age in years</i>	
Mean (stdev)	57.04 (3.8)
Minimum, maximum	32, 79
Female (%)	51
<i>BMI (kg/m<sup>2</sup>)</i>	
Mean (stdev)	26.82 (4.1)
Minimum, maximum	19.7, 44.0
<i>Comorbidities</i>	
Hypertension (%)	27
Diabetes (%)	22
Osteoporosis (%)	2
Smoker (%)	7

majority of the population was female (51%), and the mean age was  $57.04 \pm 3.8$  years old (range from 33 to 79). History of smoking was reported by seven percent of subjects. The most common comorbidities at baseline were hypertension (27%) and diabetes (22%), with one subject (2%) diagnosed with osteoporosis.

Subjects were divided in two groups, with 30 subjects being treated with CBGS and 15 with autograft. Most surgeries were performed at L4–L5 level (88.8%;  $n = 40$ ), with only five (11.2%) at L3–L4. The preferred approach side was the left ( $n = 40$ ). Mean procedure time was  $76.57 \pm 14.79$  min for the CBGS group and  $76.28 \pm 14.14$  min for the autograft group. Mean hospital stay was  $1.38 \pm 0.46$  days for CBGS subjects and  $1.56 \pm 0.67$  days for autograft subjects (Table 2). Estimated blood loss < 100 mL was observed in 86.7% versus 80.0% of CBGS and autograft subjects, respectively ( $p > 0.05$ ). These results are summarized in Table 3.

Forty-two subjects ( $n = 28$  CBGS group;  $n = 14$  autograft group) completed their 24-month follow-up with patient related outcomes (PROs) and Lenke Grade assessments.

**Table 2** Length of surgery and hospital stay

	CBGS ( $n = 30$ subjects)	Autograft ( $n = 15$ subjects)	<i>p</i> value
Mean length of surgery (min) (Length of surgery for Autograft group includes harvest time)	76.57 (39.6)	76.28 (24.5)	0.98
Mean length of hospital stay (days)—mean (stdev) (assumption: less than 24 h stay = 0.5 days)	1.38 (1.2)	1.56 (1.2)	0.64

**Table 3** Blood loss

	< 50	50–100	101–200	201–300	> 300
CBGS (cc)— <i>n</i> (%)	16 (53.3)	10 (33.3)	2 (6.7)	2 (6.7)	0 (0.0)
Autograft (cc)— <i>n</i> (%)	4 (26.7)	8 (53.3)	1 (6.7)	1 (6.7)	1 (6.7)
<i>p</i> -value	0.1185	0.1967	1.000	1.000	0.3333

*n* number of subjects (normalized to the total number of subjects in each respective cohort)

The fusion status at 12, 18, and 24 months is summarized in Table 4. The number of patients available for assessment at each time point was used to calculate the fusion rate. At 24 months, all subjects from the autograft group had a fusion rate of at least grade II with graft effectively incorporated (Fig. 1). In the CBGS group, 27 subjects (96.4%) were considered fused (Fig. 2), with one case of pseudarthrosis (3.6%). Two subjects were lost to follow-up at three months and one subject died due to Covid-19 infection before completing the study.

Seventeen subjects (37.8%; nine in CBGS and eight in autograft group) experienced complications, for a total of 19 events (Table 5). One subject from the autograft group experienced two different complications. All complications resolved without sequelae, except for one (death due to Covid-19 infection).

The complications were classified as “XLIF procedure related” or not. Twelve complications related to XLIF were reported in twelve subjects (26%), six in each group (Table 6). The most common complication was cage migration ( $n = 6$ ), but this was mild in all cases (< 3 mm) with no cage expulsion and complete fusion at 24 months. Other complications were: psoas hematoma with neural compression resulting in radiculopathy and neurological abnormality ( $n = 1$ ); deep wound infection requiring reoperation ( $n = 1$ ); incisional hernia requiring operation ( $n = 1$ ); anterior longitudinal ligament (ALL) rupture, resolved with a locked cage ( $n = 1$ ); mild postoperative neuropathic pain ( $n = 1$ ); and moderate degeneration of adjacent level ( $n = 1$ ).

Clinical outcomes were assessed by HRQOL questionnaires, with groups stratified by pain and disability. Mean pre-operative ODI in the CBGS group was 39.9 and after 24 months was 9.3 (Fig. 3). In the autograft group, mean ODI before surgery was 36.1, and 8.2 at the last follow-up (Fig. 4). VAS clinical results were divided into back and worst leg pain (WLP) and iliac crest scores. Mean VAS for back pain (BP) in the CBGS group was 7.3 preoperatively, 3.2 at one month, and 1.6 at the last follow-up. In the autograft group, mean BP was 6.1 preoperatively, 3.6 at one month, and 1.5 at 24 months. Mean VAS for WLP in the CBGS group was 5.1 preoperative, 1.6 at three month, and 1.0 at the last follow-up. In the autograft group, mean WLP was 6.6 preoperatively, 2.5 at three

**Table 4** Lenke Grade assessment

Lenke grade	12 months ( <i>n</i> = 27 subjects)		18 months ( <i>n</i> = 32 subjects)		24 months ( <i>n</i> = 42 subjects)	
	CBGS ( <i>n</i> = 16)	Autograft ( <i>n</i> = 11)	CBGS ( <i>n</i> = 21)	Autograft ( <i>n</i> = 11)	CBGS ( <i>n</i> = 28)	Autograft ( <i>n</i> = 14)
Grade I	4 (25.0%)	6 (54.5%)	9 (42.9%)	7 (63.6%)	22 (78.6%)	10 (71.4%)
Grade II	11 (68.8%)	5 (45.5%)	12 (57.1%)	4 (36.4%)	5 (17.9%)	4 (28.6%)
Grade III	1 (6.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)
Fusion rate (Grade I and Grade II)	93.8%	100.0%	100.0%	100.0%	96.4%	100.0%



**Fig. 1** Sagittal view CT Scan 18 m fusion (autograft group)



**Fig. 2** Sagittal view CT Scan 18 m fusion (CBGS group)

month, and 0.9 at 24 months. Mean VAS for worst iliac crest pain (WIP) in the CBGS group was 0.3 preoperatively, 0.4 at one month, and 0.3 at the last follow-up. In the autograft group, mean WIP was 0.4 preoperatively, 1.5 at one month, and 0.4 at 24 months. Preoperative EQ-5D index level of the CBGS group was 0.56 and increased to 0.82 at last follow-up. In the autograft group, it was 0.63 before surgery and increased to 0.94 at 24 months. The results for MCID and SCB are summarized in Tables 7 and 8, respectively.

**Table 5** Complications in all subjects

Complication at any time point ( <i>n</i> = 45 subjects)		
	Yes	No
CBGS— <i>n</i> (%)	9 (30)	21 (70)
Autograft— <i>n</i> (%)	8 (53.3)	7 (46.7)
	<i>p</i> -value	0.1280

*n* number of subjects (normalized to the total number of subjects in each respective cohort)

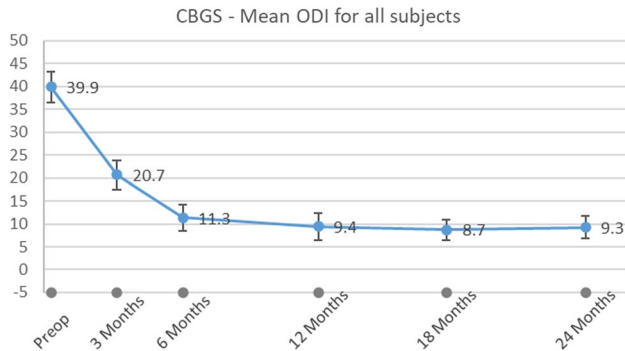
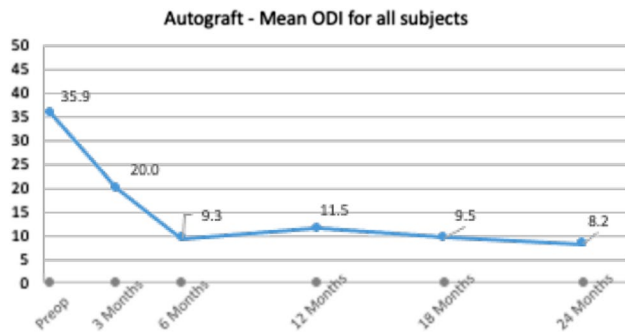
### Discussion

The fusion capacity in XLIF is widely known in the literature, mostly due to its capability to produce a sizable grafting area for insertion of large and stable cage, while

**Table 6** Complications related to procedure

Relationship to procedure ( <i>n</i> = 19 complications)		
	Yes	No
CBGS— <i>n</i> (%)	6 (66.7)	3 (33.3)
Autograft— <i>n</i> (%)	6 (60)	4 (40)
	<i>p</i> -value	1.0000

*n* number of complications (normalized to the total number of complications in each respective cohort)

**Fig. 3** Mean ODI—CBGS group**Fig. 4** Mean ODI—autograft group

preserving the anterior and posterior ligaments, favouring consolidation. This study compares different grafts for interbody fusion and evaluates the clinical success of CBGS as a bone graft substitute in XLIF procedures.

With the potential to assemble ceramics with bioactivity, there is escalating interest in these materials as standalone bone graft substitutes. Ceramic matrices are inorganic, ionically bonded preparations that embrace a vast collection of bone graft substitutes. Porosity permits mesenchymal cell adhesion, proliferation, and differentiation into mature osteoblasts [26, 27].

Nickoli and Hsu [26] conducted a systematic review on the efficacy of ceramic-based bone grafts in lumbar spinal fusion. The authors found 86.4% overall fusion rate

for all ceramic products as bone graft extender. Malhalm and Parker [28] performed a comparative study between beta tricalcium phosphate ( $\beta$ -TCP/CBGS) and recombinant human bone morphogenetic protein-2 (rhBMP-2/Infuse (Medtronic, Memphis, TN, USA)) for fusion rates and clinical outcomes in lateral lumbar interbody fusion. Fusion percentage for CBGS was 80% in 25 patients after 24 months, with no significant difference for rhBMP-2 at all follow-up points. In a study with 44 patients treated with XLIF with a ceramic-based bone grafting material, Rodgers et al. [29] reported 93.2% of fusion at follow-up period (mean 17.3 months).

Ceramics alone in XLIF procedures have been associated with fusion rates ranging from 76.3% (mean follow-up time of  $14.21 \pm 4.3$  months) to 93% mean follow-up  $21 \pm 14.2$  months) [30]. A study conducted by Pimenta et al. [31] compared stand-alone lateral interbody lumbar fusion with either silicate calcium phosphate or rh-BMP2 in 30 patients. After a 36-month follow-up period, 100% of XLIF patients achieved solid fusion.

Lehr et al. [22], in a randomized noninferiority trial of 100 patients, demonstrated that CBGS used individually provided fusion rates similar to autograft. Autograft was applied to the contralateral side of fusion trajectory implanted with CBGS. Fusion rate was 52% for autograft group and 55% for CBGS patients. In a different cohort who underwent XLIF procedures, Berjano et al. [6] studied the differences in fusion rates in 78 levels in 53 patients and the results revealed similar fusion rates for autograft, calcium triphosphate, and CBGS—75%, 89%, and 83%, respectively—as determined by CT at one year postoperatively. The differences in fusion rate by graft material (CBGS vs. calcium triphosphate) were not statistically significant (*p* value 0.837).

The fusion status at 24 months on this series corroborates that CBGS used in XLIF promotes a high fusion rate. In our study, 96.4% of the individuals in the CBGS group were considered fused at last follow-up. No statistically significant differences were found between CBGS and autograft groups. This result shows a slightly higher fusion rate than those previously demonstrated in the literature [6, 22, 28].

The results in our series endorse clinical outcomes previously shown in various reports. Rodgers et al. [29] found a reduction in VAS for BP, after 12 months, from  $8.2 \pm 1.2$  to  $4.8 \pm 3.1$ , VAS for WLP from  $7.9 \pm 2.0$  to  $3.7 \pm 3.1$ , and in ODI of  $50.9 \pm 15.2\%$  to  $33.1 \pm 19.6\%$ . Parker [28] recorded a reduction in ODI from 56.9 preoperatively to 33.5 at the last follow-up. Berjano [6] results for ODI, VAS for BP, and WLP after fusion in final follow-up were 19.0, 2.3, and 2.2, respectively. Lehr et al. [22] reported no significant difference between clinical outcomes of CBGS or rhBMP-2 patients, with similar improvements in BP (46% and 49%; *p*=0.98), WLP (31 and 52%; *p*=0.14) and ODI (38 and 41%;

**Table 7** Minimal Clinically Important Difference (MCID)

Groups	MCID_ODI		MCID_BP		MCID_WLP		MCID_EQ-5D-3L	
	Yes	No	Yes	No	Yes	No	Yes	No
CBGS ( <i>n</i> = 28)	24 (85.7%)	4 (14.3%)	26 (92.9%)	2 (7.1%)	24 (85.7%)	4 (14.3%)	15 (53.6%)	13 (46.4%)
Autograft ( <i>n</i> = 14)	14 (100%)	0	12 (85.7%)	2 (14.3%)	11 (78.6%)	3 (21.4%)	10 (71.4%)	4 (28.6%)
<i>p</i> -value*	0.2829		0.5902		0.6685		0.3308	

\**p*-value assessed by *t*-test using JMP v.15

**Table 8** Substantial Clinical Benefit (SCB)

Groups	SCB_ODI		SCB_BP		SCB_WLP	
	Yes	No	Yes	No	Yes	No
CBGS ( <i>n</i> = 28)	24 (85.7%)	4 (14.3%)	26 (92.9%)	2 (7.1%)	23 (82.1%)	5 (17.9%)
Autograft ( <i>n</i> = 14)	14 (100%)	0	11 (78.6%)	3 (21.4%)	11 (78.6%)	3 (21.4%)
<i>p</i> -value*	0.2829		0.3126		1.000	

\**p*-value assessed by *t*-test using JMP v.15

*p* = 0.81). In our series, a mean ODI improvement of 76.7% was observed in the CBGS group and of 77.1% in the autograft group. Mean VAS for BP in the CBGS group was 7.3 preoperatively and 1.6 at the last follow-up, whereas mean VAS for WLP was 5.1 preoperatively and 1.0 at 24 months. There was no statistical difference between groups for any of the clinical outcomes measured. These results support the possibility of achieving not only fusion rates comparable with "gold standard" iliac bone autograft, but also similar clinical outcomes without the morbidity of bone graft harvesting.

This series corroborates the efficiency of single position lumbar fusion surgery (SPLS), a novel minimally invasive alternative performed entirely in lateral decubitus position. SPLS decreases operative time (OpTime), blood loss (EBL), length of stay (LOS), and subsequent complications of prolonged anesthesia. Buckland et al. [3] studied 390 patients undergoing lumbar fusion surgery, of which 237 underwent SPLS and 153 were in the lateral-then-prone group. SPLS significantly reduced OpTime (103 min vs 306 min, *p* < 0.001), EBL (97 vs 313 mL, *p* < 0.001), LOS (1.71 vs 4.12 days, *p* < 0.001). The results of our series are similar for both groups treated with XLIF in SPLS: mean OpTime was < 90 min for both groups; the majority of subjects had EBL < 100 mL; LOS was 1,38 ± 0,46 days for the CBGS group and 1,56 ± 0,67 for the autograft group.

## Conclusion

The results of this prospective, randomized study support the use of CBGS as a standalone bone graft substitute for autograft in single-level XLIF surgery. The clinical

performance and safety outcomes reported here are consistent with published evidence on CBGS. Improvements in patient-reported back pain, leg pain and disability outcomes were comparable between the CBGS and autograft groups.

**Acknowledgements** The study was supported by NuVasive and incorporated as follows: Greg Williams, PhD, and Sara Thompson, MS, involved in writing—review and editing; Diane Vang, Fatemeh Nooshabadi, PhD, Lee Honig, PhD, took part in analysis.

**Authors' contributions** CMM, contributed to the study conception and design, material preparation, data collection, and writing of the manuscript. GCL, contributed to the study data collection and writing of the manuscript. GSO do V, contributed to the study data collection and writing of the manuscript. A de OA, contributed to the study data collection. EGM, contributed to the writing of the manuscript.

**Funding** This study was sponsored by NuVasive, Incorporated (7475 Lusk Boulevard, San Diego, CA 92121 USA).

**Availability of data and material** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Code availability** SAS JMP version 15 and MS Excel.

## Declarations

**Conflict of interest** Cristiano M Menezes involved in consulting, research grants, and product development, NuVasive. All other authors do not have any conflict.

**Consent to participate** All subjects who participated in this study signed an informed consent form (ICF). The ICFs are available upon request.

**Consent for publication** Identifying details of the participants will not be published; therefore, consent for publication is not applicable.

**Ethical approval** Reviewed and approved by the ethics committee at the São Francisco Hospital Foundation on December 23, 2014.

**Humans or animals rights** Not applicable.

## References

- Ozgun BM, Aryan HE, Pimenta L, Taylor WR (2006) Extreme lateral interbody fusion (XLIF): a novel surgical technique for anterior lumbar interbody fusion. *Spine J* 6(4):435–443. <https://doi.org/10.1016/j.spinee.2005.08.012> (PMID: 16825052)
- Pereira EA, Farwana M, Lam KS (2017) Extreme lateral interbody fusion relieves symptoms of spinal stenosis and low-grade spondylolisthesis by indirect decompression in complex patients. *J Clin Neurosci* 35:56–61. <https://doi.org/10.1016/j.jocn.2016.09.010> (Epub 2016 Oct 1 PMID: 27707614)
- Buckland AJ, Ashayeri K, Leon C, Manning J, Eisen L, Medley M, Protopsaltis TS, Thomas JA (2021) Single position circumferential fusion improves operative efficiency, reduces complications and length of stay compared with traditional circumferential fusion. *Spine J* 21(5):810–820. <https://doi.org/10.1016/j.spinee.2020.11.002> (Epub 2020 Nov 13 PMID: 33197616)
- Rodgers WB, Gerber EJ, Patterson JR (2010) Fusion after minimally disruptive anterior lumbar interbody fusion: analysis of extreme lateral interbody fusion by computed tomography. *SAS J* 4(2):63–66. <https://doi.org/10.1016/j.esas.2010.03.001> (PMID: 25802651; PMCID: PMC4365611)
- Malham G, Ellis N, Parker R, Seex K (2012) Clinical outcome and fusion rates after the first 30 extreme lateral interbody fusions. *Sci World J*. <https://doi.org/10.1100/2012/246989>
- Berjano P, Langella F, Damilano M, Pejrona M, Buric J, Ismael M, Villafañe JH, Lamartina C (2015) Fusion rate following extreme lateral lumbar interbody fusion. *Eur Spine J* 24(Suppl 3):369–371. <https://doi.org/10.1007/s00586-015-3929-7> (Epub 2015 Apr 17 PMID: 25893332)
- Dimar JR 2nd, Glassman SD, Burkus JK, Pryor PW, Hardacker JW, Carreon LY (2009) Two-year fusion and clinical outcomes in 224 patients treated with a single-level instrumented posterolateral fusion with iliac crest bone graft. *Spine J* 9(11):880–885. <https://doi.org/10.1016/j.spinee.2009.03.013> (Epub 2009 May 17 PMID: 19447682)
- Dimitriou R, Mataliotakis GI, Angoules AG, Kanakaris NK, Giannoudis PV (2011) Complications following autologous bone graft harvesting from the iliac crest and using the RIA: a systematic review. *Injury* 42(Suppl 2):S3–S15. <https://doi.org/10.1016/j.injury.2011.06.015> (Epub 2011 Jun 25 PMID: 21704997)
- Yuan H, Fernandes H, Habibovic P, de Boer J, Barradas AM, de Ruiter A, Walsh WR, van Blitterswijk CA, de Bruijn JD (2010) Osteoinductive ceramics as a synthetic alternative to autologous bone grafting. *Proc Natl Acad Sci U S A* 107(31):13614–13619. <https://doi.org/10.1073/pnas.1003600107> (Epub 2010 Jul 19. PMID: 20643969; PMCID: PMC2922269)
- Plantz MA, Gerlach EB, Hsu WK (2021) Synthetic Bone graft materials in spine fusion: current evidence and future trends. *Int J Spine Surg* 15(Suppl 1):104–112. <https://doi.org/10.14444/8058>. PMCID: PMC8092933
- Vaccaro AR, Greg Anderson D, Patel T, Fischgrund J, Truumees E, Herkowitz HN, Phillips F, Hilibrand A, Albert TJ, Wetzel T, McCulloch JA (2005) Comparison of OP-1 Putty (rhBMP-7) to iliac crest autograft for posterolateral lumbar arthrodesis: a minimum 2-year follow-up pilot study. *Spine* 30(24):2709–2716. <https://doi.org/10.1097/01.brs.0000190812.08447.ba> (PMID: 16371892)
- Vaccaro AR, Whang PG, Patel T, Phillips FM, Anderson DG, Albert TJ, Hilibrand AS, Brower RS, Kurd MF, Appannagari A, Patel M, Fischgrund JS (2008) The safety and efficacy of OP-1 (rhBMP-7) as a replacement for iliac crest autograft for posterolateral lumbar arthrodesis: minimum 4-year follow-up of a pilot study. *Spine J* 8(3):457–465. <https://doi.org/10.1016/j.spinee.2007.03.012> (Epub 2007 May 25 PMID: 17588821)
- van Dijk LA, Barbieri D, Barrère-de Groot F, Yuan H, Oliver R, Christou C, Walsh WR, de Bruijn JD (2019) Efficacy of a synthetic calcium phosphate with submicron surface topography as autograft extender in lapine posterolateral spinal fusion. *J Biomed Mater Res B Appl Biomater* 107(6):2080–2090. <https://doi.org/10.1002/jbm.b.34301> (Epub 2019 Jan 7. PMID: 30614621; PMCID: PMC6690075)
- Hoffmann MF, Jones CB, Sietsema DL (2013) Complications of rhBMP-2 utilization for posterolateral lumbar fusions requiring reoperation: a single practice, retrospective case series report. *Spine J* 13(10):1244–1252. <https://doi.org/10.1016/j.spinee.2013.06.022> (Epub 2013 Aug 22 PMID: 23973099)
- Veillette CJ, McKee MD (2007) Growth factors–BMPs, DBMs, and buffy coat products: Are there any proven differences amongst them? *Injury* 38(Suppl 1):S38–S48. <https://doi.org/10.1016/j.injury.2007.02.009> (PMID: 17383485)
- Oliveira ORG, Martins SPR, Lima WG, Gomes MM (2017) O uso de proteínas morfogenéticas ósseas (BMP) e pseudoartroses: uma revisão de literatura. *Rev Bras Ortop* 52(2):124–140. <https://doi.org/10.1016/j.rboe.2016.03.005>
- Benzel EC, Lieberman IH, Ferrara LA (2005) Bone void fillers: bone and bone substitutes. *Spine surgery*. Elsevier, pp 192–203. <https://doi.org/10.1016/B978-0-443-06616-0.50018-3> (ISBN 9780443066160)
- Han S, Park B, Lim J-W, Youm J-Y, Choi S-W, Kim DH, Ahn DK (2020) Comparison of fusion rate between demineralized bone matrix versus autograft in lumbar fusion: meta-analysis. *J Korean Neurosurg Soc* 63(6):673–680. <https://doi.org/10.3340/jkns.2019.0185> (Epub 2020 May 27. PMID: 32455520; PMCID: PMC7671781)
- Kadam A, Millhouse PW, Kepler CK, Radcliff KE, Fehlings MG, Janssen ME, Sasso RC, Benedict JJ, Vaccaro AR (2016) Bone substitutes and expanders in spine surgery: a review of their fusion efficacies. *Int J Spine Surg* 10:33. <https://doi.org/10.14444/3033>. PMID: 27909654; PMCID: PMC5130324
- Shepard NA, Rush AJ III, Scarborough NL, Carter AJ, Phillips FM (2021) Demineralized bone matrix in spine surgery: a review of current applications and future trends. *Int J Spine Surg* 15(Suppl 1):113–119. <https://doi.org/10.14444/8059>. PMCID: PMC8092935
- Mechteld Lehr A, Cumhuri Oner F, Delawi D, Stellato RK, Hoebink EA, Kempen DHR, van Susante JLC, Castelein RM, Kruyt MC (2020) Increasing fusion rate between 1 and 2 years after instrumented posterolateral spinal fusion and the role of bone grafting. *Spine* 45(20):1403–1410. <https://doi.org/10.1097/BRS.0000000000003558> (PMID: 32459724; PMCID: PMC7515483)
- Mechteld Lehr A, Cumhuri Oner F, Delawi D, Stellato RK, Hoebink EA, Kempen D, van Susante J, Castelein RM, Kruyt MC (2020) Efficacy of a standalone microporous ceramic versus autograft in instrumented posterolateral spinal fusion: a multicenter, randomized, inpatient controlled, noninferiority trial. *Spine* 45(14):944–951. <https://doi.org/10.1097/BRS.0000000000003440> (PMID: 32080013; PMCID: PMC7337108)
- Bridwell KH, Lenke LG, McEnery KW, Baldus C, Blanke K (1995) Anterior fresh frozen structural allografts in the thoracic and lumbar spine: Do they work if combined with posterior fusion

- and instrumentation in adult patients with kyphosis or anterior column defects? *Spine* 20(12):1410–1418. <https://doi.org/10.1097/00007632-199506020-00014>
24. Copay AG, Glassman SD, Subach BR, Berven S, Schuler TC, Carreon LY (2008) Minimum clinically important difference in lumbar spine surgery patients: a choice of methods using the Oswestry Disability Index, medical outcomes study questionnaire short form 36, and pain scales. *Spine J* 8(6):968–974. <https://doi.org/10.1016/j.spinee.2007.11.006> (Epub 2008 Jan 16 PMID: 18201937)
  25. Glassman SD, Copay AG, Berven SH, Polly DW, Subach BR, Carreon LY (2008) Defining substantial clinical benefit following lumbar spine arthrodesis. *J Bone Joint Surg Am* 90(9):1839–1847. <https://doi.org/10.2106/JBJS.G.01095> (PMID: 18762642)
  26. Nickoli MS, Hsu WK (2014) Ceramic-based bone grafts as a bone grafts extender for lumbar spine arthrodesis: a systematic review. *Global Spine J* 4(3):211–216. <https://doi.org/10.1055/s-0034-1378141> (Epub 2014 Jun 9. PMID: 25083364; PMCID: PMC4111951)
  27. Tay B, Kleinstueck F, Bradford D, Berven S (2001) Clinical applications of bone graft substitutes in spine surgery: consideration of mineralized and demineralized preparations and growth factor supplementation. *Eur Spine J* 10(0):S169–S177. <https://doi.org/10.1007/s005860100270> (PMID: 11716015; PMCID: PMC3611549)
  28. Parker RM, Malham GM (2017) Comparison of a calcium phosphate bone substitute with recombinant human bone morphogenetic protein-2: a prospective study of fusion rates, clinical outcomes and complications with 24-month follow-up. *Eur Spine J* 26(3):754–763. <https://doi.org/10.1007/s00586-016-4927-0> (Epub 2016 Dec 27 PMID: 28028645)
  29. Rodgers WB, Gerber EJ, Rodgers JA (2012) Clinical and radiographic outcomes of extreme lateral approach to interbody fusion with  $\beta$ -tricalcium phosphate and hydroxyapatite composite for lumbar degenerative conditions. *Int J Spine Surg* 6:24–28. <https://doi.org/10.1016/j.ijssp.2011.10.001> (PMID:25694867;PMCID: PMC4300873)
  30. Greene AC, Hsu WK (2019) Orthobiologics in minimally invasive lumbar fusion. *J Spine Surg* 5(Suppl 1):S11–S18. <https://doi.org/10.21037/jss.2019.04.15> (PMID:31380488;PMCID: PMC6626751)
  31. Pimenta L, Marchi L, Oliveira L, Coutinho E, Amaral R (2013) A prospective, randomized, controlled trial comparing radiographic and clinical outcomes between stand-alone lateral interbody lumbar fusion with either silicate calcium phosphate or rh-BMP2. *J Neurol Surg A Cent Eur Neurosurg* 74(6):343–350. <https://doi.org/10.1055/s-0032-1333420> (Epub 2013 Feb 26 PMID: 23444134)

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.