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Efficacy of an FDA Approved Synthetic Nano-Bioactive Glass Plus Demineralized Bone Matrix (DBM) Combination versus DBM Alone in Instrumented Lumbar Fusion for Low-Grade Degenerative Spondylolisthesis: A Prospective Randomized Controlled Trial Pilot Study --Manuscript Draft--

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Abstract:	<p>Background</p> <p>Demineralized Bone Matrix (DBM) is widely used in spinal fusion but has donor variability and supply limitations. Synthetic bioactive glass (BAG) offers osteoinductive and osteoconductive properties. NanoFuse™ DBM, an FDA-approved combination of nano-BAG and DBM, integrates bioactive nanomaterials with organic bone matrix, but its efficacy in spinal fusion remains underexplored. This study evaluates its impact on fusion success and clinical outcomes compared to DBM alone.</p> <p>Methods</p> <p>In a randomized controlled trial, 64 patients underwent single-level lumbar fusion and were followed for 36 months. Group 1 (n=29) received nano-BAG+DBM with an interspinous fixation device, while Group 2 (n=35) received DBM alone with pedicle screws and posterior lumbar interbody fusion. Both groups received an equivalent graft volume. Outcomes included radiographic fusion, Visual Analog Scale (VAS), Oswestry Disability Index (ODI), surgical parameters, and revisions.</p> <p>Results</p> <p>Both groups achieved 100% fusion at 24 months, but Group 1 demonstrated earlier fusion at 6 and 12 months. Group 1 had significantly lower VAS scores at 24 (P = 0.041) and 36 months (P < 0.001). ODI improved in both groups, with greater recovery in Group 1 (P < 0.00001). Group 1 also had shorter operative times and reduced blood loss. Two patients (5.71%) in Group 2 required revision for adjacent segment disease.</p> <p>Conclusion</p>

	Nano-BAG+DBM accelerated early bone fusion and improved clinical outcomes while reducing DBM requirements and reliance on cadaveric bone. These findings highlight its role as a synthetic alternative for spinal fusion and its potential in bone regenerative strategies.
Opposed Reviewers:	

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**1 Efficacy of an FDA Approved Synthetic Nano-Bioactive Glass Plus Demineralized Bone
2 Matrix (DBM) Combination versus DBM Alone in Instrumented Lumbar Fusion for Low-
3 Grade Degenerative Spondylolisthesis: A Prospective Randomized Controlled Trial Pilot
4 Study**

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1 **Structured Abstract**

2 **Background:** Demineralized Bone Matrix (DBM) is widely used in spinal fusion but has donor
3 variability and supply limitations. Synthetic bioactive glass (BAG) offers osteoinductive and
4 osteoconductive properties. NanoFuse™ DBM, an FDA-approved combination of nano-BAG
5 and DBM, integrates bioactive nanomaterials with organic bone matrix, but its efficacy in spinal
6 fusion remains underexplored. This study evaluates its impact on fusion success and clinical
7 outcomes compared to DBM alone.

8
9 **Methods:** In a randomized controlled trial, 64 patients underwent single-level lumbar fusion and
10 were followed for 36 months. Group 1 (n=29) received nano-BAG+DBM with an interspinous
11 fixation device, while Group 2 (n=35) received DBM alone with pedicle screws and posterior
12 lumbar interbody fusion. Both groups received an equivalent graft volume. Outcomes included
13 radiographic fusion, Visual Analog Scale (VAS), Oswestry Disability Index (ODI), surgical
14 parameters, and revisions.

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16 **Results:** Both groups achieved 100% fusion at 24 months, but Group 1 demonstrated earlier
17 fusion at 6 and 12 months. Group 1 had significantly lower VAS scores at 24 (P = 0.041) and 36
18 months (P < 0.001). ODI improved in both groups, with greater recovery in Group 1 (P <
19 0.00001). Group 1 also had shorter operative times and reduced blood loss. Two patients (5.71%)
20 in Group 2 required revision for adjacent segment disease.

21
22 **Conclusion:** Nano-BAG+DBM accelerated early bone fusion and improved clinical outcomes
23 while reducing DBM requirements and reliance on cadaveric bone. These findings highlight its
24 role as a synthetic alternative for spinal fusion and its potential in bone regenerative strategies.

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2 **Keywords:** Lumbar fusion, Demineralized Bone Matrix (DBM), Bioactive Glass (BAG),

3 NanoFuse™ DBM, Interspinous fixation, Bone Graft Alternative, Lamellar Bone.

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1 **1. Introduction**

2 Degenerative disc disease (DDD) and spondylolisthesis are prevalent spinal conditions that
3 frequently lead to chronic pain, disability, and progressive neurological deficits. DDD results
4 from the degeneration of intervertebral discs, leading to reduced disc height, diminished shock
5 absorption, and potential nerve compression [1-4]. Spondylolisthesis, defined by the anterior
6 displacement of one vertebra over another, further compromises spinal stability and may cause
7 nerve root impingement [5]. Although conservative treatments such as physical therapy, pain
8 management, activity modification, and epidural steroid injections [6-9] are typically first-line
9 management, surgical intervention becomes necessary when these measures fail or when
10 instability worsens [10].

11 Interbody cages combined with pedicle screw instrumentation have long been considered the
12 benchmark for posterior stabilization in the treatment of degenerative spondylolisthesis, offering
13 robust biomechanical support and high fusion rates [11, 12]. Despite the proven effectiveness of
14 pedicle screw fixation since its introduction in the 1940s, [13, 14] pedicle screw fixation (PSF)
15 has been associated with drawbacks, including prolonged operative times, increased blood loss,
16 screw malposition, and the development of adjacent segment disease (ASD). Consequently, non-
17 pedicular fixation alternatives such as interspinous fixation devices (IFDs) have emerged, as they
18 stabilize the spine by fixating the spinous processes and lamina posteriorly, thereby eliminating
19 the need for pedicle screws [15]. These devices have been associated with shorter operative
20 times, reduced blood loss, and decreased intraoperative complications [16, 17] and potentially
21 reducing adjacent segment disease [18].

22 With approximately 1.3 million lumbar fusion procedures billed to Medicare Part B in the United
23 States between 2000 and 2019, and annual lumbar interbody fusions nearly doubling from about

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1 61,000 to roughly 119,000, these statistics underscore the growing demand for spinal fusion
2 among an aging population [19]. The success of lumbar fusion procedures is highly dependent
3 on the selection of an appropriate bone graft material, which is critical for achieving robust
4 osseointegration and long-term spinal stability [20].

5 Historically, autologous iliac crest bone graft (ICBG) has been considered the gold standard for
6 spinal fusion owing to its osteogenic, osteoinductive, and osteoconductive properties [21-23].
7 However, the use of ICBG is limited by donor site morbidity, including pain, cluneal nerve
8 injury, infection risk, and structural compromise of the iliac crest, which has prompted the
9 exploration of alternative graft materials [24, 25]. As a result, demineralized bone matrix
10 (DBM), derived from processed allograft bone and retaining essential osteoinductive proteins
11 such as bone morphogenetic proteins (BMPs), has become widely adopted [26-28]. Although
12 DBM provides an osteoconductive properties, its clinical efficacy can be inconsistent due to
13 donor variability and a lack of mechanical support [29].

14 To address these limitations, synthetic bone substitutes like bioactive glass (BAG) have been
15 introduced to enhance osteogenesis and improve structural integrity [30]. In particular, the 45S5
16 composition of BAG, developed by Professor Larry Hench in 1969, has demonstrated significant
17 osteostimulative properties [31] by releasing biologically active calcium, phosphate, and silicon
18 ions that stimulate osteoblastic differentiation and promote bone matrix mineralization. BAG is
19 composed of inorganic metallic oxides and exhibit inherent osteoconductive properties that
20 foster bone regeneration and healing. Their dense, nonporous structure provides superior
21 durability and strength compared to other ceramic materials [32]. In addition, BAG exhibits
22 antimicrobial properties that may reduce the risk of postoperative infections. Animal studies,

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1 such as those by Pajamaki et al. [33-35], indicate that BAG can accelerate bone induction when
2 combined with DBM.

3 Despite these theoretical advantages, the efficacy of nano-BAG+DBM in lumbar fusion remains
4 largely unexplored. Given the unique biomechanical and anatomical characteristics of the lumbar
5 spine, further investigation is warranted to determine whether BAG and DBM combination can
6 yield clinical and radiographic outcomes comparable to those achieved with DBM alone. The
7 objective of this study aims to be the first to evaluate the safety and efficacy of nano-bioactive
8 glass combined with demineralized bone matrix (nano-BAG+DBM) versus DBM alone in
9 single-level instrumented lumbar fusion for grade 1 degenerative spondylolisthesis. We aim to
10 determine whether nano-BAG+DBM promotes earlier fusion at 12 months compared to DBM
11 alone in lumbar fusions.

2. Materials and Methods

2.1. Nano-Bioactive Glass and Demineralized Bone Matrix Combination

15 NanoFuse™ DBM (NanoFuse Biologics LLC, Burlington, MA) represents the only U.S. Food
16 and Drug Administration (FDA) approved osteobiologic that combines 45S5 BAG with DBM,
17 integrating the osteoinductive benefits of DBM with the osteostimulatory and antimicrobial
18 advantages of BAG. The product by weight is 33% DBM cortical bone, 33% 45S5 Bioglass and
19 33% porcine gelatin. This composite graft offers a promising alternative to autografts by
20 potentially enhancing fusion rates while reducing surgical morbidity.

2.2. Study Design

22 This prospective, randomized controlled trial (RCT) enrolled patients between 2019 and 2022 to
23 evaluate the efficacy and safety of nano-BAG+DBM versus DBM alone in single-level

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1 instrumented lumbar fusion. The study included individuals diagnosed with low-grade
2 degenerative spondylolisthesis who had not responded to conservative treatment for a minimum
3 of six months. This study was granted Institutional Review Board (IRB) approval through
4 Western Institutional Review Board (WIRB®) now known as WIRB-Copernicus Group
5 (WCG® IRB) (WIRB#20181251) and informed consent was obtained from all individual
6 participants.

7 *2.3. Participants and Eligibility Criteria*

8 A total of 64 patients meeting the inclusive criteria for instrumented fusion groups were enrolled.
9 All surgeries were performed by a single board-certified orthopedic spine surgeon in an
10 outpatient setting. Inclusion criteria included adults aged 18 to 75 years with symptomatic grade
11 1 degenerative spondylolisthesis at a single lumbar level (L2-S1) who failed nonoperative
12 treatment for at least six months and were able to comply with postoperative follow-up (Figure
13 1). Exclusion criteria included acute trauma, fractures, malignancy, active infection, prior lumbar
14 fusion or total disc replacement, severe osteoporosis or metabolic bone disease, chronic
15 uncontrolled systemic illness (e.g., diabetes, autoimmune disorders), and a body mass index
16 (BMI) >42.

17 *2.4. Randomization and Allocation*

18 Block randomization was employed to ensure balanced allocation of patients between treatment
19 groups. Eligible patients were randomly assigned to either Group 1 (nano-BAG+DBM+IFD,
20 n=29) and received fusion with IFD and 10 cc of nano-BAG+DBM (n=29) or Group 2
21 (DBM+PSF) and underwent fusion with PLIF and PSF and 10 cc of DBM Pure (n=35) using a
22 structured block system. The randomization process was managed by the surgical coordinator,
23 ensuring unbiased assignment. The treating surgeon was not aware of the randomization process

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1 or treatment allocation. No patients refused treatment, and no crossovers occurred between
2 groups.

3 *2.5. Blinding*

4 Radiologists assessing pre and postoperative radiographic images were blinded to group
5 allocation to ensure objective imaging analysis. However, due to the distinct surgical techniques
6 used in each group, blinding of participants and care providers was not feasible.

7 *2.6. Surgical Technique*

8 All patients underwent a midline posterior lumbar decompression followed by instrumented
9 fusion. For Group 1, the interlaminar space was prepared, and InSpan IFD (InSpan LLC,
10 Burlington, MA, USA) was measured and fixated to the spinous processes and lamina [16, 17].
11 NanoFuse™ DBM (Nano-BAG+DBM) was mixed with autograft and applied over the
12 decorticated facet joints and within the interlaminar space to facilitate fusion (Figure 2). For
13 Group 2, the intervertebral disc space was prepared for standard PLIF procedure and two PLIF
14 cages packed with DBM (DBM Pure, LESSpine Inc., Burlington, MA, USA) mixed with
15 autograft were inserted. Bilateral pedicle screws and rods were placed for posterior stabilization,
16 and DBM was applied over the decorticated facet joints.

17 *2.7. Follow-Up*

18 Patients were monitored postoperatively and discharged based on standard outpatient surgical
19 criteria. Follow-up visits were conducted at 3 months, 6 months, 12 months, 24 months and 36
20 months. Clinical and radiographic evaluations were conducted to assess fusion progress, pain
21 levels, and functional outcomes.

22 *2.8. Outcomes*

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1 The primary outcome of this study was radiographic fusion, assessed using dynamic X-rays
2 (flexion-extension lateral views) and CT scans at 6, 12, 24, and 36 months. Facet fusion was
3 graded using the following classification: Grade I (complete bone continuity across the facet
4 joint), Grade II (continuous but incomplete bone formation), Grade III (uncertain bony
5 continuity), and Grade IV (obvious nonunion) [36, 37]. Fusion was considered successful if
6 either one or both facet joints achieved Grade I or II fusion. Interbody fusion was defined
7 according to Lebowitz et al., where the presence of continuous bone bridging in the interspace
8 anterior to the cage on lateral radiographs was considered definitive fusion [38]. Secondary
9 outcomes included patient-reported outcome measures (PROMs), perioperative parameters, and
10 long-term surgical outcomes. PROMs were assessed using the Visual Analog Scale (VAS) and
11 the Oswestry Disability Index (ODI) at baseline and at 6, 12, 24, and 36 months to evaluate pain
12 relief and functional improvement. Perioperative parameters included operative time, estimated
13 blood loss (EBL), and intraoperative complications. Long-term surgical outcomes included
14 implant-related failures, revision rates, and the development of adjacent segment disease (ASD).

15 *2.9. Sample Size and Power Analysis*

16 The sample size was based on expected differences in fusion rates at 6 months, the primary
17 outcome. We hypothesized that Group 1 would achieve earlier fusion compared to Group 2. A
18 priori power analysis was conducted to determine the necessary sample size to detect a moderate
19 to large effect size with statistical confidence. To achieve 80% power at a 0.05 significance
20 level, a minimum of 32 patients per group (64 total) was required. This sample size balanced
21 statistical power with study feasibility. Despite unequal group sizes, 29 and 35, the total sample
22 size remained sufficient to detect meaningful differences. A post-hoc power analysis confirmed
23 that the sample size remained adequate to detect a clinically relevant effect.

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1 2.10. *Statistical Analysis*

2 All statistical analyses were performed using Python-based tools (pandas, scipy.stats,
3 statsmodels) within Visual Studio Code. Continuous variables (VAS, ODI, operative time, and
4 EBL) were analyzed using independent samples t-tests for between-group comparisons and
5 paired t-tests for within-group changes. Effect sizes were quantified using Cohen’s d. Normality
6 was assessed using the Shapiro-Wilk test, and Levene’s test evaluated homogeneity of variances.
7 When normality or variance assumptions were violated, non-parametric comparisons were
8 performing using the Mann-Whitney U test for between-group analyses and the Wilcoxon test
9 for within-group paired data. Categorical variables, including fusion status, revision rates, and
10 complication rates, were analyzed using the Chi-square test with Yates' continuity correction or
11 Fisher’s exact test when expected frequencies were <5. For multiple comparisons with unequal
12 variances, the Games-Howell test was applied to adjust for standard errors. Statistical
13 significance was set at $P < 0.05$.

15 **3. Results**

16 A total of 64 patients were enrolled and randomized into two groups. Group 1 (n = 29, 62.1%
17 female) received nano-BAG+DBM+IFD, while Group 2 (n = 35, 51.43% female) received
18 DBM+PSF. All participants completed their assigned treatments and follow-up visits, with no
19 dropouts. Baseline characteristics, including age (P = 0.513) and BMI (P = 0.648), were
20 comparable between groups.

21 *Radiographic Fusion Outcomes*

22 Radiographic evaluations confirmed 100% fusion at 24 months in both groups (Figures 3 and 4).
23 However, fusion patterns differed between groups. Group 1 demonstrated earlier interspinous

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1 fusion and unilateral Grade II facet fusion by 6 months, with definitive Grade I facet fusion by
2 12 months. In contrast, Group 2 showed early interbody fusion within the cage at 12 months,
3 reaching definitive fusion and Grade II facet fusion at 24 months.

4 *Pain and Functional Outcomes*

5 Both groups demonstrated significant postoperative improvements in pain and function. In
6 Group 1, VAS scores decreased from 8.08 ± 1.62 preoperatively to 4.05 ± 3.14 at 12 months ($P <$
7 0.001). Between 12 and 24 months, VAS remained stable (4.04 ± 2.62), but further improved at
8 36 months (3.04 ± 2.31 , $P = 0.02$). In Group 2, VAS scores declined from 8.17 ± 0.95 to $5.5 \pm$
9 0.66 at 12 months ($P < 0.001$), but remained comparable at 24 months (5.54 ± 0.95 , $P = 0.301$)
10 and 36 months (5.08 ± 0.65 , $P = 0.458$). Between-group comparisons revealed no significant
11 difference in VAS at 12 months ($P = 0.162$), but Group 1 had significantly lower pain scores at
12 24 months ($P = 0.041$) and 36 months ($P < 0.001$), compared to Group 2 with a moderate and
13 large effect size of 0.76 and 1.15.

14 Functional outcomes also improved significantly in both groups. Group 1 showed a greater
15 reduction in ODI from $51.45\% \pm 7.76$ preoperatively to $16.30\% \pm 8.96$ at 24 months, compared
16 to Group 2, which decreased from $51.57\% \pm 6.19$ to $33.34\% \pm 3.85$. Group 1 exhibited
17 significantly greater functional improvement ($P < 0.00001$).

18 *Operative and Surgical Outcomes*

19 Group 1 demonstrated shorter operative times (94 ± 13 minutes vs. 146 ± 21 minutes; $P < 0.001$)
20 and lower EBL (72.90 ± 44.65 mL vs. 297.43 ± 80.31 mL; $P < 0.00001$). No intraoperative
21 complications occurred in either group. Although no revisions were required in Group 1, two
22 patients (5.71%) in Group 2 required revision surgery for adjacent segment disease; however,

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1 this difference was not statistically significant (Fisher’s exact test, P = 1.0). No implant-related
2 failures were reported in either group.

4. Discussion

4.1. Brief Summary and Purpose of This Study

6 This study assessed the safety and efficacy of nano-BAG+DBM combination in single-level
7 instrumented lumbar fusion compared to DBM alone for patients with low-grade
8 spondylolisthesis. BAG is recognized for its ability to enhance osteogenic activity, stimulate
9 angiogenesis, exert antimicrobial properties due to its ionic release and contribute to high
10 fusion rates in cervical and lumbar spine surgery [31, 39-41]

4.2. Summary of Key Findings

12 Our results demonstrated that both groups achieved 100% radiographic fusion at 24 months,
13 confirming that the addition of BAG to DBM does not compromise fusion success. Notably,
14 Group 1 (nano-BAG+DBM+IFD) exhibited earlier facet fusion, with Grade II fusion evident at 6
15 months and definite Grade I fusion by 12 months, compared to the Group 2 (DBM+PSR), which
16 showed definitive fusion at 24 months. This accelerated fusion in Group 1 may be attributed to
17 BAG’s dual function as both a scaffold and a source of biologically active ions that enhance the
18 osteogenic potential of DBM. In contrast, Group 2’s use of interbody cages likely delayed
19 interbody fusion, while pedicle screws and rods may have contributed to stress shielding of the
20 facets and interbody space, slowing the overall fusion process. The less rigid fixation provided
21 by the IFD in Group 1 appeared to promote bone remodeling in accordance with Wolff’s Law
22 [42], resulting in earlier and more pronounced radiographic fusion.

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1 An *in vivo* animal model demonstrated that instrumentation improved fusion rates for
2 posterolateral spine fusion; however, more rigid instrumentation led to the formation of
3 histologically woven bone [43], which is less mineralized and appears more radiolucent.
4 According to Wolff's law, Group 1, where mechanical stress is maintained at the facets, is
5 expected to form lamellar bone, whose highly organized and mineralized structure creates clear,
6 dense (radiopaque) images on radiographs, making it superior for visualizing facet fusion
7 compared to the stress-shielded woven bone seen in Group 2.
8 No complications were reported in either group; however, Group 1 benefited from significantly
9 reduced operative times and lower blood loss, likely due to the reduced instrumentation and the
10 absence of interbody cages. The achievement of 100% facet fusion highlighted the effectiveness
11 of the nano-BAG+DBM combination independent of pedicle screw and cage use. While no
12 implant failures occurred in either group, it is noteworthy that, despite the known strength of
13 pedicle screws coupled with interbody cages for three-column fixation [44, 45], the earlier facet
14 and interspinous fusion observed in Group 2 may have helped protect the less rigid fixation
15 construct from developing ASD by reducing stress on adjacent segments. In contrast, two
16 patients in the Group 2 developed ASD that required revision surgery.

17 *4.3. Comparison with Existing Literature*

18 Our findings align with previous studies that highlight the osteoinductive and osteoconductive
19 properties of BAG, supporting its role as an effective bone graft substitute that promotes bone
20 healing and structural integrity. For instance, animal studies by Pajamaki et al. [33-35]
21 demonstrated that BAG implants can accelerate bone induction when combined with DBM,
22 which may explain the earlier facet fusion observed in our nano-BAG+DBM group compared to
23 DBM alone. Moreover, a meta-analysis by Cottrill et al. [46]. confirmed that BAG enhances

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1 spinal fusion rates via its osteostimulatory effects, offering a viable alternative to both DBM and
2 autografts without increasing the risk of deep wound infections. A 4-year randomized controlled
3 trial reported that BAG spacers achieved fusion rates and clinical outcomes comparable to those
4 of autologous bone grafts and titanium cages in single-level PLIF [47], while another
5 randomized trial found no significant difference in fusion success between BAG spacers (89.7%)
6 and titanium cages (91.2%) at 12 months post-surgery [48]. Szadkowski et al. reported that in
7 anterior lumbar interbody fusion (ALIF) procedures performed at L5-S1 or L4-L5, fusion rates
8 achieved using BAG were equivalent to those obtained with autologous ICBG [49]. This finding
9 indicates that BAG can effectively replace autologous grafts, thereby reducing operative time,
10 blood loss, and the complications associated with donor site morbidity.

11 In the context of instrumented lumbar fusion, high fusion rates have been achieved using PSR
12 constructs combined with interbody cages; however, these techniques are often associated with
13 complications such as ASD [50]. Consequently, IFDs have been explored as alternatives, as they
14 provide adequate stabilization with the added benefits of shorter operative times, reduced blood
15 loss, and decreased tissue disruption, potentially mitigating the risk of ASD. Stand-alone
16 interspinous lumbar instrumented fusion with bone grafting has also shown promising results in
17 promoting fusion in patients with unstable grade 1 degenerative spondylolisthesis with
18 comparable outcomes to PLIF [51]. When IFD is used in conjunction with anterior or lateral
19 lumbar interbody fusion (ALIF/LLIF), significant improvements in early postoperative patient-
20 reported outcomes (≤ 12 months) were observed with robust posterior fusion and minimal
21 complications [15].

22 *4.4. Clinical Implications*

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1 Our study indicates that integrating BAG with DBM offers a promising alternative to using
2 DBM alone in lumbar fusion, particularly in outpatient settings where less invasive techniques
3 are favored. BAG provides a standardized, reproducible graft option that mitigates the donor
4 variability issues often seen with DBM, when used in equivalent volumes. Furthermore, as a
5 synthetic inorganic material, bioactive glass circumvents the need for harvesting cadaveric or
6 autologous bone, ensuring a reliable and cost-effective supply [32].

7 *4.5. Limitations*

8 This study’s single-center design and relatively small sample size (n=64) may affect the
9 generalizability of our findings. Although the follow-up period extended to 36 months, it may
10 not fully capture long-term outcomes such as implant subsidence, adjacent segment
11 degeneration, or late-stage nonunion. Additionally, two different fixation methods were used:
12 Group 1 employed an IFD, which provides less rigid stabilization compared to the pedicle
13 screws and interbody cages used in Group 2. This methodological difference, particularly in light
14 of the earlier facet fusion observed in Group 1, could potentially confound the results. Future
15 multi-center studies with larger cohorts and extended follow-up periods are needed to validate
16 fusion rates, assess efficacy against other synthetic grafts and autograft alternatives with similar
17 instrumentation, and evaluate performance in multi-level fusion procedures, ultimately clarifying
18 the clinical utility of nano-BAG+DBM in spinal fusion.

20 **5. Conclusion**

21 Posterior instrumentation using both nano-bioactive glass and DBM combination and DBM
22 alone achieved 100% radiographic fusion. Notably, the nano-BAG+DBM group with
23 interspinous fixation devices demonstrated earlier facet fusion compared to the DBM group

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1 utilizing a pedicle screw-rod construct. These findings support the use of nano-BAG+DBM as a
2 viable alternative for instrumented lumbar fusion procedures that do not require pedicle screws
3 or interbody cages in selected patients. Moreover, using an equivalent volume of the nano-
4 BAG+DBM composite compared to DBM alone suggests that BAG’s enhanced osteogenic
5 capabilities can lower the total DBM needed, thereby reducing reliance on cadaveric bone. The
6 osteoconductive and osteostimulatory properties of BAG further augment the bone-forming
7 potential of DBM [33-35], offering a reproducible, synthetic alternative to human-derived grafts.

8
9 **CRedit authorship contribution statement:**

10 William M. Costigan MD – Conceptualization, Supervision. Erik Spayde MD –
11 Conceptualization, Supervision. Vito Lore PE – Supervision. Hope Estevez – Project
12 administration. Sukanya Chebrolu MS - Writing – original draft, Project administration.
13 Chukwunonso C. Ilogu MD - Data curation, Writing – original draft, Formal analysis. Jason A.
14 Seale MBBS - Writing – review and editing, Visualization. Kingsley R. Chin MD -
15 Conceptualization, Methodology, Supervision.

16
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19 or not-for-profit sectors.

20
21 **Data availability:**

22 Data will be made available on request.

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1 **Figure Legend:**

2 **Figure 1:** Female patient with L3-4 grade 1 degenerative spondylolisthesis and ligamentum
3 flavum hypertrophy, Modic endplate changes, disc desiccation and spinal stenosis on MRI.

4 **Figure 2:** NanoFuse™ DBM inserted following decompression and fusion with InSpan
5 interspinous fixation device

6 **Figure 3:** Postoperative Computed Tomography (CT) Scan at 24 months showing (A) Grade I
7 facet fusion and (B and C) Interspinous Fusion.

8 **Figure 4:** L5-S1 decompression and instrumented fusion with bilateral PLIF cages and pedicle
9 screws-rod construct. Postoperative Computed Tomography (CT) Scan at 24 months showed
10 interbody fusion and grade II facet fusion.

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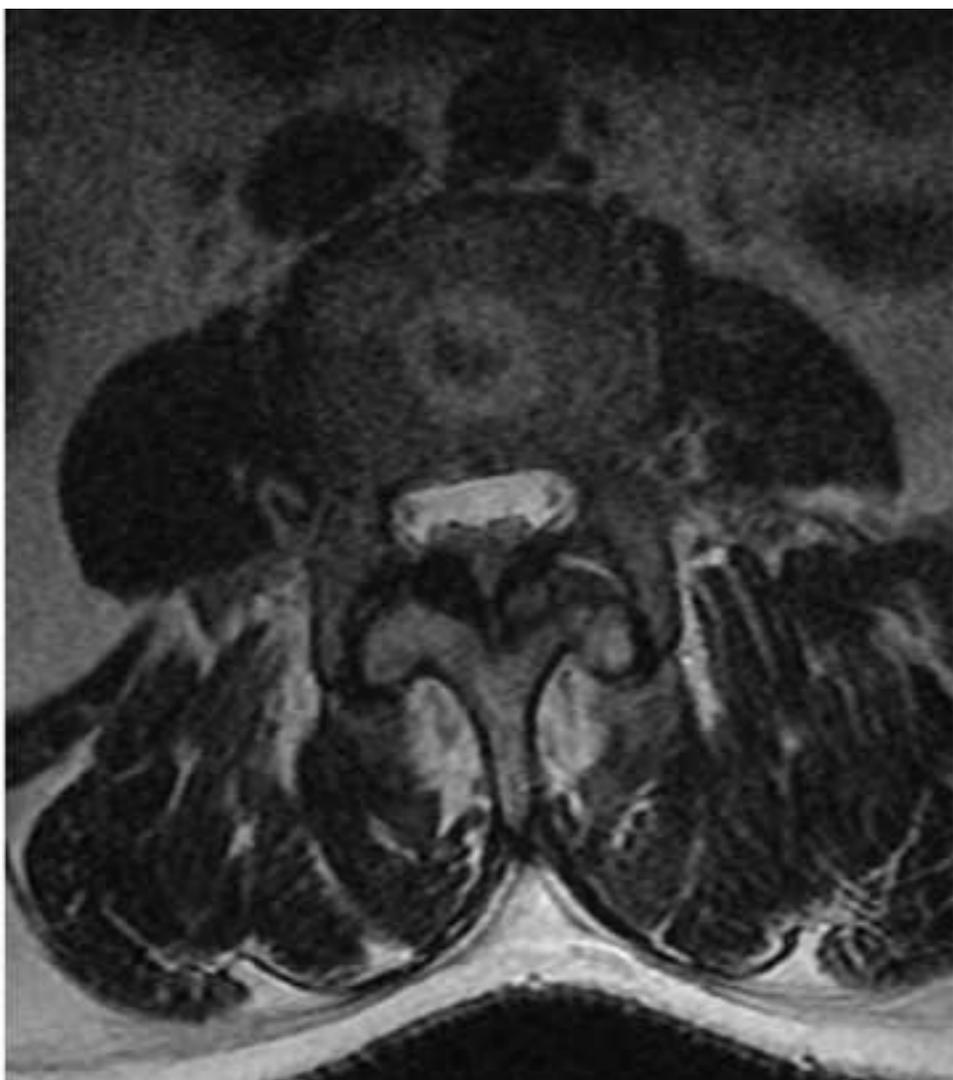
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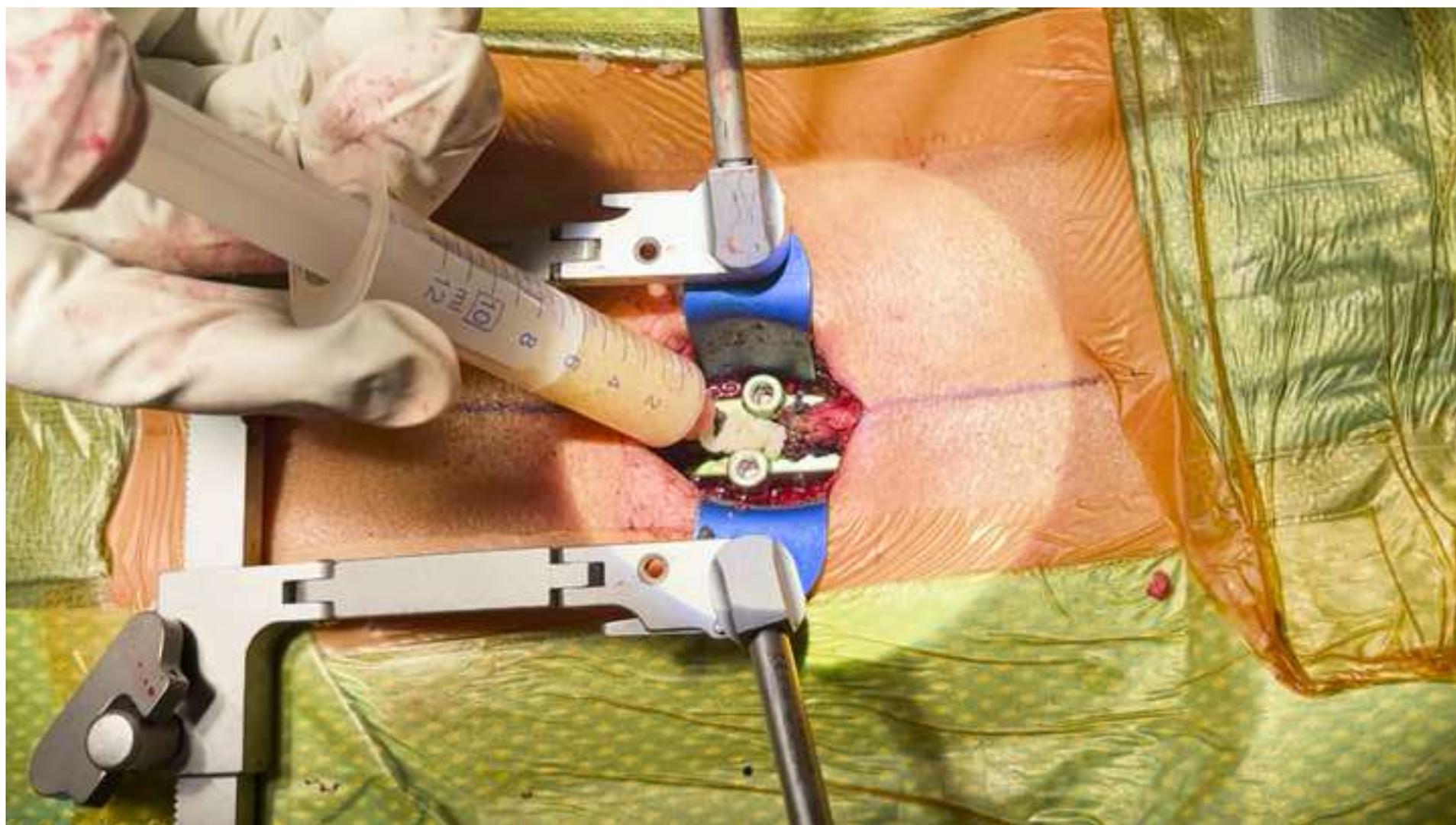
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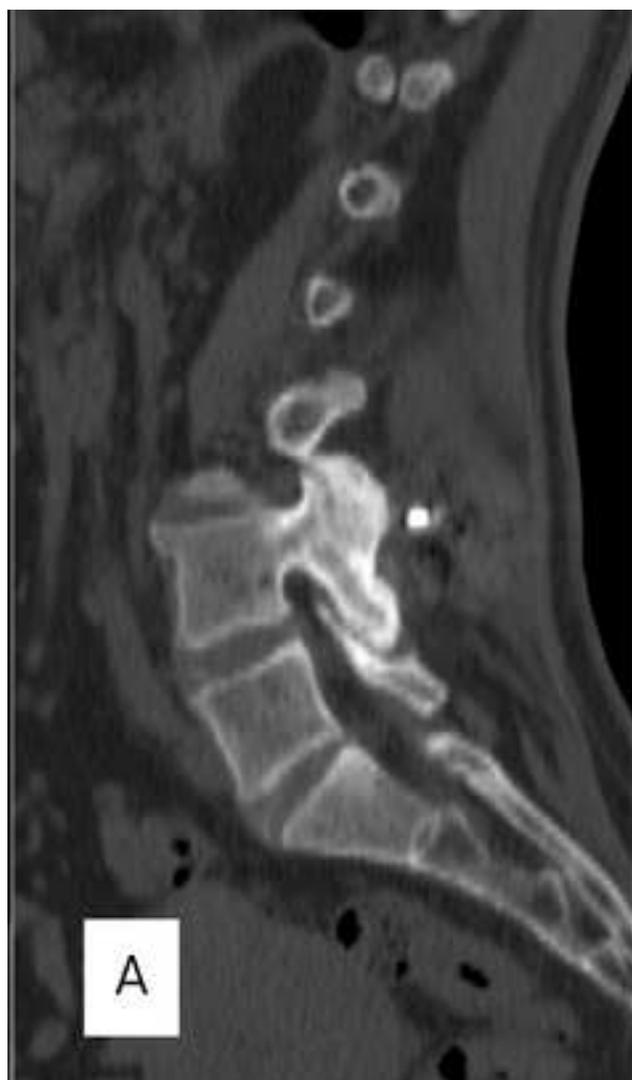
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Figure(s)



Figure(s)





Figure(s)



1 **Highlights**

- 2 1. Nano-BAG+DBM fused earlier at 6 months compared to DBM alone at 12 months.
- 3 2. Fusion rates were similar using equal volumes of nano-BAG+DBM and DBM.
- 4 3. Nano-BAG+DBM lowered VAS pain scores and improved ODI functional outcomes.
- 5 4. BAG's osteogenic properties may reduce DBM needs and reliance on cadaveric bone.
- 6 5. Nano-BAG+DBM is a synthetic alternative for spinal fusion biomaterials.

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