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An innovative advance in bone grafting: initial clinical results using a novel integrative bone graft in spinal fusion

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Introduction: Although autologous iliac crest bone graft (ICBG) has long been the gold standard for spinal fusion, complications related to its harvest and availability issues with local bone autograft have encouraged the development of bone graft substitutes that provide safer alternatives with consistent clinical efficacy and potential for applications across musculoskeletal health, including spinal fusion. This study evaluates the initial safety and efficacy of a novel integrative bone matrix (IBM) in spinal fusion procedures.
Methods: The charts of twenty patients who underwent spinal fusion surgery at 1–5 contiguous interbody levels and/or 1–15 contiguous posterolateral levels with the novel IBM between November 2022 and May 2023 were retrospectively evaluated for safety and efficacy endpoints at standard of care 3, 6, and 12 months postoperative follow up visits. Radiographic fusion rate was evaluated by plain radiographs using the Bridwell interbody fusion grading system and/or the Glassman posterolateral fusion grading system, as appropriate. Subjective pain, disability, and quality of life assessments included the EuroQoL 5 Dimensions Visual Analogue Scale (EQ-5D VAS), Oswestry Disability Index (ODI), and the revised Scoliosis Research Society Score (SRS-22r).
Results: No adverse events occurred that were related to the graft, and no subjects required unplanned revision surgery. Radiographic fusion was achieved in all (100%) of the interbody and posterolateral levels by 12 months. There was no significant difference in overall fusion rate between subjects receiving short vs. long segment constructs. At 3, 6, and 12 month follow up, significant ($p < 0.001$) improvements were observed compared to baseline values for all patient reported outcome measures, and the cohort reached the minimum clinically significant mean improvements.
Discussion: This study highlights the potential of this novel IBM as a safe and effective bone graft substitute in spinal arthrodesis procedures. Patients had a high rate of fusion without any graft-related adverse events. Larger, controlled studies with longer-term follow-up are warranted for further validation.

KEYWORDS

spinal fusion, bone graft, spine surgery, biologics, regenerative medicine, integrative bone matrix, IBM

Introduction

Spinal fusion plays a pivotal role in managing pain from a diverse range of spinal disorders, including degenerative disc disease, spinal stenosis, spondylolisthesis, and spinal fractures. From 1998 to 2008, the frequency of spinal fusion discharges was reported to have increased by 137%, which further increased between the years 2002 and 2014 to 276% for elective lumbar fusion procedures (1–3). The use of autologous iliac crest bone graft (ICBG) has been considered the gold standard for bone grafting in spinal fusion surgery, due to its natural osteoconductive, osteoinductive, and osteogenic properties. However, harvesting ICBG can lead to complications such as pain, blood loss, and infection (4, 5).

One systematic review and meta-analysis compared ICBG to local autologous bone in spinal fusion procedures and found that the use of local bone resulted in significantly higher fusion rates compared to ICBG (5). However, although autologous local bone from the operative site may serve as an alternative, its limited availability and variable quality present challenges in achieving consistent surgical outcomes (6). Thus, there is an unmet need for bone graft substitutes that can offer comparable efficacy in supporting bone healing while circumventing the limitations of autologous grafting (5, 7). Bone graft substitutes, such as those from either allogeneic (donor) or synthetic sources, can fulfill this need, however not all bone graft substitutes are biomimetic alternatives for autologous bone (4, 5, 7, 8).

Specifically in the field of regenerative medicine, extensive research efforts have focused on identifying novel osteobiologics capable of enhancing bone healing and integration in spinal fusion procedures (4, 5, 7). Bone graft substitutes with osteoconductive and osteoinductive characteristics accelerate bone healing by releasing growth factors and cytokines, which facilitates cell proliferation, angiogenesis, and extracellular matrix deposition for optimal bone regeneration and integration (4, 7). A recent advancement in bone grafting technology was the development of cellular bone matrices (CBMs) or viable bone matrices (VBMs) that preserve viable cells, aiming to enhance osteogenesis and improve patient outcomes (4, 9). As with many advancements, improvements in grafting technology often come with compromise. The focus on preserving viable cell populations in CBMs and VBMs often comes at the price of reducing inductive factors and/or suboptimal handling of the bone graft during manufacturing. However, the latest advancement in bone grafting technology (integrative bone matrix, IBM) provides viable and functional cells while including improved graft handling and the preservation of a greater concentration of inherent osteoinductive and angiogenic proteins compared to what has been previously reported for manufactured demineralized bone (10–12). Due to the critical role of angiogenesis in bone healing, there is an unmet need for an advanced viable bone graft that can provide high levels of both osteoinductive and angiogenic growth factors to support clinical success.

This article provides preliminary observational data on the use of a novel integrative bone matrix (IBM) in spinal fusion procedures and summarizes the regenerative properties of advanced viable bone grafts such as IBM.

Materials and methods

This study was reviewed and approved by our institutional IRB review process. A waiver of Informed Consent and HIPAA was obtained due to the retrospective nature of the work performed. This study was conducted in accordance with the ethical principles in the Declaration of Helsinki and conducted according to U.S. and international standards of Good Clinical Practice in accordance with applicable Federal regulations, International Council for Harmonization guidelines, and institutional research policies and procedures.

Subject population

This retrospective observational study was performed to evaluate initial safety and efficacy outcomes of INFLUX™ SPARC integrative bone matrix (IBM) implanted between November 2022 and May 2023 in patients aged 18–80 years undergoing spinal fusion surgery. Only patients receiving the novel IBM as a bone graft were included in the study. Enrolled subjects included those with spinal fusion surgery at 1–5 contiguous interbody levels and/or 1–15 contiguous posterolateral levels. Subjects with fusion constructs from 1 to 3 interbody or posterolateral levels were defined as short segment, and those that had greater than 3 interbody or posterolateral levels in their fusion constructs were defined as long segment.

Endpoints

The primary endpoint was evaluation of fusion of the treated levels, as assessed by the operative surgeon through radiographic examination of plain films (and CT imaging when available) collected at baseline (preoperative) and 3, 6, and 12 months postoperatively utilizing the Bridwell interbody fusion grading system and the Glassman posterolateral fusion grading system as appropriate (Tables 1, 2) (13, 14). Grades I and II on the Bridwell system and Grades 4 and 5 on the Glassman system were classified as successful fusion based on established literature (14, 15).

The operative physician's standard of care patient-reported assessments collected at baseline (preoperative) and 3-, 6-, and

TABLE 1 Bridwell interbody fusion grading system.

Fused	Grade I	Fused with remodeling and trabeculae present
	Grade II	Graft intact, not fully remodeled and incorporated, but no lucency present
Not fused	Grade III	Graft intact, potential lucency present at top and bottom of graft
	Grade IV	Fusion absent with collapse and/or resorption of graft

12-months postoperatively for pain, function, and quality of life were the secondary endpoints of the study: EuroQoL 5 Dimensions Visual Analogue Scale (EQ-5D VAS), Oswestry Disability Index (ODI), and the revised Scoliosis Research Society Score (SRS-22r). The EQ-5D VAS scale ranges from 0 to 100, with 0 indicating "the worst health you can imagine" and 100 indicating "the best health you can imagine" (16). ODI scores can range from 0% (no disability) to 100% (most severe disability) (17). SRS-22r has a minimum score of 1 and a maximum score of 5, with higher scores indicating better patient quality of life (18). Minimal clinically significant improvements were defined as an increase of 12 points for EQ-5D VAS, a 10% decrease in points for ODI, and a mean increase of 0.4 for SRS-22r, as established in the literature (19–21). Safety evaluation included incidence of pseudoarthrosis or unplanned reoperation related to the use of IBM.

Statistical analysis

Continuous variables are presented as means with standard deviations and categorical data are represented as counts with percentages. Fusion rates were considered noncontinuous variables, whereas pain and disability scores were treated as ordinal variables. The number of levels treated was correlated with preoperative quality of life scale scores using Spearman correlations. Independent median samples tests were used to compare median time to fusion for short vs. long segment subjects, and those with vs. without comorbidities. The nonparametric, related-samples Friedman's Analysis of Variance was used to examine change in quality-of-life outcomes over time. The Bonferroni correction was applied to pairwise *post hoc* analyses. Statistical significance was set at $p < .05$. SPSS software version 27 (IBM Corp.; Armonk, New York, USA) was used for statistical analysis.

Results

Patient and procedural details

A total of 20 patients met the inclusion criteria for this study, 50% ($n = 10$) of which were male. Table 3 provides a summary of subject demographics and health profiles. Subjects had a mean age of 60.4 years (range 45–79) and a mean body mass index (BMI) of 31.9 kg/m^2. A quarter (25.0%) of the subjects were current smokers and 35.0% were currently taking steroids. Diagnoses within patient charts revealed a range of health conditions: 45.0% of subjects were obese (BMI > 30), 30.0% had cardiovascular disease, 20.0% had kidney disease, 5.0% had Type II diabetes, and 35.0% were undergoing a revision surgery.

TABLE 2 Glassman posterolateral fusion grading system.

Not fused	Grade 1	No fusion
	Grade 2	Partial or limited unilateral fusion
	Grade 3	Partial or limited bilateral fusion
Fused	Grade 4	Solid unilateral fusion
	Grade 5	Solid bilateral fusion

TABLE 3 Patient demographics & clinical characteristics.

Demographic Variables	
Age, Years, mean ± SD	60.4 ± 10.2
(Min – Max)	45–79
Gender, Male	10 (50.0%)
BMI (kg/m^2, mean ± SD)	31.9 ± 6.9
Race	
White	16 (80.0%)
Black or African American	4 (20.0%)
Ethnicity	
Non-Hispanic or Latino	7 (35.0%)
Hispanic or Latino	1 (5.0%)
Unknown	12 (60.0%)
Smoker	7 (35.0%)
Current	2 (10.0%)
Former	5 (25.0%)
Steroids (Current)	7 (35.0%)
Diagnoses at enrollment	
None	5 (25.0%)
Hypertension	12 (60.0%)
Obesity (>30 BMI)	9 (45.0%)
Cardiovascular Disease	6 (30.0%)
Kidney Disease	4 (20.0%)
Diabetes (Type II)	1 (5.0%)
Reoperative Surgery	7 (35.0%)

On average, each subject had 3.6 ± 1.4 indications for surgery (Table 4). The most common indications were stenosis (90.0%), followed by herniated nucleus pulposus (HNP) (75.0%), spondylolisthesis (60.0%), and spondylosis (50.0%). There were no cases of degenerative disc disease (DDD). Other indications (85.0%) included scoliosis, radiculitis/radiculopathy, kyphosis, and revision. Most subjects underwent interbody with posterior spinal fusion (90.0%), but some underwent posterolateral fusion alone (10.0%). The cohort was split evenly between short (50.0%) vs. long segment (50.0%) fusion constructs. The average number of levels treated per interbody subject was 2.1 (ranging from T8 to S1), and 5.0 for posterolateral subjects (ranging from C2 to S1). However as expected, the most treated levels were between L3 – S1 (70.2% of interbody and 32.3% of posterolateral). The number of levels treated was not associated with preoperative EQ-5D [$r(19) = -0.075$, $p = 0.752$], ODI [$r(19) = 0.123$, $p = 0.604$], or SRS-22r [$r(19) = 0.004$, $p = 0.985$] scores.

Approximately half of the procedures were performed using minimally invasive approaches (55.0% TLIF or LLIF). All interbody subjects (100.0%) received an expandable titanium interbody device (Globus Medical, Audubon, Pennsylvania) and bilateral percutaneous pedicle screw constructs with posterolateral grafting. A total of 5.0cc of IBM was used per fusion area (i.e., 5.0cc for posterolateral fusion alone, 10.0cc for both interbody and posterolateral), and all posterior fusions also included the use of available local autograft (approximately 6cc per level). All subjects who underwent ALIF, LLIF, or TLIF also underwent

TABLE 4 Procedural details.

Indications for Surgery[a]	
# Indications per subject, mean ± SD	3.6 ± 1.4
Stenosis	18 (90.0%)
Herniated Nucleus Pulposus (HNP)	15 (75.0%)
Spondylolisthesis	12 (60.0%)
Spondylosis	10 (50.0%)
Degenerative Disc Disease (DDD)	0 (0.0%)
Other[b]	17 (85.0%)
Surgical Approach	
Interbody with Posterior Fusion	18 (90.0%)
Posterior Fusion Alone	2 (10.0%)
Construct Size	
Short Segment (≤3 levels)	10 (50.0%)
Long Segment (>3 levels)	10 (50.0%)
Interbody Levels Treated	*N* = 37
# Levels Treated (1–5), mean ± SD	2.1 ± 1.2
T8 – T9	1 (2.7%)
T9 – T10	1 (2.7%)
T10 – T11	1 (2.7%)
T11 – T12	1 (2.7%)
T12 – L1	0 (0.0%)
L1 – L2	3 (8.1%)
L2 – L3	4 (10.8%)
L3 – L4	7 (18.9%)
L4 – L5	12 (32.4%)
L5 – S1	7 (18.9%)
Interbody Implant Used During Procedure (per level)	*N* = 37
Titanium Cage	37 (100.0%)
Posterolateral Levels Treated	*N* = 99
# Levels Treated (1–15), mean ± SD	5.0 ± 4.3
C2 – C3	1 (1.0%)
C3 – C4	1 (1.0%)
C4 – C5	1 (1.0%)
C5 – C6	1 (1.0%)
C6 – C7	1 (1.0%)
C7 – T1	1 (1.0%)
T1 – T2	1 (1.0%)
T2 – T3	2 (2.0%)
T3 – T4	2 (2.0%)
T4 – T5	3 (3.0%)
T5 – T6	3 (3.0%)
T6 – T7	3 (3.0%)
T7 – T8	3 (3.0%)
T8 – T9	5 (5.1%)
T9 – T10	5 (5.1%)
T10 – T11	5 (5.1%)
T11 – T12	7 (7.1%)
T12 – L1	8 (8.1%)
L1 – L2	6 (6.1%)
L2 – L3	8 (8.1%)
L3 – L4	9 (9.1%)
L4 – L5	14 (14.1%)
L5 – S1	9 (9.1%)

IBM, integrative bone matrix; SD, standard deviation.
[a]Percentages do not equal 100, as most patients had multiple indications for spinal fusion.
[b]Other indications included scoliosis, radiculitis/radiculopathy, kyphosis, and revision.

TABLE 5 Radiographic fusion rates.

Interbody Fusion Rate, *n* (%) (Bridwell grading system)	*N* = 37
3 months	28 (77.8%)
6 months	35 (94.6%)
12 months	37 (100.0%)
Time to Fusion, median (25th – 75th percentile)	3.0 (3.0–4.5)
Posterior Fusion Rate, *n* (%) (Glassman grading system)	*N* = 99
3 months	2 (2.0%)
6 months	57 (57.6%)
12 months	99 (100.0%)
Time to Fusion, median (25th – 75th percentile)	6.0 (6.0–12.0)
Combined Fusion Rate[a], *n* (%)	*N* = 37
3 months	1 (2.7%)
6 months	23 (62.2%)
12 months	37 (100.0%)
Time to Fusion, median (25th – 75th percentile)	6.0 (6.0–12.0)

[a]Combined fusion rate indicates time level achieved fusion per both measurement scales (i.e., Bridwell Grade I or II and Glassman Grade 4 or 5) for subjects with interbody and posterolateral grafting.

PSF. When preparing the fusion graft for implantation during intervertebral fusion, the expandable cage was first packed with bone graft and implanted in a collapsed state, then was expanded to the desired height and backfilled with bone graft. No patients required harvesting of ICBG.

Clinical and radiographic outcomes

Radiographic fusion rates per level are summarized in Table 5. For interbody fusion ($n = 37$ levels), assessed using the Bridwell grading system (Table 1) and literature definition for successful fusion (grade I or II), fusion rates steadily increased over time, with 77.8% at 3 months, 94.6% at 6 months, reaching 100.0% at 12 months post-surgery (13, 15). The median time to interbody fusion was 3.0 months (range 3.0–4.5). Posterior fusion rates ($n = 99$ levels), evaluated via the Glassman grading system (Table 2) and literature definition for successful fusion (grade 4 or 5), showed a slower progression with only 2.0% achieving fusion at 3 months, increasing to 57.6% at 6 months, and eventually reaching 100.0% by 12 months, with a median fusion time of 6.0 months (range 6.0–12.0) (14). The combined fusion rate, i.e., scores of Bridwell grade I or II and Glassman grade 4 or 5 for subjects with interbody and posterolateral grafting ($n = 37$ levels), was 2.7% at 3 months, 62.2% at 6 months, and 100.0% at 12 months, with a median fusion time of 6.0 months (range 6.0–12.0). Although excellent reference images can be found in the original publications, example radiographs representing the interbody and posterolateral scoring systems from our subject cohort are shown in Figure 1 (13, 14).

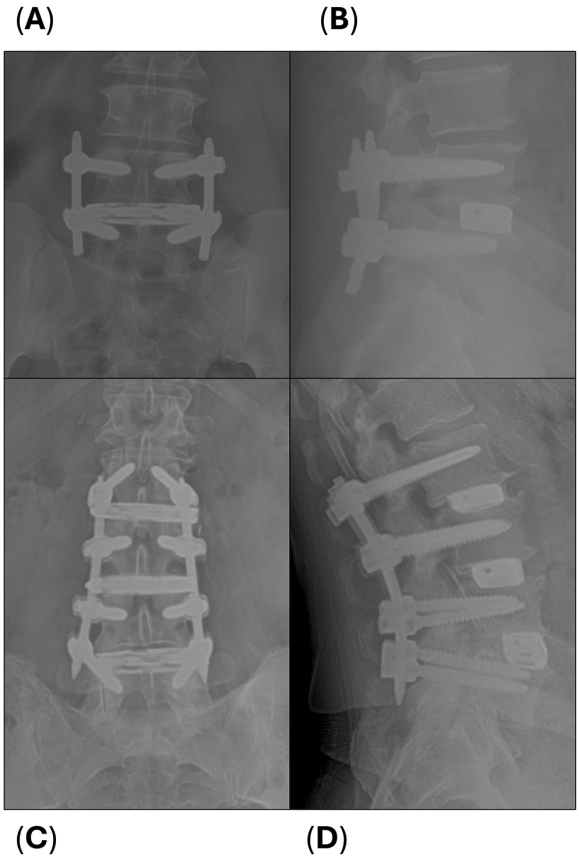

FIGURE 1
Example radiographs of interbody (Bridwell) and posterolateral (Glassman) scoring. **(A)** At 3 months, this single level LLIF subject was scored as Bridwell Grade III (not fused) and **(B)** Glassman Grade 2 (not fused). **(C)** At 12 months, this 3-level LLIF subject was scored as Bridwell Grade I (fused) and **(D)** Glassman Grade 5 (fused) at each level.

Radiographs and CT imaging that display baseline and successful fusion at 6- and 12-month follow-up are provided of two subjects in Figure 2: a low-risk subject undergoing a single level interbody and posterior fusion, and a high-risk subject undergoing an 11-level revision posterior fusion. One subject achieved their single level fusion on both scales at only 3 months: a high risk 77-year-old obese female who was a current smoker, hypertensive, with coronary artery and peripheral vascular disease, and was currently taking corticosteroids. No patients experienced pseudarthrosis or required unplanned revision surgery. When fusion rates between subjects receiving short vs. long segment constructs were compared, no significant differences were found ($p > 0.05$ for interbody, posterolateral only, and combined median times to fusion), and there were no differences in comorbid risk factors between these groups. Further, no significant differences were found in median time to fusion for subjects who were current smokers, currently on steroids, or obese (>30 kg/m^2), however obesity trended with a shorter time to fusion ($p = 0.057$).

Subjective clinical outcomes

Subject-reported outcomes, including: EuroQoL 5 Dimensions Visual Analogue Scale (EQ-5D VAS) for pain, Oswestry Disability Index (ODI) for disability, and Scoliosis Research Society Score (SRS-22r) for quality of life demonstrated statistically significant main effects ($p < 0.001$). Additionally, post-hoc comparisons at 3-, 6-, and 12 months were significantly improved compared to baseline ($p < 0.001$ for all comparisons) (Table 6, Figures 3–5).

In terms of pain perception measured by EQ-5D VAS, subjects exhibited significant improvements over the follow up times (Table 6, Figure 3). At baseline, the median pain score was 45.0 (IQR: 30.0–60.0), which notably increased to 67.5 (IQR: 60.0–82.5) at 3 months ($p < 0.001$), further improving to 70.0 (IQR: 52.5–80.0) at 6 months ($p < 0.001$), and 70.0 (IQR: 61.3–85.0) at 12 months ($p < 0.001$). Regarding disability levels assessed by ODI, subjects experienced a significant reduction in disability from baseline (median score: 62.0, IQR: 50.5–72.0, $p < 0.001$) to 3 months (median score: 31.0, IQR: 24.5–42.3, $p < 0.001$), remaining relatively stable at both 6 months (median score: 31.0, IQR: 26.0–39.0, $p < 0.001$) and 12 months (median score: 29.0, IQR: 22.0–34.0, $p < 0.001$) (Table 6, Figure 4). Quality of life, as measured by SRS-22r, also showed significant improvement throughout the study period: the median score increased from 2.4 (IQR: 2.1–2.6) at baseline to 3.5 (IQR: 3.1–3.8) at 3 months ($p < 0.001$) and 6 months ($p < 0.001$), reaching 3.8 (IQR: 3.4–4.0) at 12 months ($p < 0.001$), indicating a consistent enhancement in patients' overall well-being over time (Table 6, Figure 5).

The most substantial improvements compared to baseline were at the 12-month assessment, however the cohort reached the minimum clinically significant mean improvements in EQ-5D VAS (+12 points), ODI (−10%), and SRS-22r (+0.4 points) by 3 months (19–21). The mean changes in EQ-5D VAS scores at 3, 6, and 12 months were +19.3, +21.5, and +25.8, respectfully. At 3, 6, and 12 months, the mean change in ODI percentage points were −26.9%, −29.3, and −32.0%, respectively. For SRS-22r, the mean score changes at 3, 6, and 12 months were +1.0, +1.1, and +1.3. Overall, from baseline to 12 months there was a 54.9% improvement in EQ-5D VAS, 52.4% in ODI, and 54.2% in SRS-22r.

Safety

No adverse events related to the graft were reported. Only 1 report of mild, procedure-related proximal junctional kyphosis (PJK) was found in an obese 78-year-old white female with chronic kidney and cardiovascular disease.

Discussion

Expanding capabilities in regenerative medicine research and manufacturing have resulted in osteobiologic substitutes that reduce dependence on autologous bone grafts, and therefore effectively lower the risk of related complications (4, 5, 7, 8). The

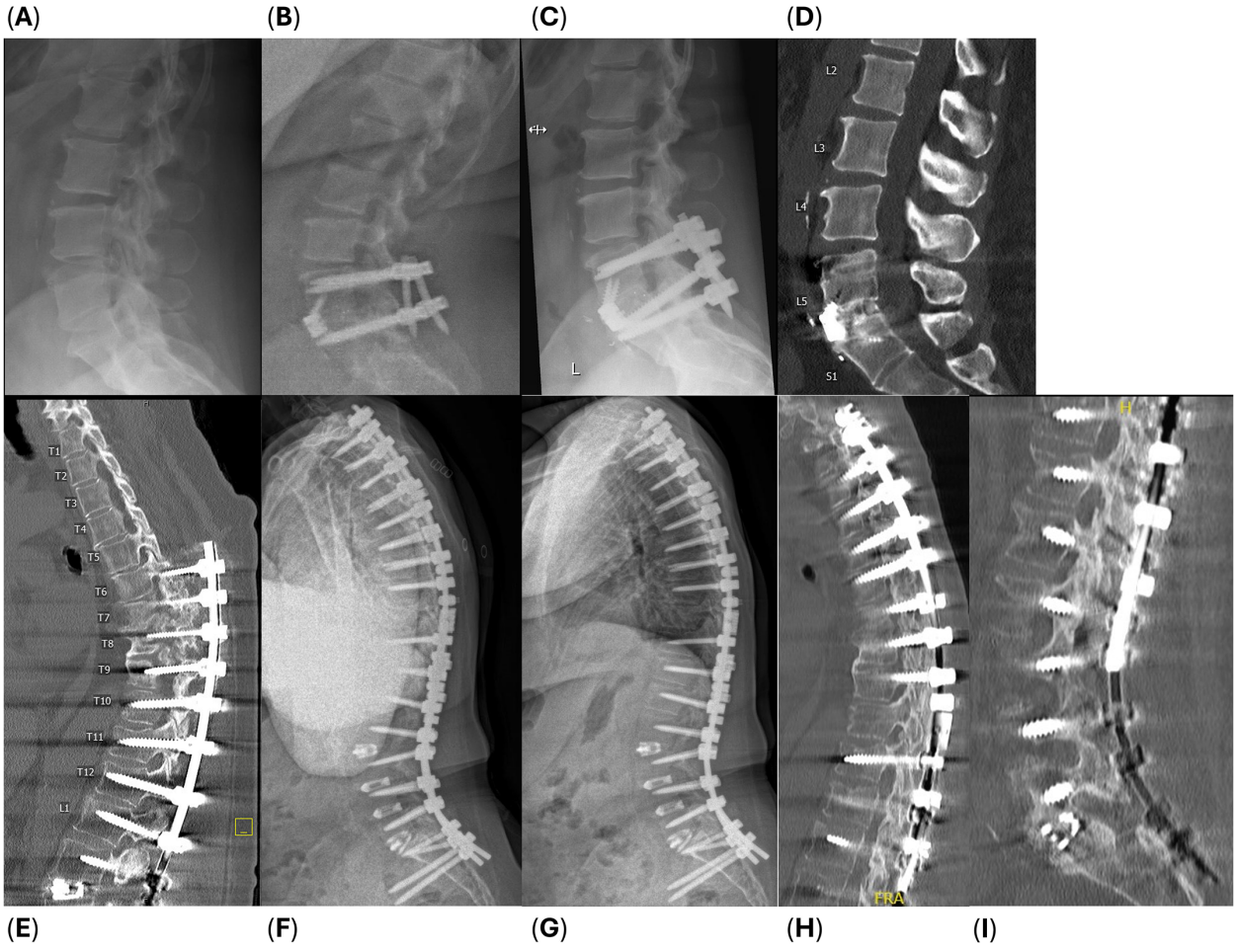

FIGURE 2
Example radiographs of two subjects: **(A–D)** a 51-year-old obese female who underwent a single level ALIF from L5 to S1, and **(E–I)** a 61-year-old obese, current smoker female with hypertension who underwent a revision T2 to L1 posterolateral fusion after a L1 to L3 TLIF with T6 to pelvis posterior fusion 8 months prior, and a L3 to L5 PLIF 6 years prior (subject experienced PJF and pseudarthrosis in the thoracic spine and underwent hardware removal with revision in the latest procedure). **(A,E)** Baseline radiographic imaging and successful fusion apparent at **(B,F)** 6-month follow up, **(C,G)** 12-month follow-up, and **(D,H,I)** CT images at 12 months postoperative.

clinical success of these grafts is mainly attributed to the inclusion of osteoconductive, osteoinductive, and/or osteogenic properties that mimic those of autologous bone (5, 12). During bone healing, tissue remodeling and neovascularization are conducted by osteogenic cells and cytokines such as insulin-like growth factors (IGFs), bone morphogenetic proteins (BMPs), platelet-derived growth factor (PDGF), transforming growth factors (TGF-βs), vascular endothelial growth factor (VEGF), and endothelial growth factor (EGF) (22). Thus, bone grafts that preserve viable bone forming cells and a high concentration of these supportive growth factors and cytokines may provide clinical benefit over bone grafts which only provide osteoconductive properties.

Currently in the United States, synthetic scaffolds, bone morphogenetic proteins (BMPs), demineralized bone matrices (DBMs), bone marrow aspirate (BMA) byproducts, and viable bone matrices (VBMs) are available for use. Each osteobiologic has shown promising potential to enhance fusion rates and alleviate pain associated with autologous harvesting in musculoskeletal fusion procedures, however some provide more limited characteristics compared to others which could affect clinical outcomes (23). Synthetic bone graft scaffolds provide consistent structure but have lower reported fusion rates (77% to 90%) when used alone compared to using as an extender with iliac crest autograft (78% to 100%) (24, 25). Demineralized bone matrix (DBM) was designed to enhance fusion with osteoinductive properties, however growth factor concentration variability between individual DBMs and within lots is thought to be responsible for the differing reported rates of fusion (52% to 100%) (23, 26, 27). Bone morphogenetic proteins (BMPs) have high reported fusion rates (93% to 99%) due to strong osteoinductive effects but carry risks such as inflammation and malignancy (23, 28–30). Bone marrow aspirate (BMA) relies on osteogenic cells and growth factors to drive osteogenesis, and depending on which scaffold it is combined with, has similar reported arthrodesis rates to iliac crest autograft (76% to 100%)

TABLE 6 Pain and disability scores.

		*p-value**
EQ-5D VAS (Pain) median (IQR, 25th – 75th%)		
Baseline	45.0 (30.0–60.0)	–
3 months	67.5 (60.0–82.5)	*<0.001*
6 months	70.0 (52.5–80.0)	*<0.001*
12 months	70.0 (61.3–85.0)	*<0.001*
ODI (Disability) median (IQR, 25th – 75th%)		
Baseline	62.0 (50.5–72.0)	–
3 months	31.0 (24.5–42.3)	*<0.001*
6 months	31.0 (26.0–39.0)	*<0.001*
12 months	29.0 (22.0–34.0)	*<0.001*
SRS-22r (Quality of Life) median (IQR, 25th – 75th%)		
Baseline	2.4 (2.1–2.6)	–
3 months	3.5 (3.1–3.8)	*<0.001*
6 months	3.5 (3.1–3.7)	*<0.001*
12 months	3.8 (3.4–4.0)	*<0.001*

EQ-5D VAS, EuroQoL 5 dimensions visual analogue scale; ODI, oswestry disability index; IQR, interquartile range; SRS-22r, Scoliosis Research Society Score.
**p-value* represents baseline scores versus scores at each follow up timepoint from model *post hoc* pairwise comparison with Bonferroni adjustment.

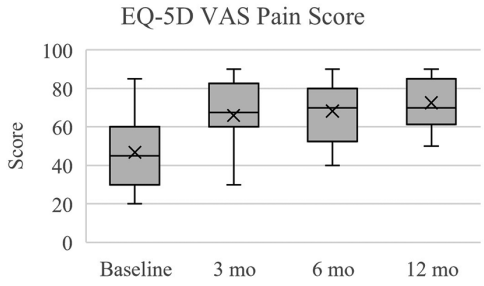

FIGURE 3
EuroQoL 5 dimensions visual analogue scale (EQ-5D VAS) for pain. Scores reported here and in Table 6 are presented as median (IQR, 25th – 75th percentile). At each follow up timepoint, mean scores were: 46.8 ± 19.8 (baseline), 66.0 ± 16.6 (3 months), 68.3 ± 16.3 (6 months), and 72.5 ± 12.7 (12 months).

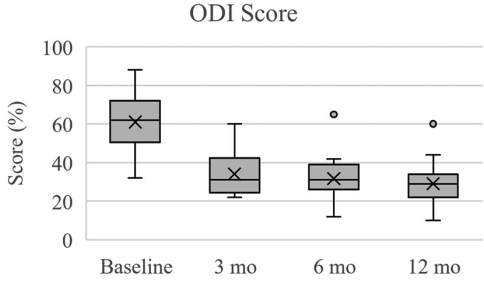

FIGURE 4
Oswestry disability Index (ODI) for disability. Scores reported here and in Table 6 are presented as median (IQR, 25th – 75th percentile). At each follow up timepoint, mean scores were: 61.1 ± 14.0 (baseline), 34.2 ± 11.0 (3 months), 31.8 ± 10.8 (6 months), and 29.1 ± 11.4 (12 months).

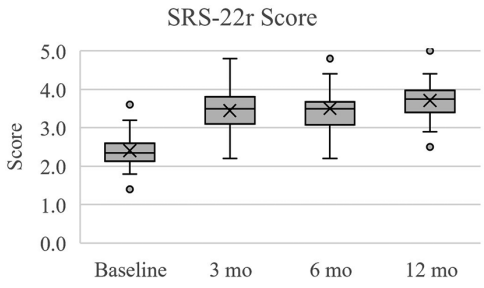

FIGURE 5
Scoliosis research society score (SRS-22r) for quality of life. Scores reported here and in Table 6 are presented as median (IQR, 25th – 75th percentile). At each follow up timepoint, mean scores were: 2.4 ± 0.5 (baseline), 3.4 ± 0.6 (3 months), 3.5 ± 0.6 (6 months), and 3.7 ± 0.5 (12 months).

(31, 32). Currently there is a lack of evidence supporting the utilization of DBM or BMA derivatives as standalone orthobiologics (4). The only class of osteobiologic that incorporates all three required components to support bone healing are VBMs or IBMs (Table 7).

VBMs have shown equivalent or greater clinical success compared to ICBG even in complex cases and with patients with higher risk factors in spinal fusion (33, 34), foot and ankle arthrodesis (35–38), and craniomaxillofacial repairs (39, 40). The ability of advanced grafts to overcome potential healing deficiencies caused by these risk factors could explain the lack of significant differences in fusion rates between short vs. long segment arthrodesis and low vs. high comorbid risk factors in this dataset, however larger studies are needed to confirm these relationships. Recent studies have also suggested that VBMs may be more cost-effective compared to other alternatives such as rhBMP2, in part due to their lower complication rates which potentially can lead to lower healthcare costs over a 2-year period postoperatively (41, 42). In fact, the higher rates of complications from using rhBMP2 could explain the 50% decrease in utilization during thoracolumbar spine fusion surgeries observed between the years 2008–2014 (43). There are many different VBMs commercially available, yet differences exist between products in manufacturing processes which can affect the quantity and quality of cells and growth factors, shelf life, thaw time, use of carrier(s), and time of post-thaw viability (44). Differences in the presence and bioavailability of these factors may explain the differences in clinical fusion success, as reported by others (44, 45). Integrative bone matrix (IBM) includes the same three bone-supportive characteristics as VBM yet provides a greater concentration of native osteoinductive proteins compared to what has been previously reported for demineralized bone (10–12).

As this is the first reporting of results for this application, the purpose of this study was to assess the initial safety and efficacy of a novel IBM in spinal fusion procedures. The use of SPARC IBM was considered safe, as it led to zero related adverse events and circumvented the need for harvesting iliac crest autograft. The

TABLE 7 Comparison of osteobiologic adjunct characteristics within the US.

	Osteoconductive	Osteoinductive	Osteogenic
Synthetic scaffolds	+		
Bone morphogenetic proteins (BMPs)		+	
Demineralized bone matrix (DBM)	+	+	
Bone marrow aspirate (BMA) byproducts		+	+
Viable bone matrix (VBM)	+	+	+
Integrative bone matrix (IBM)	+	++	+

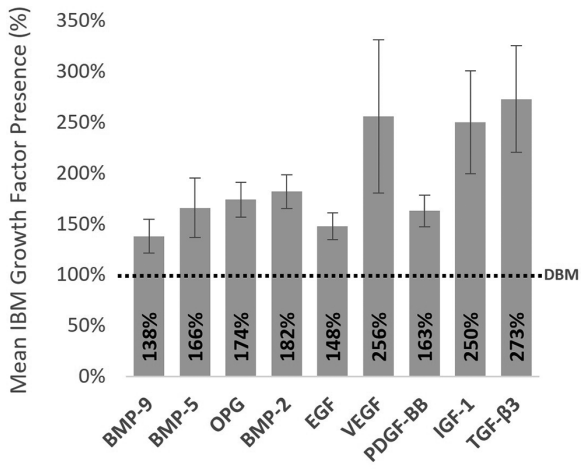

FIGURE 6
Advanced proprietary processing resulted in heightened growth factor preservation and bioavailability for the IBM compared to demineralized bone matrix (DBM) concentrations. These preserved growth factors can promote osteoinduction, angiogenesis, and cellular proliferation. Values were assessed from donor matched samples across 8 donors (lots). Proteins were extracted from bone samples using standard guanidine hydrochloride protein extraction methods, then each target protein was quantified via a commercially available custom multiplex fluorescent ELISA. *Dashed line represents normalized level of growth factors measured from a common DBM.

only procedure-related complication was proximal junctional kyphosis (PJK) in a patient with obesity, which is a well-known risk factor for PJK (46). Increasing fusion levels also heightens the risk of PJK, nonunion, and mechanical strain, with severe cases requiring revision surgery. However, these outcomes are highly dependent upon differing surgical techniques, patient factors, and follow-up protocols. It is worth noting that the PJK in this study was asymptomatic and did not require any subsequent intervention by 1-year follow up. Efficacy outcomes included radiographic fusion success, which occurred in 100% of interbody and posterolateral levels by 12 months, and subjective clinical evaluations for pain, function, and quality of life which reached the minimum clinically significant mean improvements by 3 months and was maintained through 12 months of follow up.

Previously published VBM spinal fusion rates and pain, disability, and quality of life score improvements align with those reported in this IBM study. A recent systematic review including VBM studies published through January 2023 reported lumbar segment fusion rates of 68% – 99% at 12 months (9). However, the reported rate of reoperation (up to 8.7% in one study with a similar number of enrolled subjects) (47) is significantly higher than our observed rate of 0%. Only one VBM study was identified that included similar subjective outcome measures (48), reporting a 57.1% improvement in mean ODI scores at 12 months, similar to the improvements reported in this study (52.4%).

This innovative IBM combines cancellous chips and cortical DBM fibers to optimize both handling and osteoconduction, and is processed using a gentle manufacturing protocol that preserves viable osteoprogenitor cells with viability for up to 5 h post-thaw, per the IFU. Mitigation of the risk of infection and disease transmission are due to advanced screening of donors and aseptic processing methods. Unlike what has been previously reported for conventional DBM grafts, the IBM retains greater levels of native growth factors extracted from the bone lining cells (Figure 6) (10–12). These include a diverse array of bioavailable osteoinductive, angiogenic, and mitogenic growth factors such as: BMPs, PDGF, TGF-β3, VEGF, and EGF. Unlike VBMs, the IBM thaws quickly in approximately 10 min in room temperature sterile water or saline and is dimethyl sulfoxide (DMSO)-free, which eliminates the need to rinse and decant prior to implantation. The graft comes in a surgeon-friendly ready-to-use syringe.

These favorable radiographic fusion results combined with early improvements in pain, function, and quality of life highlight the potential of this novel IBM as a promising bone graft extender and substitute in spinal fusion procedures. Aside from its retrospective nature, limitations for this study include lack of a control group, a small cohort size, short-term follow up, use of local autograft alongside the IBM, radiographic evaluation by the operative surgeon, lack of CT fusion evaluation for all subjects, and use of a Ti cage which may have contributed to challenges in fusion determination. Larger, controlled studies with longer-term follow-up are needed to further validate these results.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by New York University Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The Ethics Committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because of the retrospective nature of the work performed.

Author contributions

PP: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing, Formal Analysis, Project administration, Validation. OO: Formal Analysis, Methodology, Project administration, Validation, Writing – review & editing. AD: Formal Analysis, Methodology, Project administration, Validation, Writing – review & editing. JM: Formal Analysis, Methodology, Project administration, Validation, Writing – review & editing. AY: Data curation, Formal Analysis, Project administration, Validation, Writing – review & editing. MF: Data curation, Formal Analysis, Project administration, Validation, Writing – review & editing.

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Conflict of interest

PGP reports that they are a consultant for ISTO Biologics, Inc. (manufacturer of SPARC IBM).

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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