

Preliminary study showing safety/efficacy of nanoss bioactive versus vitoss as bone graft expanders for lumbar noninstrumented fusions

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Abstract

Background: The lateral fusion mass for multilevel lumbar laminectomies with noninstrumented posterolateral fusions now often utilizes lamina autograft and bone marrow aspirate (BMA) mixed with one of two bone graft expanders: either Vitoss (Orthovita, Malvern, PA, USA) or NanOss Bioactive (Regeneration Technologies Corporation: RTI, Alachua, FL, USA).

Methods: Here, we compared two sequential prospective the times to fusion, fusion rates, complications, and infection rates for two prospective cohorts of patients utilizing either Vitoss (first 213 patients) or NanOss (subsequent 45 patients) respectively, undergoing multilevel lumbar laminectomies (average 4.6 vs. 4.5 levels) with noninstrumented fusions (average 1.3 vs. 1.2 levels). Surgery addressed stenosis/ossification of the yellow ligament (OYL) (all patients), with subsets exhibiting degenerative spondylolisthesis synovial cysts, and disc disease. Fusion was documented by two independent neuroradiologists blinded to the study design, utilizing dynamic X-rays and two dimensional computed tomography (2D-CT) studies up to 6 months postoperatively, and up to 1 year where indicated.

Results: Comparison of patients receiving Vitoss versus NanOss as bone graft expanders revealed nearly comparable; times to fusion (5.3 months vs. 4.8 months), fusion rates (210 [98.6%] vs. 45 [100%] patients), pseudarthroses (3 [1.4%] vs. 0), postoperative seromas (2 [0.94%] vs. 0), and deep wound infections (2 [0.94%] vs. 0).

Conclusion: In this preliminary study of patients undergoing multilevel lumbar laminectomies with posterolateral noninstrumented fusions, results were nearly comparable utilizing Vitoss or NanOss as bone graft expanders. Although the number of NanOss patients was substantially lower, the comparable efficacy and absence of postoperative complications for noninstrumented fusions is promising.

Key Words: Autograft, Beta-TriCalcium phosphate, noninstrumented lumbar fusion, NanOss Bioactive, pseudarthrosis rates, Vitoss

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INTRODUCTION

Two successive prospective cohorts of patients underwent multilevel lumbar laminectomies with noninstrumented posterolateral lumbar fusions (PLF) utilizing lamina autograft and bone marrow aspirate (BMA) mixed with one of two bone graft expanders. The first 213 patients received Vitoss (Orthovita, Malvern, PA, USA), while the latter 45 patients received NanOss Bioactive (Regeneration Technologies Corporation (RTI: Alachua, FL, USA). We asked whether utilization of these two bone graft expanders would result in comparable times to fusion, rates of fusion versus pseudarthrosis, incidence of postoperative seromas, and infection.

METHODS

Vitoss

Vitoss, a form of Beta Tri-Calcium Phosphate (B-TCP), is a synthetic cancellous bone graft substitute/bone void filler that contains 39% calcium and 20% phosphorous, in a 1:5 ratio.^[1-4,6] Vitoss' porous low-density construct is prepared by fusing nano particles (100 nm in diameter) that increase its microporosity (e.g., a scaffold that is 90% interconnected; pores ranging from 1 to 1000 microns) and fusion rates by facilitating bone ingrowth/infiltration, resorption, dissolution, and new bone formation.

NanOss Bioactive

NanOss' nano-crystalline conformation (15–100 nm) is similar to normal human bone crystals (25–500 nm) both in composition and shape; alternatively, other calcium phosphate crystals are typically 1000–10,000 nm in size.^[7,8] NanOss contains highly purified porcine collagen that is unwound producing much more surface area for the attachment of osteoclasts/osteoblasts. This manufactured extracellular matrix-bioscaffold facilitates greater cell infiltration/osteoconduction, and fusion, with an open scaffold that optimizes bone mineralization/remodeling.

Two prospective cohorts utilizing Vitoss (213 Patients) followed by NanOss (45 Patients) as bone graft expanders

The first cohort of 213 patients received Vitoss (2007–2011) while the subsequent cohort of 45 patients received NanOss (2012–2014) as bone graft expanders to supplement noninstrumented posterolateral fusions (average 1.3 vs. 1.2 levels) following multilevel lumbar laminectomies (average 4.6 vs. 4.5 levels) [Table 1]. For patients receiving Vitoss or NanOss, average ages, major comorbid factors, average estimated blood loss (EBL) (163 cc vs. 177 cc, respectively), and operative times (respectively 4.125 vs. 4.0 h) were similar. Pathology documented

Table 1: Clinical data utilizing vitoss versus nanoss bioactive as bone graft expanders/supplements

Variables	Laminectomy/ noninstrumented fusion (LamF) with Vitoss 213 patients (2007-11)	Laminectomy/ noninstrumented fusion (LamF) with NanOss 45 patients (2012-14)
Age		
Average	65.8	62.5
STDEV	11.11	10.0
Range	34-83	51-83
Sex		
Males	87	13
Females	126	32
Comorbidities		
Hypertension	119	22
Diabetes	38	4
Osteoporosis	120	36
Obesity	73	14
Pathology		
Ossification of yellow ligament	213	45
Spondylolisthesis with Lysis	173 (81.2%) (8)	41 (91%) (1)
Synovial cysts	35 (16.4%)	19 (42.2%)
Disc herniations	98 (46%)	14 (31.1%)
Far lateral discs	(33)	(6)
Laminectomy levels		
Average	4.6	4.5
STDEV	1.2	1.01
Range	3-11	3-7
Fusion levels		
Average	1.3	1.2
STDEV	0.51	0.4
Range	1-3	1-2
Operative time		
Average	4.125	4.0
STDEV	0.6	0.6
Range	3.5-6	3-5.5
Duration of follow-up		
Average	2.7	1.2
Range	1-5 years	6 months to 2 years

on dynamic X-rays, magnetic resonance imaging (MR), and computed tomography (CT) studies uniformly included ossification of the yellow ligament (OYL) with varying frequencies of spondylolisthesis, synovial cysts, and disc herniations [Table 1]. The average follow-up duration, however, was longer as anticipated for the Vitoss (average 2.7 years) versus NanOss (1.2 years) patients due to the longer duration (4 years vs. 2 years) of the Vitoss series.

Table 2: Operative data utilizing Vitoss versus NanOss Bioactive as bone graft expanders/supplements

Variables	Lumbar noninstrumented fusion with Vitoss 213 patients	Lumbar noninstrumented fusion with NanOss Bioactive
Time to fusion (months)		
Average	5.3	4.8
Range	3-7	3-7
Pseudarthrosis	3	0
Delayed 10-12 months	2	0
Complications/reoperations		
Infection/dehiscence	3	0
Seroma (no infection)	2	0
Estimated blood loss (cc)		
Average	163	177
STDEV	128	112
Range	200-1000	50-600

Posterolateral fusion mass utilizing vitoss and NanOss

Posterolateral fusion masses applied over decorticated transverse processes utilized lamina autograft (first layer), supplemented with Vitoss or NanOss (second layer). Both products come in a 10 × 2.5 cm sheets that are readily soaked in 10 cc of BMA. Each sheet may be cut in half or quarters for better handling. For a one-level fusion, each side receives half a strip applied dorsal to the lamina autograft, while two-level fusions in larger patients, may occasionally warrant a full strip on each side.

Dynamic X-rays and two dimensional computed tomography (CT) documentation of fusion

All patients underwent dynamic X-rays (3, 4.5, and 6 months postoperatively) and two dimensional CT (2D-CT) studies (at 3 months and repeated as needed) until fusion or pseudarthrosis was documented (e.g. up to 1 year postoperatively). Studies were independently analyzed by two neuroradiologists blinded to the study design.

RESULTS

Patients in both groups also exhibited comparable; times to fusion; 5.3 months vs. 4.8 months [Figures 1-4 and Table 2]. Despite the much greater number of patients in the Vitoss versus NanOss cohorts, both groups exhibited similar fusion rates; 210 (98.6%) of 213 Vitoss patients fused versus 100% fusion rate for the 45 NanOss patients. However, likely due to the larger number of patients in the Vitoss series, three patients exhibited pseudarthrosis (1.4%), two of whom had developed early wound infections (0.94%), while two others developed postoperative seromas (0.94%) warranting debridement. Alternatively, for the smaller

sample of NanOss patients, no pseudarthroses, infections, or seromas were observed.

DISCUSSION

Prior studies documenting efficacy of Vitoss as a bone graft expander for fusion

Efficacy of Vitoss as a bone graft expander for instrumented posterolateral lumbar fusions

Epstein previously documented the efficacy of Vitoss as a bone graft supplement/expander in two instrumented PLF studies.^[1] In the 2006 study, Vitoss, BMA, and lamina autograft (50:50 mix) constituted the posterolateral fusion mass for 40 multilevel lumbar laminectomies (average 3.7 levels) with one (27 patients) or two level (13 patients) instrumented fusions. At 6 postoperative months, 26 of 27 single level procedures fused (1 pseudarthrosis), while 11 of 13 two level fusions (2 pseudarthroses) succeeded. In 2009, Vitoss, BMA, and lamina autograft were again successfully utilized to perform 100 posterolateral lumbar instrumented fusions.^[3] For single-level fusions, 74 (93.7%) of 79 patients fused “early” (average 6.5 postoperative months), 2 (2.5%) fused “late” (average 6.5–12 months), while 3 (3.8%) exhibited pseudarthrosis. For two-segment fusions, 14 (66.7%) of 21 patients showed “early” fusions, 5 (23.8%) demonstrated “late” fusions, while 2 (9.5%) exhibited pseudarthroses.

Efficacy of Vitoss as a bone graft expander for noninstrumented posterolateral lumbar fusions (earlier study)

In a prior series from 2008, Epstein evaluated fusion rates for 60 patients undergoing average 5.4 level laminectomies with 1-2 level posterolateral noninstrumented fusions utilizing Vitoss/BMA/autograft.^[2] Although radiographic pseudarthrosis was documented in nine (15%) patients on both dynamic X-rays and 2D-CT studies performed 3–12 months postoperatively, only one patient was sufficiently symptomatic to required secondary surgery (e.g., younger patient on early postoperative aspirin due to severe cardiac disease).

Efficacy of Local bone with Vitoss/B-TCP (bone graft extender) for posterior adolescent idiopathic scoliosis surgery

In a 2009 prospective randomized scoliosis pilot study (EBM-Level 1), Lerner *et al.* compared the clinical/radiographic results of utilizing Vitoss/B-TCP (20 patients) with local bone versus autogenous iliac crest bone graft (ICBG) (20 patients) for adolescent idiopathic scoliosis (AIS) surgery.^[6] With an average postoperative follow-up of 20 months, Vitoss/local bone graft resulted in equal fusion rates (e.g., only 1 pseudarthrosis) versus ICBG (e.g. no pseudarthrosis).

Efficacy of bone morphogenetic protein (BMP/INFUSE) and calcium phosphate salts for posterolateral lumbar fusion

In 2014, Kaiser *et al.* proposed using local laminectomy autograft, calcium-phosphate salts, and bone morphogenetic



Figure 1: A 73-year-old female underwent a multilevel L2-S1 lumbar laminectomy and noninstrumented L4-5 posterolateral fusion (for grade I degenerative spondylolisthesis) utilizing lamina autograft/BMA/Vitoss. The 6-month postoperative axial CT study demonstrated continuity of the fusion mass consistent with adequate arthrodesis



Figure 2: For the same patient from Figure 1, the 6-month postoperative parasagittal 2D soft tissue CT scan demonstrated continuity of the lamina autograft/BMA/Vitoss over the L4-L5 transverse processes consistent with posterolateral noninstrumented arthrodesis



Figure 3: A 75-year-old female underwent a multilevel L1-S1 laminectomy and noninstrumented L4-L5 posterolateral fusion (for grade I degenerative spondylolisthesis) utilizing lamina autograft/BMA/NanOss. The 6-month postoperative axial CT study demonstrated similar continuity of the fusion mass consistent with arthrodesis



Figure 4: For the same patient from Figure 3, the 6-month postoperative parasagittal 2D bone window CT demonstrated continuity of the lamina autograft/BMA/NanOss over the L4-L5 posterolateral noninstrumented fusion mass consistent with arthrodesis

proteins (BMPs) to perform lumbar interbody fusions, thus avoiding the morbidity of harvesting autologous ICBG (AICB).^[5] Although they noted comparable fusion rates using BMP, they cited increasing concern regarding BMPs risks of heterotopic bone formation.

Comparison of NanOss with Vitoss and other products as bone graft expanders

NanOss, autograft, Vitoss, and Actifuse in a rabbit posterolateral fusion model

In 2009, Hill and Walsh (*presentation North American Spine Society Meeting 2009*) observed that NanOss has a high surface area for osteoblastic adhesions due to its unwinding of the triple helix structure, thus separating

the strands to provide more sites for cell infiltration/ attachments, and greater bone formation. Surface areas for the various compounds included; NanOss 70 m²/g, human bone 20–100 m²/g, Vitoss 0.3 m²/g, Actifuse 0.26 m²/g (Baxter Corporation Franklin Lakes, NJ, USA). Evaluating CT studies following L5-L6 PLF performed in rabbits at 8 and 12 postoperative weeks, they documented greater fusion for NanOss versus Actifuse versus Autograft, greater biomechanical strength/ stiffness, and more histological ossification/fusion. In 2012, Walsh *et al.* (*Orthopedic Research Society Meeting 2012*) again confirmed greater fusion utilizing NanOss to perform L5-L6 PLF in rabbits; at 6, 12, and 26 weeks greater fusion was observed for NanOss/BMA/autograft versus Vitoss BA/BMA versus autograft/BMA).

Nanocrystalline hydroxyapatite versus autologous BMA versus local bone in the lumbar spine: A retrospective CT analysis of PLF
In 2014, Robbins *et al.* performed a retrospective, multicenter 1-year review of postoperative CT studies in 46 patients (average age 58.6) undergoing 1–3 segment instrumented posterolateral fusions (PLF) utilizing NanOss/BMA/autograft.^[8] Patients' comorbid factors included: obesity (19 patients), hypertension (HTN) (4 patients), Type II DM (2 patients), smoking (6 patients), steroid use (1 patient), and osteopenia (3 patients). CT-documented fusion (e.g. bridging bone) over the transverse processes was confirmed in 94% of patients either unilaterally or bilaterally; fusion rates for 1–3 segments were 88%, 93%, and 100%, respectively, with only 6% of segments showing no fusion. Furthermore, there were no complications attributed to NanOss.

NanOss nanocrystalline hydroxyapatite most comparable to normal bone vs. Vitoss

In 2014, MacMillan *et al.* evaluated osteoblast and osteoclast activity for NanOss Bioactive (e.g. nanocrystalline hydroxyapatite [HA]; nanomaterials < 100 nm; porous low crystalline nano HA, B-TCP (RTI Surgical Corporation)) versus other micron crystalline ceramics (e.g. calcium phosphate products; HA, and biphasic calcium phosphates (TCP/HA), porous micron-TCP (Vitoss; Stryker, Corporation, Kalamazoo MI, USA) various types of nanoceramics).^[7] Focusing on improved bone formation utilizing nanoceramics (NanOss) versus micron ceramics, they demonstrated similar osteoblast and osteoclast activity for NanOss and normal bone, noting that micron crystalline HA products were not as effective. They concluded that NanOss resulted in increased bone growth, reduced pseudarthrosis, and fewer infections.

Comparable posterior cervical fusion rates utilizing Vitoss versus NanOss to supplement ICBG and BMA

In 2014, Epstein evaluated the efficacy of utilizing two bone graft expanders to achieve fusion in two separate sequential patient cohorts undergoing 1–3 level cervical laminectomy with posterior instrumented fusions (range 5–9 levels).^[4] The first cohort of 72 patients received Vitoss/BMA/ICBG, while the next cohort of 20 patients received NanOss/BMA/ICBG. Utilizing dynamic X-ray and 2D-CT studies, the time to fusion for both groups were comparable (5.65 months vs. 5.35 months). As

anticipated, however, the larger series of 72 patients receiving Vitoss/BMA/ICBG demonstrated more complications (e.g., 2 [2.8%] instances of pseudarthrosis, 2 infections [2.8%]) versus none for the smaller NanOss sample of 20 patients.

CONCLUSION

Following multilevel lumbar laminectomies and 1-2 level posterolateral noninstrumented fusions, Vitoss (213 patients) and subsequently NanOss (45 patients) proved to be successful bone graft expanders, demonstrating nearly comparable fusion rates. Despite the smaller number of NanOss patients in this study, the comparable fusion efficacy and lack of significant postoperative complications make it a promising product to use in the future.

REFERENCES

1. Epstein NE. A preliminary study of the efficacy of Beta Tricalcium Phosphate as a bone expander for instrumented posterolateral lumbar fusions. *J Spinal Disord Tech* 2006;19:424-9.
2. Epstein NE. An analysis of noninstrumented posterolateral lumbar fusions performed in predominantly geriatric patients using lamina autograft and beta tricalcium phosphate. *Spine J* 2008;8:882-7.
3. Epstein NE. Beta tricalcium phosphate: Observation of use in 100 posterolateral lumbar instrumented fusions. *Spine J* 2009;9:630-8.
4. Epstein NE. Preliminary Documentation of the Comparable Efficacy of Vitoss vs. NanOss Bioactive as Bone Graft Expanders for Posterior Cervical Fusion. *Surg Neurol Int Spine Suppl* [In Press 2015].
5. Kaiser MG, Groff MW, Watters WC 3rd, Ghogawala Z, Mummaneni PV, Dailey AT, *et al.* Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 16: Bone graft extenders and substitutes as an adjunct for lumbar fusion. *J Neurosurg Spine* 2014;21:106-32.
6. Lerner T, Bullmann V, Schulte TL, Schneider M, Liljenqvist U. A level-I pilot study to evaluate of ultraporous beta-tricalcium phosphate as a graft extender in the posterior correction of adolescent idiopathic scoliosis. *Eur Spine J* 2009;18:170-9.
7. MacMillan AK, Lamberti FV, Moulton JN, Geilich BM, Webster TJ. Similar healthy osteoclast and osteoblast activity on nanocrystalline hydroxyapatite and nanoparticles of tri-calcium phosphate compared to natural bone. *Int J Nanomedicine* 2014; 9:5627-37.
8. Robbins S, Laurysen C, Songer MN. Use of Nanocrystalline Hydroxyapatite with Autologous BMA and Local Bone in the Lumbar Spine. A Retrospective Ct Analysis of Posterolateral Fusion Results. *J Spinal Disord Tech* 2014; Feb 27 (EPUB ahead of print).

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