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Allografts and Spinal Fusion

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ABSTRACT

Background: Back pain is a common chief complaint within the United States and is caused by a multitude of etiologies. There are many different treatment modalities for back pain, with a frequent option being spinal fusion procedures. The success of spinal fusion greatly depends on instrumentation, construct design, and bone grafts used in surgery. Bone allografts are important for both structural integrity and providing a scaffold for bone fusion to occur.

Method: Searches were performed using terms ‘allografts’ and ‘bone’ as well as product names in peer reviewed literature Pubmed, Google Scholar, FDA-510k approvals, and clinicaltrials.gov.

Results: This study is a review of allografts and focuses on currently available products and their success in both animal and clinical studies.

Conclusion: Bone grafts used in surgery are generally categorized into 3 main types: autogenous (from patient’s own body), allograft (from cadaveric or living donor), and synthetic. This paper focuses on allografts and provides an overview on the different subtypes with an emphasis on recent product development and uses in spinal fusion surgery.

Special Issue

Keywords: spine fusion, allograft, bone graft material, bone grafts

INTRODUCTION

Back pain is a common chief complaint within the United States and is caused by a multitude of etiologies. According to the National Center for Health Statistics, more than 650 000 spinal fusion surgeries are performed annually.¹ The success of arthrodesis in spine surgery depends on multiple factors; however, an important component to success depends on the bone graft and graft substitutes used in surgery. Bone grafts and graft substitutes are materials that are used to rapidly induce or support biologic bone remodeling after surgical procedures to reconstruct bony structures and/or to provide initial structural support.² The graft material used in spinal fusion procedures can be categorized generally into 3 main types of materials: autogenous bone graft (autograft) from the patient’s own body, allograft from human cadavers and/or living donors, and synthetic bone graft or substitutes.^{3,4} Autograft is considered the “gold standard”; however, the authors believe allograft and synthetics are currently replacing separate surgical site–harvested autografts as the standard because of patient donor site morbidity,

advancement in the development of other products, limited quantity available, host limiting bone quality, and lack of training of young surgeons in the technique of autograft harvest.⁴ This paper focuses on allografts and recent advancements in product development and uses in spinal fusion surgery.

BONE GRAFT PROPERTIES

Osteogenesis, or bone formation, occurs via 2 mechanisms: endochondral ossification or intramembranous ossification. Intramembranous ossification involves direct conversion of mesenchymal tissue into bone, does not require cartilage as an intermediate, and does require bone morphogenic proteins and CBFA1 transcription factors.⁵ Endochondral ossification requires cartilage as an intermediate and can be divided into 5 stages. The stages of endochondral ossification are as follows:—mesenchymal cells differentiate to cartilage cells, formation of chondrocytes, proliferation of chondrocytes to form the model for the bone, formation of hypertrophic chondrocytes, and invasion of blood vessels.⁵ Both mechanisms of bone formation

rely on complex intracellular signaling events, and each contributes to bone formation after spinal fusion surgeries.

Critical elements that are required for bone formation and are important in bone graft properties include osteoconduction, osteoinduction, osteogenesis, mechanical stability, and vascularization. Osteoconduction relies on a scaffold that supports cell ingrowth, facilitates vascularization, and provides a network for cells to attach.⁴ Osteoinduction relies on the provision of signals that act on the precursor cells and encourage cell migration, proliferation, and differentiation into bone-forming cells, leading to rapid bone formation.⁴ Osteogenesis relies on the immediate provision of viable cells emanating from the host to the defect site differentiating into bone-forming cells.⁴ Autologous bone is the only bone graft available that intrinsically contains all 3 properties and is therefore considered the “gold standard.” However, with advancements in allograft processing and development, recent products have theoretically been able to acquire all 3 properties of bone development.

ALLOGRAFT

Allograft bone is obtained from either living or deceased donors and then processed for sterility. Common preparation includes freezing or lyophilization (ie, freeze drying), which involves dehydration and vacuum packaging to store at room temperature.⁶ In general, allografts are primarily osteoconductive with minimal osteoinductive potential and are traditionally not osteogenic because the donor cells are eradicated during processing.^{7,8} Surgeons prefer allografts because they are readily accessible, available in various forms delivering handling properties, facilitate bone formation, and do not require donor site morbidity. However, traditionally available allografts consist of nonviable tissue and cannot stimulate bone formation without the addition of bone-stimulating factors and cells.^{9–11} These limitations lead to slower and less complete incorporation with native bone. Additionally, allografts have a potential risk of disease transmission even if the incidence is very low and the risk can be controlled during the procurement and sterilization process.⁷ Allogenic bone is traditionally available in many forms: cortico-cancellous, demineralized bone matrix (DBM), morselized and cancellous chips, and osteochondral and whole bone-segments.¹²

Recently, a new class of allograft has emerged called *viable cellular allografts* or *cellular bone matrices* (CBMs), which are designed to have all 3 properties of bone formation: osteoconduction, osteoinduction, and osteogenesis. CBMs are created using osteoconductive cadaveric bone with the retention or addition of allogeneic stem cells (ie, mesenchymal stem cells) to initiate an osteogenic process.¹³ The efficacy of mesenchymal stem cells has been shown to be as efficacious as rhBMP and allograft.¹² Overley et al¹⁴ retrospectively examined 78 patients (98 fusion levels) and found no difference in radiographic fusion and rate of revision surgery in patients who underwent MSLIF with either rhBMP-2 or CBM as fusion adjuncts.

Table 1 provides a description of the different types of allografts and their corresponding characteristics. For a more thorough description of all classes of bone grafts, please refer to the chapter by Yang et al⁴ in the *Handbook of Spine Technology* or the review article by Gruskin et al.³ A comprehensive review of bone graft characteristics can be found in the chapter by Bae et al²³ in *AAOS Comprehensive Orthopaedic Review 2*.

Allo-bone Graft: Cortico-Cancellous Allograft

Cortico-cancellous allografts are the most commonly used allograft today. They are strictly osteoconductive without any osteoinductive or osteogenic properties. These grafts can be prepared as whole pieces, such as rings of femoral head/neck used traditionally for interbody fusion, or prepared as chips to aid in void-filling scenarios or postero-lateral fusion.²⁴ Cortical allograft is most commonly used as a mechanical strut graft, whereas cancellous allograft functions as a osteoconductive scaffold for bone formation.⁴ In a study by Park et al,²⁵ 46 patients underwent ACDF with either a cortico-cancellous allograft or iliac crest autograft, and there was no significant difference in fusion status between the 2 groups. Another study by Suchomel et al²⁶ evaluated fibular allografts versus autologous iliac crest grafts in 80 patients undergoing ACDF procedures and found in single-level procedures that there was no difference in fusion rates and graft collapse between autograft and allograft. Table 2 provides a list of commercially available cortico-cancellous allografts used for spinal fusions and specifics on each product.

Table 1. Description characteristics of different types of allografts.

Grafting Material	Grafting Material (Typical Abbreviation)	Grafting Material Category and Description	Variability	Osteogenic	Osteoinductive	Osteoconductive	Immunogenicity/ Disease Transmission	Strength (Immediate)	Donor Site Morbidity
Allograft	Fresh ¹⁵	1. Living donor (patient-to-patient transfer) 2. Cadaveric donor (harvested within 12 h and allo-transplantation within 72 h) → Femoral head (as osteochondral form)	Lot-to-lot variability donor's bone condition + sterilization techniques +/- (Only chondrocyte viability remains)	? (No data for osteogenic graft for human) ? (No data for osteogenic graft for human)	?	?	+++ (Generally causes an unacceptable host immune reaction as osteogenic graft) → Not used commercially, only animal studies.	+++ (Generally causes an unacceptable host immune reaction as osteogenic graft for human)	—
Allograft	Fresh (osteochondral graft) ¹⁶	1. Living donor (patient-to-patient transfer) 2. Cadaveric donor (harvested within 12 h and allo-transplantation within 24 h) → Femoral head (as osteochondral form) ¹⁷	+/- (Only chondrocyte viability remains)	—	++	+	+ (Reduced/mild immune reaction by cartilaginous portion of graft) + (Infection risk due to storage media)	++ (Grafted at articular portion for weight support)	—
Allograft	Fresh-frozen ¹⁸	From 1. living donor 2. cadaveric donor	—	—	—	++ (Less than autogenous bone) ¹⁹	+ (Reported cases)	++	—
Allograft	Freeze-dried	From 1. living donor 2. cadaveric donor	—	—	++	+/-	+/- (Significantly affected by drying process) ²⁰	+/-	—
Allograft	Gamma sterilization	—	—	—	++	+/-	+ (By radiation effect) ²¹	—	—
Allograft	Demineralized bone matrix ²²	Mostly cadaveric donors	Demineralization processes + particle sizes	+/-	++	+/-	—	—	—
Selective cell retained allografts	Osteogenic cell	Patient characteristics	+/-	—	—	—	—	—	—

+++ Characteristic is definitely observed from biologic, clinical, and preclinical studies.

++ Characteristic is somewhat observed from biologic, clinical, and preclinical studies.

+ Suggested by clinical and preclinical studies. There may be some controversy or effect is minimal.

+/- Debate status; for demineralized bone matrix osteoconductive depending on the processing and sterilization techniques (product variability).

— None/no effect.

Table 2. Commercially available allograft mineralized products, structural and/or nonstructural.^a

Company	Allograft Spinal Graft Products	Product Composition	Clinical Evidence: Clinical Trials.gov/ Ongoing Study	Regulatory Clearance/Approvals: US by FDA-Registered Tissue Bank Establishments; 21CFR1270, CFR 1271 AATB; US Pharmacopoeia USP standard 71
AlloSource, Centennial, Colorado, 1995 Allosource.org	AlloFuse Spinal grafts—freeze-dried	Cortical/cancellous spacers Cancellous cervical spacers Cortical cervical spacers Bicortical blocks Dowel Patella wedge Cervical spacers, parallel spacer/textured lordotic Femoral rings Fibular rings, radial rings, ulna rings Cortical Strut TriCortical ilium wedges, strips	n/a n/a	Regulated human tissue CFR 1270, 1271 Regulated human tissue CFR 1270, 1271
	Spinal grafts—freeze-dried/ frozen			Regulated under CFR 1270, 1271 as a human tissue http://activitiv.com/wp-content/uploads/2014/05/Allograft-Catalog.pdf
AlloSource	Allofuse cortical fibers Allofuse cortical chips Cancellous	Cortical/cancellous chips Cancellous chips, crushed, cubed, block, unicortical dowels, tricortical ilium, femoral shafts, Allo>true terminal sterility gamma irradiation Vacuum-level allograft designed to hydrate	(None in spine) NCT01413061 Subtalar arthrodesis	AATB standards and Good Tissue Practices
ATEC, Carlsbad, California Australian Biotechnologies	AlphaGRAFT Structural Allografts Cervical spacers Femoral ring	Vacuum-level allograft designed to hydrate PureCleanse, then chemical soak; low-temperature, high-pressure CO ₂	n/a	Therapeutic Good Administration (TGA), code of Good Manufacturing Practice for Therapeutic Goods—Human Blood and Blood Components, Human Tissues and Human Cellular Therapy Products, 2013 Tissue banks in China products are now approved by the National Medical Products Administration, China.
Beijing Datsing Bio-Tech Co Ltd, Beijing, China	BioCage	Cortical bone (from donor femur) contoured wedge-shaped, end plates large contact area with dentine protrusions (saw-tooth), sagittal convex angle, center open “window” and side hole	Spinal fusion anterior portion with BioCage 2 y (30/33, 90.9% vs 30/ 34, 88.2%) PEEK [†] (360° posterior rods and screws), 1-level lumbar spine ²⁷	Previously CFDA/State Food and Drug Administration, China
BoneBank Allografts, Texas	SteriSorb*	Osteoconductive sponge allografts (100% cancellous bone) Characteristics of a sponge by absorbing saline, blood, or bone marrow aspirate	n/a	Bone Bank Allografts Registration—FDA BBA Manufacturing Registration—FDA (previously THB) Bone Bank Allografts—Accreditation AATB CTO Registration Certificate—Bone Bank Allografts (International Registration)
SteriFlex		Wrappable bone allografts (100% cortical bone) Can be bent, contoured, rolled, trimmed, molded, or sewn, making this flexible bone material	n/a	

Table 2. Continued.

Company	Allograft Spinal Graft Products	Formulation, Product Composition	Clinical Evidence: ClinicalTrials.gov / Ongoing Study	Regulatory Clearance/Approvals: US by FDA-Registered Tissue Bank Establishments; 21CFR1270, CFR 1271 AATB; US Pharmacopoeia USP standard 71
SteriGraft	cervical ACF SteriGraft—ACF cortical-cancellous spacer SteriGraft – ALIF SteriGraft—PLIF SteriGraft—unicortical dense cancellous block SteriGraft—dense cancellous block	Fully machined, constructed of 100% human cortical bone (femur or tibia) Fully machined, constructed of 100% human cortical bone with an internal cancellous plug (femur or tibia) Fully machined, constructed of 100% human cortical bone (femur) Fully machined, constructed of 100% human cortical bone (femur or tibia) Unicortical dense cancellous block (femoral head, patella, distal tibia, talus, or calcaneus) Dense cancellous block (femoral head, patella, distal tibia, talus or calcaneus)	n/a	21 CFR 888.3060, K152239 (December 2, 2015) FDA 510(k) cleared
Traditional bone/cancellous bone allografts	Traditional bone/cortical-cancellous bone allografts	Traditional-type cancellous bone chip or tricortical alloiliac bone	n/a	21 CFR 888.3060, K152239 (December 2, 2015) FDA 510(k) cleared
DePuy Synthes Spine	Zero-P Natural Plate System*	Zero-profile plate with allograft spacer (cervical spine) Traditional cortical/cancellous bone graft Available freeze-dried (FD) or frozen (FZ) Sterilized SAL 10 ⁻⁶	n/a	21 CFR 888.3060, K152239 (December 2, 2015) FDA 510(k) cleared
Hospital Innovations	Ilium tricortical strips* Bone blocks* Whole shaft and hemishift*		n/a	
Globus Medical Inc	FORGE* FORGE Oblique*	Fully machined corticocancellous spacer (cervical spine fusion) Fully machined cortical spacer designed to provide a natural option for transformaminal lumbar fusion Fully machined cortical-cancellous spacer (from femur and tibia) for cervical spine	n/a	K153203 (December 3, 2015) FDA 510(k) cleared
Life Link Tissue Bank	Cortical cancellous spacer*	Fully machined cortical spacer (from femur and tibia) for cervical spine	AATB FDA	Florida, California, and New York Holds a permit to provide tissue in Maryland Processed at an AATB-accredited facility
Maintain States Medical → Merged into Zimmer	OsteoStim*		ClinicalTrials.gov identifier: NCT01491399, no results posted	
Medtronic Spinal and Biologics	Allograft structural Cornerstone SR* Cornerstone ASR* Cornerstone-RESERVE*	Fully machined cortical block (from femur or tibia) with capital D shape Fully machined cortical lateral wall with a cancellous center with capital D shape Fully machined cortical ring with cancellous plug Freeze-dried cortical/cancellous (iliac crest) Freeze-dried cortical/cancellous (iliac crest) Freeze-dried anterior cortical wall with cancellous center Freeze-dried dense cancellous with capital D shape Freeze-dried cortical ring	AATB standards, FDA regulations, and applicable Public Health Service guidelines for donor screening	AATB standards, FDA regulations, and applicable Public Health Service guidelines for donor screening

Table 2. Continued.

Company	Allograft Spinal Graft Products	Formulation, Product Composition	Clinical Evidence: ClinicalTrials.gov/ Ongoing Study	Regulatory Clearance/Approvals: US by FDA-Registered Tissue Bank Establishments; 21CFR1270, CFR 1271 AATB; US Pharmacopoeia USP standard 71
Orthofix	AlloQuents [®] , Monolithic Cortical [*] Structural allograft*	Structural allograft (cervical fusion, lumbar fusion) Different sizes and shapes (ALIF, PLIF, TLIF)	NCT00637312, has results posted—cervical disc Trial was stopped; approval not being pursued for device (clinicaltrial.gov) n/a	Unknown
RTI Surgical	Elenax cortical spacer allograft* Elenax cortical spacer allograft* Elemax PLIF allograft*	Precision-machined cortical spacer for anterior cervical discectomy and fusion procedures Fully machined cortical lateral wall with a cancellous center with capital D shape for anterior cervical discectomy and fusion procedures Fully machined cortical spacer designed to provide a natural option for PLIF	AATB Accreditation Certificate (Florida) FDA Establishment Registration and Listing for Human Cells, FDA-HCT/Ps Florida Tutogen Medical, GmbH (Germany) International Organization of Standards (ISO) CMDCAS—RTI Surgical (Florida) CE certificates Pioneer Surgical Technology (Michigan) International Facility Registrations Canada—CTO Registration State Tissue Banking Licenses California, Florida, Maryland, New York, Oregon, Illinois, Delaware FDA Establishment Registration and Listing for Human Cells, FDA-HCT/Ps	
	AlloWedge bicortical allograft bone	Options for approaching opening wedge osteotomies in the foot and ankle Preshaped bicortical allografts	n/a	
	Cross-Fuse Advantage lateral allograft	All-cortical bone implant designed for a lateral approach to provide maximum potential for fusion Produced from femoral or tibial tissue	n/a	
	Bigfoot ALIF allograft	All-cortical bone implant designed for use as an intervertebral spacer in ALIF approach Freeze-dried: rehydrate for a minimum of 30 s Frozen: thaw for a minimum of 15 min	n/a	FDA Establishment Registration and Listing for Human Cells, FDA-HCT/Ps
	Traditional cortical and/or cancellous strut allogeneic cancellous strut allograft	Femoral head, hemifemoral shaft, humeral head, ilium tricortical block, ilium tricortical strip, proximal and distal femur, proximal and distal humerus, proximal and distal tibia, unicortical block, whole femur, fibula and humerus, and bicortical block	n/a	FDA Establishment Registration and Listing for Human Cells, FDA-HCT/Ps
SeaSpine, Carlsbad, California	Capistrano System*	Cervical allograft spacer system is precision machined from cortical and cancellous allograft bone	n/a	361-HCT/P US-FDA 21 CFR 1271 Restricted to homologous use for the repair, replacement, or reconstruction of bony defects by a qualified health care professional (eg, physician) AATB US FDA regulations for tissue management. US-FDA 21 CFR 1271
Stryker	AlloCraft CA, CL, CP, CS*	Machined from femoral/tibial allograft → ACDF Freeze-dried Chamfered edge	n/a	

Demineralized Bone Matrix

DBM is derived from human allografts and prepared by acid extraction of innate minerals to create an osteoconductive organic matrix with differing quantities of proteins that aid in osteoinduction.⁵ DBM is a composite of collagens (mostly type I), noncollagenous proteins and growth factors, residual calcium phosphate mineral (1%-6%), and some cellular debris.³ The use of DBM was developed in 1965 by Urist,²⁹ who observed that soluble signals contained within the organic phase of bone were capable of promoting bone formation. After processing, DBM lacks structural integrity but retains osteoconductive and osteoinductive properties.³ DBM base is available, and when mixed with other substances these DBM-based products come in many forms, including powders, granules, gels, putties, and strips.³⁰ Importantly, the concentration of native BMP in DBM products differs significantly by manufacturer, donor lot, and batch, making it difficult to study the efficacy of DBM in clinical trials.³⁰⁻³³ In an athymic rat model, Bae et al³⁴ observed significant lot-to-lot variability of a single DBM-based product, commercially available “off-the-shelf” with regard to BMP concentrations and associated in vivo bone formation for fusion rates.³⁵ Therefore, it is important to note the efficacy of DBM’s osteoconduction and osteoinduction properties in clinical studies is limited by mainly narrative study designs with limited levels of evidence, small sample size, and lack of appropriate controls.²⁶

In current clinical practice, because DBM-based products lack structural integrity, they are exclusively/mostly used in spinal applications as bone graft extenders, typically mixed with surgical site local bone or morselized harvested bone from the iliac crest (ICBG) autografts, and/or exogenous peptide/differentiation factors (rhBMP-2) to promote bone growth.⁴ Kang et al³⁶ completed a 2-year prospective randomized clinical trial comparing outcomes of Grafton DBM with local bone to those of ICBG in a single-level instrumented posterior lumbar fusion. In the study, 46 patients (30 Grafton, 16 ICBG) were evaluated, and primary outcome was solid posterolateral lumbar fusion. Results indicated no significant difference in overall fusion rates between the 2 study groups (86% for Grafton, 92% for ICBG). Lower blood loss was recorded in the patients who received an implant of DBM-base

Table 2. Continued.

Company	Allograft Spinal Graft Products	Formulation, Product Composition	Regulatory Clearance/Approvals: US by FDA-Registered Tissue Bank Establishments; 21CFR1270, CFR 1271; AATB; US Pharmacopeia USP standard 71	
			Clinical Evidence: ClinicalTrials.gov / Ongoing Study	n/a
Xtant USA	Ilium tricortical blocks,* unicortical blocks,* fibula segments,* and femoral struts*	Traditional allografts		Processed by tissue banks that are members of the AATB
X-spine Systems Inc/ Xtant USA	Atrix-C cervical allograft spacer	Precision-milled cortical bone with teeth like keel surfaces	n/a	Processed by tissue banks that are members of the AATB
Zimmer Biomet	OsteoStim cervical allograft system*	Fully machined cortical spacer bone for cervical and lumbar with teeth like keel surfaces	n/a	Processed by tissue banks that are members of the AATB
	OsteoStim PLIF*			
	OsteoStim ALIF*			

Abbreviations: AATB, American Association of Tissue Banks; ALIF, anterior lumbar interbody fusion; FDA, US Food and Drug Administration; n/a, not available on ClinicalTrials.org/no clinical data found or clinical trial registered (December 31, 2020); PLIF, posterior lumbar interbody fusion; THB, xxxx.

* Indicates cancellous chips “crunch” available.
†PEEK cage made from engineered plastic polyetheretherketone.

matrix (Grafton DBM-Matrix), but with equal or slightly greater improvement in Oswestry Disability Index scores for the DBM-base matrix patients.

Cammisa et al³⁷ completed a multicenter, prospective, side-to-side (right versus left) comparison of a DBM-based gel (Grafton DBM gel) combined with iliac crest autograft (2:1 ratio) placed on one side of the fusion construct versus iliac crest autograft alone on the other side in 120 patients who underwent posterolateral spinal fusion (PLF) procedures. At 24 months nearly equivalent fusion rates between the sides implanted with a composite of DBM-based gel (Grafton DBM gel) + one-third iliac autograft were 52% fused (42 of 81 sides) versus contralateral sides at 54% fused (44 of 81 sides) after being implanted with autograft alone. Specifically, radiographically fused rates of 40.7% bilateral (33 of 81 consistently both right and left sides fused) or 24.7% unilateral (only autograft side fused in 14% [11 of 81] versus DBM-based gel + autograft composite fused in 11% [9 of 81]). Although 34.6% (28 of 81) were not radiographically fused, the pseudarthrosis revision surgery rate was <1% (1 of 81). Interestingly, the fusion rate in this study is substantially lower than the accepted solid fusion rate of PLF surgery (90%),^{38–40} and the authors ascribe this discrepancy to a difficult patient population, strict radiologic criteria for fusion, and only evaluating bone graft lateral to the instrumentation on anteroposterior film.

These authors conclude that DBM-based allograft products may be used to augment the amount of autograft bone graft needed for successful lumbar fusion. Cammissa et al³⁷ report that one third the quantity of autograft may be used with this DBM-based gel graft extender to achieve consolidated bony fusion, and Kang et al³⁶ used 15 to 20 cm³ of autograft with DBM compared with 25 to 30 cm³ ICBG for successful fusion. The studies by Kang et al and Cammissa et al provide level 1 evidence that Grafton can be used as a bone graft extender for lumbar spinal fusion.³⁷

Interestingly, Grafton is the only bone graft extender to have level 1 evidence and shows different efficacy in the lumbar spine versus the cervical spine. As the above studies showed Grafton to be effective in lumbar spinal fusions, a study by An et al showed level 1 evidence that Grafton DBM is not useful for cervical spinal fusion.^{41,42} In a randomized control trial, An et al⁴² compared 77

ACDF patients with either Grafton DBM + tricortical bone versus tricortical bone alone. Nonunion developed in 46% of patients in the Grafton group compared with 26% of patients in the standalone tricortical bone group.

Table 3 provides a list of commercially available DBM-based products used for spinal fusion and specifics on each product.

Viable Cellular Allografts (Cellular Bone Matrices)

The advancement in the field of stem cell procurement has generated the development of allogenic bone grafts containing live mesenchymal stem cells (MSCs), also known as cellular bone matrices.⁶³ Mesenchymal stem cells were identified in 1966 by Fridenstein et al in bone marrow and have been shown to differentiate into chondroblasts and osteoblasts.^{63,64} These commercially available bone allografts are composed of osteoconductive partially demineralized cadaveric bone as matrix carriers with components of cryopreserved allogeneic cells (MSCs) that promote osteogenesis and osteoinduction.^{6,65} MSCs can be isolated from bone marrow, placenta, umbilical cord blood, connective tissue, skin, synovial fluid, fat, and teeth.^{63,66} MSCs are capable of evading the immune system because they uniquely do not express human leukocyte antigen class II molecules, which are essential for activation of the cellular immune response.^{63,67–69}

In the United States, the process to manufacture these materials involves the American Association of Tissue Banks (AATB) approval processes for cadaveric human bone recovering (contract with independent US Food and Drug Administration [FDA]-registered tissue recovery groups), processing, storing, and preserving cellular components of the bone, or addition of cells, and removal of noncellular proteins. Marketed under FDA-HCT wherein the regulation of product directive is safety, safety is exercised by restricted donor screening. Unlike other DBM-based allografts approved via 510(k) or premarket approval pathways, CBMs are not required to be terminally sterilized, relying on the donor screening and aseptic processing to ensure safety. The exact procedures vary by manufacturer. The HCT/P classification does not require lot-to-lot cell composition or validation of growth factor production. (Per FDA guidance documents on HCT/P products, to “rely on the metabolic activity of living

cells for their primary function" would render a product as a biologic drug [section 360], which would require a biologic license application and clinical trials.)

CBMs are commercially provided as frozen products and must be stored at -80°C , and they require thawing prior to surgical implantation. Neither the reproducibility of cell recovery, after thaw, nor the viability of the cells following implantation has been established for commercially available products or production lots of them. The average number of cells across products is claimed to range from 66 000 to 3 million. Attempting to preserve the viable cells, these products are not terminally sterilized, like 510(k) DBMs or premarket approval products, but rely on aseptic processing to ensure safety. Table 4 provides a list of commercially available CBMs used for spinal fusion and specifics on each product.

The efficacy of viable cellular allografts in spinal fusion is difficult to determine. Given the properties of mesenchymal stem cells, their ability to promote osteogenesis, and their ability to evade the immune system, it is reasonable to think they would be advantageous for bone fusion. Several *in vivo* studies have demonstrated theoretical benefits of using CBMs. Cui et al⁹⁰ compared cloned osteoprogenitor cells to mixed marrow cells and found that cloned cells produced a greater amount of mature osseous tissue at an earlier time point during spine fusion in an athymic rat model. Gupta et al⁹¹ used an ovine posterolateral lumbar fusion model and found similar fusion rates with osteoprogenitor-enriched graft compared with autograft.

To date, there have been very few non-industry-sponsored clinical trials. McAnany et al⁹² evaluated 57 patients who underwent a 1- or 2-level ACDF using interbody allograft with Osteocel (NuVasive, San Diego, California). The patients were matched to a control group of 57 patients where only interbody allograft was used. At the 1-year follow-up, 87% in the Osteocel cohort had solid fusion compared with 94.7% in the control group.⁸¹

There are many factors that can influence the efficacy of CBMs and therefore result in limitations to these products. Hernigou et al⁹³ showed that bone marrow aspirates containing fewer than 1500 MSC/cc were ineffective for the treatment of tibial nonunion, suggesting that this is the minimal MSC concentration for bony healing.⁶³ Preparation of

MSCs is not standardized, and variation in donor age, donor site, and viability of stem cells after thawing the allograft can all influence the effectiveness of CBM.

Although human clinical data are lacking, the athymic rat model allows for direct testing of CBM bone graft products. In a well-established rat model, fusion is assessed by manual palpation of a bony mass 6 to 8 weeks after implantation of DBM-based or CBM-based graft placed between the transverse processes during a posterolateral fusion procedure.^{33,34,76} Using this model, Bhamb et al³³ reported at 8 weeks a 0 of 16 fusion rate in rats implanted with CBM Osteocel Plus Pro (NuVasive) compared with 88% to 100% fusion rate after noncellular human DBM-based products were implanted (Acell Evo3, DBX Mix, DBX Strip, Grafton Crunch, Grafton Flex, and Grafton Matrix), and 13% (2 of 16) were manually fused when implanted with syngeneic bone graft. Lin et al⁷⁶ at 6 weeks detected manual palpation fusion in 73% (11 of 15) of Cellentra (Zimmer Biomet, Warsaw, Indiana), 53% (8 of 15) of Trinity Elite (OrthoFix, Lewisville, Texas), 13% (2 of 15) of Vivi-Gen (Dupey Synthes, Raynham, Massachusetts) and 0 of 15 for each of Osteocel Plus Pro, Bio4 (BIO, Stryker, Kalamazoo, Michigan), and Map3 (RTI Surgical, Marquette, Michigan) implanted rats; 33% (5 of 15) were manually fused for syngeneic bone graft-implanted rats. Johnstone et al⁸⁰ recently evaluated manual palpation results after posterolateral fusion performed with several commercially available human CBM grafts; the highest manual palpation fusion rates were 71% (10 of 14) for Trinity Evolution and 77% (10 of 13) for Trinity Elite compared with 7% (1 of 14) for Osteocel Plus Pro and 40% (6 of 15) for syngeneic bone-implanted rats.

The findings of these studies highlight the variability among CBM commercial products and potentially among production lots.³² Yet, interestingly, there are common observations across these studies: Syngeneic bone graft, a proxy for ICBG in this model, containing some live cells yielded low fused rates (13%, 33%, and 40%) across the studies, whereas the Osteocel Plus preparations consistently yielded almost no sites fused (0%, 0%, and 7%). Trinity Elite (53% and 77%) and Trinity Evolution (71%) formulations, along with Cellentra (73%), seem to yield somewhat comparable results. Preparations, sterilization, formulation, manufacturing

Table 3. Commercially available demineralized bone matrix (DBM)-based products.^a

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study Clinical Trials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
AlloSource Inc Centennial, Colorado, 1995 Allosource.org	AlloFuse Gel Stimublast Putty (identical to AlloFuse Putty and Gel manufactured for Arthrex)	Injectable gel and putty	DBM, RPM carrier Carrier composed of polyethylene oxide/polypropylene oxide block copolymer dissolved in water exhibiting reverse-phase characteristics (ie, an increase in viscosity as temperature increases)	n/a	K071849, December 2008
Amend Surgical Inc	Allofuse Plus Alloflex	Paste, putty Strips, blocks, fillers	DBM, RPM, cancellous chips Cancellous bone allograft, DBM, strip form, no carriers added DBM + 4555 bioactive glass Bond void filler 4555 bioactive glass + porcine gelatin + DBM 4555 bioactive glass; osteoconductive scaffold, DBM; osteoconductive potential	Kirk et al, ⁴³ 2013 In vivo mouse muscle Kirk et al, ⁴³ 2013 In vivo mouse muscle	K103036, January 2011 Marketed as human tissue K161996, February 2017 Regulated under CFR 1270, 1271 as a human tissue K110976, May 2011 www.accessdata.fda.gov/cdrh_docs/pdf1/K110976.pdf www.accessdata.fda.gov/cdrh_docs/pdf1/6/K161996.pdf 510(k) DCI fiber classification LIT-84817A, LIT-84806A Linked to K150621, August 2015 (Bacterin International Inc)
A-TEC, Carlsbad, California/Aphatec Spine Inc	ALPHAGRAFT DBM	Putty or gel	DBM of 100% demineralized fiber, an RPM DBM with superior handling characteristics and ready-to-use application. RPM. Thickens at body temperature	n/a	
Australian Biotechnologies, Sydney, Australia	Allowance Fibre Mat	Demineralized bone fibers	Demineralized bone long fibers cut (low-energy technique) preserving bone collagen alignment and microstructure	Rajadurai et al, ⁴⁴ 2019 Case report ALIF	Australian Therapeutic Goods Administration (TGA), Code of Good Manufacturing Practice for ~2017 K091321, September 2009 K130498, May 2013
Bacterin International Inc → Changed to Xtant Medical	OsetoSelect DBM	Putty	74% DBM dry weight	Yao et al, ⁴⁵ 2020 MI-TLIF, lumbar spine Yao et al, ⁴⁶ 2019 MI vs open TLIF n/a	HCT/P (FEI 3005168462) HCT/P (FEI 3005168462), November 2017 HCT/P (FEI 3005168462), November 2017
OsteoSelect Plus DBM	Putty	74% DBM dry weight + demineralized cortical chips (1-4 mm)	Shehabdi and Elzain, ⁴⁷ 2017	K150621, August 2015 HCT/P (FEI 3005168462)	
OsteoSponge	The malleable sponge	DBM (100% human demineralized cancellous bone)	Galli et al, ⁴⁸ 2015, 717-722, <i>Journal of Foot & Ankle Surgery</i>	HCT/P (FEI 3005168462), November 2017	
OsteoSponge SC	The malleable sponge	Demineralized cancellous bone intended to treat the pathology of damaged subchondral bone of the articulating joints	100% Human demineralized cortical bone		
OsteoWrap	Flexible handling characteristics with a scalpel or scissors	Contain BMPs and other growth factors	100% Human demineralized cortical bone fiber	n/a	HCT/P (FEI 3005168462), November 2017
3Demin	Various shape (fiber, boat shape, strip)	3Demin allografts are also available as loose cortical fibers in 3 volume options	100% DBM putty and crush-mix	n/a	Compliance with FDA guidelines regarding human cells, tissues, and cellular tissue-based products HCT/P 361 regulated viable allogeneic bone scaffold AATB guidelines
Berkeley Advanced Biomaterials, California Biomet Osteobiologics → Merged into Zimmer Biomet	H-GENIN InterGro DBM	Putty Matrix sponge Powder Putty (40% DBM) Paste (35% DBM)	Shehabdi and Elzain, ⁴⁷ 2017 Prospective case series	510(k) cleared (as B-GENIN, R-GENIN) K092046, March 2010 510(k) cleared K082793, April 2009 K031399, February 2005	

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
Bioventus surgical	Exponent	Putty form	Demineralized bone matrix is composed of human demineralized bone (DBM) mixed with resorbable carrier, carboxymethylcellulose	n/a	AATB US FDA 21 CFR 1271. (HCT/P)
PUREBONE		Sponge shape (available in block or strip format)	100% Demineralized cancellous bone (osteoconductive matrix with osteoinductive potential that provides a natural scaffold for cellular ingrowth and revascularization)	n/a	FDA 510(k) Cleared AATB US FDA 21 CFR 1271. (HCT/P)
BoneBank Allografts 2017/ Texas Human Biologics	SteriFuse DBM Putty	Flowable, formable putty	SteriFuse DBM putty with cortical cancellous bone chips (composition?)	n/a	Regulated under 21 CFR Part 1271 (h) FDA requirements for HCT/P
	SteriFuse Crunch	Flowable, formable crunch	DBM + sodium hyaluronate	n/a	Regulated under 21 CFR Part 1271 (h) FDA requirements for HCT/P
DePuy Synthes	DBX	Putty type Paste Mix		NCT0205081: DBX and Autograft vs Actifuse in ACC Cervical Spine (translational PLF, Russell et al. ⁴⁹ 2020; Bhamb et al. ³³ 2019) NCT04635865	K103795, April 2011 K080399, October 2008
SYNTHERIS Dent		Powder type Granule type Putty type Paste	Powder type: demineralized cortical powder, mineralized cancellous powder, mineralized cortical powder Granule type: demineralized cortical (80%)/cancellous granules, mineralized cortical (80%)/cancellous granules DBM putty type: 93% DBM Synthetic calcium phosphate, an inert carrier, carboxymethyl cellulose, and DBM (81% by dry weight), hydrogel carrier	n/a	
ETEX/Zimmer Biomet	CaP Plus	Cap Plus		NCT00254852 (terminated)	K063050, November 2007 K080329, April 2008
Exactech	Optecure	Injectable paste		NCT02127112 Optecure + CCC vs allograft Adams BD 2016 Wrist Arthrodesis ⁵⁰	K121989, November 2012 K061668, September 2006 K050806, February 2006 K061668, September 2006 K121989, November 2012
	Optecure + CCC	Injectable paste	Polymer powder, DBM, cortical cancellous chips (1-3 mm)	n/a (Translational Wang et al. ³² 2007; Togawa et al. ⁵¹ 2003)	K043420, February 2005
OSTEOFIL DBM Paste, OSTEOFIL RT DBM Paste		DBM paste or Dry powder—hydrated to become injectable paste Putty or dry powder—hydrated to become paste	DBM in gelatin carrier Gelatin, DBM, and cortical-cancellous bone chips	n/a	K043421, February 2005
Optiform					

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
Integra Orthobiologics (IsoTis OrthoBiologic) Inc, Irvine, California, SeaSpine 2018	Acell Connexus Acell Evo3TM	Injectable putty Injectable putty	DBM (70% by weight), RPM DBM (Accel Bone Matrix), RPM	Retrospective comparative Schizas et al. ⁵² 2007 NCT02018445 Instrumented Lumbar PLF (Accel Evo3) Evo3) + LB NCT01714804 Instrumented Lumbar PLF (Accel Evo3) Orndorff DG 2019, NASS 2019 ⁵³ NCT01430299 Prospective cohort, PLF DBM (Accel Evo3) vs rhBMP-2 (Infuse) Klineberg et al. ⁵⁴ 2020 AO Spine	K060306, March 2006 K061880, August 2007 K103742, March 2011 K081817, September 2008 K040419, March 2005 K050642, December 2005 Regulated under CFR 1270, 1271 as a human tissue
	Accel TBM Dynagraft II Orthoblast II	Preformed matrix (strip, square, round) Injectable gel, putty Injectable paste, putty	100% DBM (Accel Bone Matrix) DBM (Accel Bone Matrix), RPM, cancellous bone chips DBM (Accel Bone Matrix), RPM, cancellous bone chips from same donor	n/a n/a Lee et al. ⁵⁵ 2019 ADCF plate fixation + DBM (Orthoblast II) vs tricortical iliac autograft	K081817, September 2008 K040419, March 2005 K050642, December 2005 Regulated under CFR 1270, 1271 as a human tissue
	IC Graft Chamber	Freeze-dried in injectable delivery chamber, can be mixed with whole blood, PRP, or BMA	DBM, cancellous chips	n/a	
Lifenet Health	Optium DBM Putty Optium DBM Gel Collect DBM	Putty Gel Provided in a specialized cartridge	DBM, glycerol carrier Particulate DBM and glycerol DBM fibers + cancellous chips	Lee et al. ⁵⁶ 2009—case reports treat secondary osteonecrosis Prospective case series Epstein et al. ⁵⁷ 2007	K053098, November 2005 K053098, November 2005 Regulated under CFR 1270 and 1271
Medtronic Spinal and Biologics	Osteofil DBM Progenix TM Plus Progenix Putty	Injectable paste, moldable strips Putty with demineralized cortical chips Injectable putty	DBM (24% by weight) in porcine gelatin DBM in type I bovine collagen and sodium alginate DBM in type I bovine collagen and sodium alginate	n/a	K043420, February 2005 K081950, July 2008 K080462, May 2008
	Magnifuse Family 1. Magnifuse Bone Graft substitute/bone void filler 2. Magnifuse II Bone Graft		DBM mixed with autograft in 1:1 ratio packed into polyglycolic acid resorbable mesh bag 1. DBM + surface-deminer- alized chips 2. Combination of surface de- mineralized cortical chips and allograft fibers that have been processed, removing the mineral component and leav- ing only the organic portion	NCT02684045; PLF 1- to 2- level retrospective review cases Spine (Smucker et al., ⁵⁹ 2008)	K123691, January 2013 K082615, October 2008

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
MTF/Synthes	DBX	Paste, putty mix, strip	DBM (32% by weight), sodium hyaluronate carrier (mix varies for paste, putty, mix), processed human cortical bone	NCT02005081: DBX and Autograft vs Actifuse SHAPE (Baxter) in ACC cervical spine	K040262, March 2005 (putty, paste, matrix mix)
Nanotheapeutics Inc NanoFUSE Biologics LLC, Malden, Massachusetts	Origin DBM with Biosotve Glass (NanoFUSE DBM)	A malleable, puttylike, bone-void filler	Human DBM and synthetic calcium phosphor-silicate particulate material particles (45S5 bioactive glass), both coated with gelatin derived from porcine skin	NCT03751943 PLF with autograft NCT03762811 (NanoFUSE with autograft in voids fusion) (See: Table 4 NCT02023372)	K091217, October 2009 (putty) K091218, September 2009 (putty) K103795, April 2011 (putty) K103784, April 2011 (putty) K042829, January 2006 (strip) DBX approved in more than 50 countries
NuTech Medical Inc	Matrix Osteoconductive Matrix Plus	Putty type	Allograft cancellous and demineralized cortical mixture Freeze-dried for convenient ambient temperature storage Demineralized cortical fibers, mineralized cortical powder, and demineralized cortical powder Gamma-sterilized for patient safety Freeze-dried for convenient ambient temperature storage	RCT, prospective case series RCT, retrospective case series	K120279, April 2012 K110976, May 2011
Osteotech/Medtronic	GRAFTON A-Flex GRAFTON Crunch GRAFTON Flex	Round, flexible sheet Packable graft Flexible sheets, varying sizes	DBM DBM, demineralized cortical cubes DBM	Retrospective comparative study n/a n/a	K051188, January 2006 K051188, January 2006 K051195, December 2005
	GRAFTON Gel GRAFTON Matrix PLF Strips	Injectable syringe Troughs Strips, various sizes	DBM DBM DBM	RCT, prospective case series RCT, retrospective case series	K051195, December 2005 K051195, December 2005 (Recalled October 18, 2012)
	GRAFTON Orthoblast Large Defect GRAFTON Orthoblend Small Defect	Packable graft	DBM, crushed cancellous chips	n/a	510(k) cleared
	GRAFTON PLUS DBM Paste	Paste	DBM, crushed cancellous chips Human bone allograft DBM + inert starch-based carrier has been added	n/a	510(k) cleared
	Grafton Putty 22076647	Packable, moldable graft	DBM (17% by weight), glycerol	K043048, November 2005 (Osteotech)—traditional K051195, December 2005 (Osteotech)	Kang et al., ³⁶ 2012 PLF RCT Grafton and local bone vs ICBG Park 2013 ³⁵ ACDF, prospective case series PEEK cage packed with Grafton Cannissa et al., ³⁷ 2004 PLF Prospective comparative study, side-by-side in same patient: Grafton DBM gel vs ICBG An et al., ⁴² 1995, cervical ACDF Prospective comparative study DFDBA tricortical graft filled with Grafton vs ICBG

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study Clinical Trials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
Pioneer Surgical Technology and Regeneration Technologies → All companies merged into RTI Surgical	BioSet	Injectable paste, putty, strips, and blocks with cortical cancellous chips	DBM, gelatin carrier	n/a	510(k) cleared Regulated under 21 CFR Part 1271 (h) FDA requirements for HCT/P - December 7, 2016 (validated by FDA)
	BioAdapt DBM	Powder form	Dried powder form (70% DBM by weight) donated from 100% donated human musculoskeletal tissue •Putty; 56% DBM by weight •Putty with chips; 42% DBM by weight + small or large mineralized cortical cancellous chip	n/a	Regulated under 21 CFR Part 1271 (h) FDA requirements for HCT/P December 7, 2016 (validated by FDA)
	BioReady DBM Putty and Putty with Chips	Putty/putty with bone chip	Putty with chips; 42% DBM by weight + small or large mineralized cortical cancellous chip	n/a	Regulated under 21 CFR Part 1271 (h) FDA requirements for HCT/P December 7, 2016 (validated by FDA)
Seaspine, Carlsbad, California	OsteoBallast Demineralized Bone Matrix OsteoSurge 300 Demineralized Bone Matrix OsteoSurge 300c Demineralized Bone Matrix	DBM in resorbable mesh The moldable putty form	→ 100% allograft DBM 100% DBM DBM + Accell bone matrix (it is an open-structured, dispersed form of DBM) + cancellous bone	NCT01430299 (Same Accell Evo3)	FDA 510(k) cleared Accell/Evo3, same material
	OsteoSpary Demineralized Bone Matrix OsteoSpary C Demineralized Bone Matrix Accell Total Bone Matrix Accell Evo3c	The moldable putty, including cancellous chips	DBM + Accell bone matrix (it is an open-structured, dispersed form of DBM) + cancellous bone + biore sorbable, RPM carrier DBM + RPM carrier	NCT01430299 (Same Accell Evo3)	Accell/Evo3, same material (SeaSpine, new sponsor)
	OsteoSpary Demineralized Bone Matrix OsteoSpary C Demineralized Bone Matrix Accell Total Bone Matrix Accell Evo3c	Gel or puttylike consistency Gel or puttylike consistency Prefomed shape (round or rectangular) Putty	DBM + RPM carrier + cancellous bone DBM + Accell bone matrix → 100% DBM DBM + Accell bone matrix (it is an open-structured, dispersed form of DBM) + cancellous bone + biore sorbable, RPM carrier DBM + Accell bone matrix (it is an open-structured, dispersed form of DBM) + biore sorbable, RPM carrier	NCT01430299 (Same Accell Evo3)	It is the same material as Accell Evo3
	Accell Evo3	Putty	Putty	NCT01430299	It is the same material as Accell Evo3
				n/a	K103742, March 2011
Capistrano	DBM + allobone	DBM + machined cortical and cancellous allograft bone 100% demineralized bone fibers with (Powered by Accell Bone Matrix)	NCT02018445 Case study PLIF (December 2013 ~ June 2017) DBM (Accell Evo3) + LB NCT01714804 Prospective PLF vs retrospective PLF rhBMP-2 (December 2017 ~ January 2018)	K103742, March 2011	
SeaSpine Orthopaedics Corp. Irvine, California (IsoTis Orthobiologics)	OsteoStrand Plus OsteoStrand	Bone matrix	NCT04629807, ALIF DBM vs DBM NCT04629794 PLF deformity correction: DBM (OsteoStrand [Fibers]) vs rhBMP-2	n/a	FDA 510(k) cleared 361 HCT/P

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
SeaSpine Inc	All Products SeaSpine			NCT04364295 (Global Registry Study) Effectiveness of SeaSpine products n = 500 n/a	K 043209, December 2005
Smith & Nephew	VIAGRAF	Putty, paste, gel, crunch, and flex	DBM, glycerol	n/a	Regulated under CFR 1270, 1271 as human tissue
Spinal Elements	Hero DBM	Putty, paste, gel	DBM, RPM	n/a	Regulated under CFR 1270, 1271 as human tissue
SpineFrontier, Malden, Massachusetts	Hero DBM Powder	Powder	DBM	n/a	K 193106 (likely a combination product, June 2020)
Wright Medical Technology	ALLOMATRIX	Included DBM Various volumes, consistency varies depending on proportion of cancellous chips used	Interbody fusion device DBM (86% by volume) with or without CBM in surgical-grade calcium sulfate powder	Fu et al. ⁶¹ 2016, TLIF/PLIF with DBM (Allomatrix) + LB HA/ β -TCP vs ABG + LB + HA/ β -TCP; retrospective comparative study n/a	K 041663, September 2004
ALLOMATRIX RCS	Formable putty		DBM, synthetic RCS, calcium sulfate, and hydroxypropylmethylcellulose	n/a	K 041663, September 2004
ALLOMATRIX C	Putty		ALLOMATRIX + small cancellous chips	n/a	510(k) cleared K 040980 (July 14, 2004)
ALLOMATRIX CUSTOM	Putty		ALLOMATRIX + large cancellous chips	n/a	K 040980 September 2004
ALLOMATRIX	Injectable		DBM (86% by volume) + OSTEOSET (surgical-grade calcium sulfate)	NCT00274378 Injectable DBM (Allomatrix) putty in distal radius fracture n/a	510(k) cleared K 020895
ALLOMATRIX DR	Putty		Calcium sulfate, DBM, and small cancellous chips	n/a	K 040980, July 2004
PRO-STIM	Procedure kits, various volumes of injectable paste/formable putty		50% Calcium sulfate, 10% calcium phosphate, and 40% DBM by weight	n/a	FDA 510(k) cleared

Table 3. Continued.

Company	DBM-Based Product (Human)	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier		Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271
				Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier	Regulatory Clearance/Approval FDA 510(k), CFR 1270, CFR 1271	
Zimmer → it merged into Zimmer Biomet company	IGNITE	Percutaneous graft for fracture malunion/ nonunion Packable pellets	DBM in surgical-grade calcium sulfate powder to be mixed with DBM	n/a	K1052913, November 2005	510(k) cleared
Osteoset DBM Pellets			3.0- or 4.8-mm pellets Surgical-grade calcium sulfate, DBM (53% by volume), stearic acid	Xie et al. ⁶² Cervical fusion (ACDF) PEEK with either Osteoset vs ICBG	K022828, April 2004 K053642, January 2006	510(k) cleared
PRO-STIM Injectible Inductive Graft		Injectable paste/formable putty	DBM (40% by weight), calcium sulfate (50% by weight), calcium phosphate (10% by weight) DBM, RPM, ground cancellous bone <td>NCT03112772 (Socket Preservation)</td> <td>K190283, February 2019</td> <td>Regulated under CFR 1270, 1271 as human tissue</td>	NCT03112772 (Socket Preservation)	K190283, February 2019	Regulated under CFR 1270, 1271 as human tissue
Puros DBM with RPM Gel and Paste	Gel, paste	Puttty	DBM, RPM, with or without cortical bone chips (850 microns to 4 mm) DBM (100%)	n/a		Regulated under CFR 1270, 1271 as human tissue
Puros DBM with RPM Putty & Putty with chips	Putty		50% Demineralized cortical bone (DBM) + 50% mineralized cancellous chips	n/a		Regulated under CFR 1270, 1271 as human tissue
Puros DBM Block and Strip	Blocks, strips in varying sizes		All-inclusive bone grafting kit DBM + natural lecithin carrier + resorbable coralline hydroxyapatite/ calcium carbonate granules.	n/a		FDA registration number: FEI 1000160576 (until June 30, 2020) AATB and HTCP
Bonus CC Matrix	Putty type (molded, packed)		Available as a 40% DBM Putty or 35% DBM PLUS	n/a		FDA registration number: FEI 1000160576 (until June 30, 2020)
StaGraft DBM Putty and Plus	Putty/granules (molded, packed)		Cancellous DBM sponge and strips are machined from a single piece of cancellous bone.	n/a		FDA registration number: FEI 1000160576 (until June 30, 2020)
StaGraft Cancellous DBM Sponge and Strips	Sponge strips from a single piece cancellous bone		Osteoinductive bone, trabecular structure, spongelike handling Manufactured entirely from cortical bone, which has been demonstrated to maintain higher osteoconductivity than cancellous bone after demineralization	n/a		FDA registration number: FEI 1000160576 (until June 30, 2020)
FiberStack Demineralized Bone Matrix	Molded, packed		100% DBM (without carrier)			

Abbreviations: AATB, American Association of Tissue Banks guidelines; ACC, anterior cervical corpectomy with fusion; ACDF, anterior cervical discectomy fusion; ABG, autologous bone chips; ALIF, anterior lumbar interbody fusion; BMA, bone marrow aspirate; BRC, bone repair cells; CBM, cellular bone matrix, cellular bone allograft; FDA, US Food and Drug Administration; HA/β-TCP, hydroxyapatite β-tricalcium phosphate; ICBG, iliac crest bone graft; LB, local bone; LIIF, lumbar interbody fusion; OLIF, oblique lateral lumbar interbody fusion; PEEK, a polyetheretherketone material used for cage devices employed as instrumentation in anterior interbody spinal fusion procedures; PLIF, posterolateral lumbar fusion; PLIF, posterior lumbar interbody fusion; RCS, resorbable conductive scaffold; RCT, randomized control trial; RhBMP-2, recombinant human morphogenic protein-2, infuse; RPM, reverse-phase medium; TLIF, transforaminal lumbar interbody fusion; VBM, viable bone matrix; VCBM, viable bone matrix; XLIF, extreme lateral interbody fusion

⁶²510(k) is a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective as, that is, substantially equivalent to, a legally marketed device that is not subject to premarket approval. 501 (k) documentation for individual products is available via the FDA online database (<http://www.accessdata.fda.gov>). CFR Code of Federal Regulations 1270 (human tissue intended for transplantation) and 1271 (human cells, tissues, and tissue-based products) are federal regulations relating to the procurement and processing of human-derived tissues. Human Tissue Banks: https://images.magnetmail.net/images/clients/AATB/attach/Bulletin_Links/18_2/AATB_Accreditation_Policies_February_08_2018.pdf (last update February 2018). TBI, Tissue Banks International National Processing Center (an AATB-accredited tissue bank) license states: California, Florida, Maryland, and New York.

Table 4. Commercially available combination grafting products, naturally occurring peptides, growth differentiating factors, cellularized grafts, and cellular bone matrices (CBMs).

Company	Combination Product	Formulation	Product Composition	Regulatory Clearance/Approval	
				Peer-Reviewed Clinical Evidence/Ongoing Study	ClinicalTrials.gov Identifier:NCT
Advanced Biologics, Carlsbad, California, 2009 (marketed OsteoAMP in the USA since 2009/ Bioventus)	OsteoAMP	Granules or sponge	OsteoAMP, an allogeneic growth factor implant, exploits the angiogenic, mitogenic, and osteoinductive growth factors that are within marrow cells Growth factor-rich naturally occurring growth factors, including BMP-2, BMP-7, aFGF, and TGF- β 1 bone graft substitute; intended for homologous use repair, replacement, or reconstruction of musculoskeletal defects	Field et al, ⁷⁰ 2014 Cervical Spine-Fusion NCT02225444 Roh et al, ⁷¹ 2013 Yeung et al, ⁷² 2014, evaluation of donor bone, processing aseptically terminal sterilization in cervical/lumbar	Bioventus manufactures orders and sales of HCT/Ps (not a distributor, FDA) Regulated under CFR 1270, 1271 as a human tissue, registration held by Tissue Bank Permit: Millstone Medical Outsourcing LLC, Olive Branch, Mississippi (Bone, Demineralized Bone Matrix, Ligament, Musculoskeletal Tissues, Tendons) Maryland, New York State
AlloSource, Centennial, Colorado, 1995 Allosource.org	Allostem Cellular Bone Autograft (ACBM) AlloWrap	Strips, blocks, cubes, morselized Amniotic membrane	Partially demineralized allograft bone combined with adipose-derived MSCs Amniotic membrane dual-sided epithelial layer	NCT01413061 ACBM (69.2%) vs tibia/ICBG (45.6%). Nonunion rate after Subtalar Arthrodesis Myerson et al, ⁷³ 2019 NCT04684901 (Cervical Spine, 2-level, ACDF)	Regulated under CFR 1270, 1271 as a human tissue
Aziyo Biologics Inc Richmond, California	FiberCel (Medtronics) OsteoGro V OsteoGro V ViBone	Putty	OsteoGro V Fiber Cancellous bone particles with preserved cells combined with demineralized cortical particles Viable Bone Matrix (ViBone, Aziyo gentle VBM processes)	Reduction of Soft Tissue Swelling NCT03896347 (3-level OLFIF) NCT03425682 Lumbar (PLIF, TLIF) or Cervical (ACDF) Fusion using ViBone	Regulated under CFR 1270, 1271 as a human tissue
BBS-Bioactive Bone Substitutes Oyj, Finland	ARTEBONE		OsteoAMP	NCT02480868: case series study for ankle fusion	FDA 510(k) cleared
Bioventus Surgical Durham, North Carolina Hoofddorp, Netherlands	OSTEOAMP	Granule, putty, and sponge form	Cervical and lumbar spine fusion procedures Allograft with growth factors (such as BMP-2, BMP-7, TGF- β 1, aFGF, VEGF, and ANG1, within bone marrow cells)	PLF with OsteoAMP NCT02225444 (Roh et al, ⁷¹ 2013) Comparative study with rhBMP-2 with OsteoAMP (Roh et al, ⁷¹ 2013)	FDA 510(k) cleared ATB US FDA 21 CFR 1271. HCT/P

Table 4. Continued.

Company	Combination Product	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study	Clinical Trials.gov Identifier: NCT	Regulatory Clearance/Approval
				Peer-Reviewed Clinical Evidence/Ongoing Study	Clinical Trials.gov Identifier: NCT	
Bone Biologics Corp, Victoria, Australia	BIONESUPPORT AB: Lund, Sweden	Injectable type With MSCs + cytokines	Demineralized bone, sodium hyaluronate (DBX) + rhNell-1 (osteogenic factor) Injectable antibiotic-eluting bone graft substitute that provides local sustained	NCT03810573 (TLIF) NBI rhNELL-1(DBX) low vs high dose NCT02820363 (RCT) for open tibial fracture (recruiting status) NCT012128256; case series study (reinfection prophylaxis)	NCT03810573 (TLIF) NBI rhNELL-1(DBX) low vs high dose NCT02820363 (RCT) for open tibial fracture (recruiting status) NCT012128256; case series study (reinfection prophylaxis)	Regulated Australia Regulation
CERAMENT V With MSCs + cytokines		Injectable type	CERAMENT (40% hydroxyapatite + 60% calcium sulfate) + 17.5 mg gentamicin/mL paste. Injectable antibiotic-eluting bone graft substitute that provides local sustained	NCT04244942 (Registry Study) Cell study Alfootawi et al, ⁷⁴ 2013 Cell study Alfootawi et al, ⁷⁴ 2013	NCT04244942 (Registry Study) Cell study Alfootawi et al, ⁷⁴ 2013	CE Mark approval FDA Approvals Separate for Cеремент/Bone Void Filler K090871 September 2009 K073316, June 2008 Iobexol, initial approval 1985
ViviGen Synthes	ViviGen Cellular Bone Matrix Vertigraft	Cryo Cortical cortical cancellous bone matrix and demineralized bone	ViviGen Cellular Bone Matrix is composed of cryopreserved viable cortical cancellous bone matrix and demineralized bone. ViviGen Cellular Bone Matrix is an HCT/P. ViviGen Cellular Bone Matrix is processed from donated human tissue, resulting from the generous gift of an individual or his or her family	NCT02814825 (ACDF cervical) HCT/P Divi SN 2017 Divi SN 2017 ⁷⁵ NCT03733626 (Lumbar) NCT04007094 (PLF lumbar) Translational PLF CBMs (Lin et al, ⁷⁶ 2020) NCT03527966 (n = 3, V-CBA (ViviGen) vs rhBMP-2, Lumbar Fusion	NCT02814825 (ACDF cervical) HCT/P Divi SN 2017 Divi SN 2017 ⁷⁵ NCT03733626 (Lumbar) NCT04007094 (PLF lumbar) Translational PLF CBMs (Lin et al, ⁷⁶ 2020) NCT03527966 (n = 3, V-CBA (ViviGen) vs rhBMP-2, Lumbar Fusion	(HCT/P) as defined by the FDA in 21 CFR 1271.3(d). 21CFR 1271
CONFORM CUBE	Cube shape		Demineralized Cancellous Bone, organic matrix (osteoinductive, promotes cellular ingrowth and vascularization)	V-CBA vs rhBMP-2, Lumbar Fusion (Wetzell et al, ⁷⁷ 2020)	n/a	(HCT/P) as defined by the FDA in 21 CFR 1271.3(d). 21CFR 1271
CONFORM SHEET	Sheet shape		General bone-void filler and use with lumens of allograft spinal spacers Demineralized cancellous bone, organic matrix (osteoinductive, promotes cellular ingrowth and vascularization) For PLF (posteriorlateral gutters of the spine)		n/a	(HCT/P) as defined by the FDA in 21 CFR 1271.3(d). 21CFR 1271

Table 4. Continued.

Company	Combination Product	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study EvidenceTrials.gov Identifier: NCT	
				Regulatory Clearance/Approval	
Mesoblast Ltd, Australia	NeoFuse	Cells + granules	Allogenic mesenchymal precursor cells combined with MasterGraft in PEEK cage	FDA 510(k), FDA 361, 21 CFR Part 1271 CFR 1270, CFR 1271 21 CFR 3.2(e)	K153615, May 2016
Angioblast Systems Inc, USA	NeoFuse	Cells + granules	Allogenic mesenchymal precursor cells combined with MasterGraft in ACDF	HCT/P 361, Human Allografts (No Clinical Studies) Biologic Drugs and Devices 351 (Clinical Trials)	FDA 510(k) cleared K170318, July 2017
MTF Orthofix	Trinity Evolution	Moldable allograft fibers, varying sizes	Anterior cervical plate fixation Allogenic DBM, OPC, MSC (minimum of 500 000 cells/cc, 100 000 of which are MSC and/or OPC)	NCT01106417 NCT01097486 (ACDF) NCT00951938 Anterior Cervical Vanichkachorn et al, ⁷⁸ 2016 Peppers, 2017 JOSR Lumbar Observational Musante et al, ⁷⁹ 2016 JOSR NCT00965380 (PLIF/TLIF) Observational (completed)	Regulated under CFR 1270, 1271 as a human tissue
Trinity Elite		Moldable allograft fibers, varying sizes	DBM, OPC, MSC (minimum of 500 000 cells/cc, 100 000 of which are MSC and/or OPC)	NCT029696169 (PLF, TLIF, ALIF, XLIF) lumbar fusion Bone graft	Regulated under CFR 1270, 1271 as a human tissue

*Johnstone et al,⁸⁰ 2020 (translational
PLF, Trinity Elite vs Trinity
Evolution)

Table 4. Continued.

Company	Combination Product	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study Identifier: NCT	
				Clinical Trials.gov Identifier: NCT	Regulatory Clearance/Approval
NuVasive	Osteocel	Moldable bone matrix	DBM, OPC, MSC (<50 000 cells/cc, >70% viability)	McAnamey et al, ⁸¹ 2016, retrospective comparative study; NCT00948532	FDA 510(k), FDA 361, 21 CFR Part 1271 CFR 1270, CFR 1271 21 CFR 3.2(e)
	Osteocel Plus	Moldable bone matrix	DBM, OPC, MSC (<50 000 cells/cc, >70% viability)	(Osteocel Plus in eXtreme Lateral Interbody Fusion [XLIF]; Kerr et al, ⁸² 2011; Tohmeh et al, ⁸³ 2012 Extreme lateral interbody fusion [XLIF])	HCT/P 361, Human Allografts (No Clinical Studies) Biologic Drugs and Devices 351 (Clinical Trials)
				Osteocel Plus in a polyetheretherketone cage and anterior plating at 1 or 2 consecutive levels	Prospective case series Retrospective case series, clinical trial: ClinicalTrials.gov identifier: Evaluation of Radiographic and Patient Outcomes
				Lumbar spine: NCT00948831 (ALIF, observational) NCT00941980 (PLIF, observational) NCT00947583 (TLIF, observational) Ammerman et al, ⁸³ 2013	Regulated under CFR 1270, 1271 as a human tissue
				NCT03649490 (XLIF 1 or 2 levels, comparative: interbody implant [PEEK] with cancellous allograft + BMA vs with cellular allograft [Osteocell])	AATB and FDA guidelines for banked human tissues (is a minimally manipulated allograft tissue)
				Attienello et al 2018 LLIF XLIF (open vs percutaneous) IBF with PEEK + DBM (Osteocel Plus cellular bone matrix)	Other: Nunley et al, ⁸⁵ 2016 (ALIF, LLIF, TLIF) retrospective
				Cervical spine: NCT00942045 (ACDF) Eastlack et al, ⁸⁴ 2014	
				*Johnstone et al, ⁸⁰ 2020 (translational PLF, Osteocel Plus)	
				NCT02023372: LLIF NuCel and Autograft	
				NCT02808234: Prospective, DDD Lumbar spine LLIF Efficacy NuCel NCT02070484 (RCT) for PLF NuCel vs DBX	
				Other:	
NuTech Medical Inc	NuCel	Putty type	Cryopreserved, bioactive amniotic suspension allograft Cellular, growth factor, and extracellular matrix components		

Table 4. Continued.

Company	Combination Product	Formulation	Product Composition	Regulatory Clearance/Approval	
				Peer-Reviewed Clinical Evidence/Ongoing Study	Evidence/gov Identifier: NCT
Osteotech Merged into Medtronic	Plexur P Plexur M	Moldable type (puttylike)	Human cortical bone allograft fibers + resorbable polymer Processed human bone particles that are mixed with resorbable/ biodegradable nontissue components.	NCT00837473 (Pilot Study, iliac crest backfill) Note MAUDE Adverse Event Report	FDA 510(k) cleared K073405 (March 3, 2008)
RTI Surgical Inc Alachua, Florida	map ³ Cellular Allogeneic Bone Graft	Putty type Strip type	Cortical cancellous bone chips (or strip shape bone) + DBM + cryogenically preserved, viable multipotent adult progenitor-class cells	NCT02161016: case series study in foot and ankle. Results posted Dekker et al. ⁸⁶ 2016 Dekker et al. ⁸⁷ 2017 (revisions nonumbers) NCT02628210: A Prospective, Multi- Center, Non-Randomized Study for lumbar interbody fusion (active status) Other: Lee, ⁸⁸ 2017	Unknown Status Cell Components, 2018 (FDA biologics license needed [201(g)]FDA 21 USC 321(q)(3)(i) of PHS Act 42 USC262] based product [HCT/ P]. Also bone chip DBMs regulated under 361 PHS Act 42 USC 264 and reg. tissues part 21 CFR 1271.3 + 21 CFR 1271.10)
Stryker Spine, Allendale, New Jersey	BIO ⁴	Putty type (1, 2.5, 5, and 10 cc)	Allograft bone (cortical and cancellous) + periosteum A viable bone matrix containing endogenous bone-forming cells (including MSCs, OPCs, and osteoblasts) as well as osteoinductive and angiogenic growth factors	NCT03077204: Clinical case series study (ACDF, cervical spine), completed	AATB US FDA regulations for tissue management. US FDA 21 CFR 1271 (Osiris Therapeutics—data on file)
Manufactured by Osiris Therapeutics Inc	Vivex Biomedical, Marietta, Georgia Miami, Florida	Via Graft ^M Via Form ^M Via Form ^M	"Wet Sand" (matrix + gel) Putty type (matrix + gel) M = added bone gel component	Tally et al. ⁸⁹ 2018, MIS-TLIF case review (level of evidence IV, n = 75) Inserted expandable cage prefilled with ViaGraft sponge-soaked BMA (from pedicles) was placed interbody with posterior pedicle screws and packed Beta TCP + BMA ⁸⁹	US FDA regulations for tissue management. US FDA 21 CFR 1271
Xtant/distribution agreement with Vivex, Marietta, Georgia (formerly Bacterin International Holdings Inc)	OsteoVive	Putty type	A cell population derived from vertebral body that includes MIAMI cells (Vivex) Blend of microparticulate cortical, cancellous, and demineralized cortical allograft bone (particle size range of 100-300 microns) DMSO-free cryoprotectant (to protect MIAMI cells)	Application: Spine, Extremity, Foot & Ankle	FDA 510(k) cleared, compliance with FDA guidelines regarding human cells, Tissues, and cellular tissue-based products, HCT/P 361 regulated viable allogeneic bone scaffold AATB guidelines

Table 4. Continued.

Company	Combination Product	Formulation	Product Composition	Peer-Reviewed Clinical Evidence/Ongoing Study ClinicalTrials.gov Identifier: NCT	Regulatory Clearance/Approval
Zimmer Biomet	Cellentra Viable Cell Bone Matrix	Naturally occurring cells in fresh frozen, cryopreserved allograft comprising cancellous bone mix with cortical bone	NCT02182843; prospective ACDF interventional, results 2018 clinicaltrials.org Lin et al, ⁷⁶ 2020 (translational)	AATB US FDA regulations for tissue management. US FDA 21 CFR 1271	FDA 510(k), FDA 361, 21 CFR Part 1271 CFR 1270, CFR 1271 21 CFR 3.2(e) HCT/P 361, Human Allografts (No Clinical Studies) Biologic Drugs and Devices 351 (Clinical Trials)

Abbreviations: AATB, American Association of Tissue Banks guidelines; ACDF, anterior cervical discectomy fusion; ALIF, anterior lumbar interbody fusion; BMA, bone marrow aspirate; BRC, bone repair cell; DBM, demineralized bone matrix; FDA, US Food and Drug Administration; IBF, XXXXX; LB, local bone (from surgical site dissection); LIIF, lumbar interbody fusion; MIAMI, marrow-isolated adult multilineage-inducible; MSC, mesenchymal stem cell; OLIF, oblique lateral lumbar interbody fusion; OSC, osteoprogenitor cell; PEEK, a polyetheretherketone material used for cage devices employed as instrumentation in anterior interbody spinal fusion procedures; PLIF, posterolateral lumbar fusion; PLIF, posterior lumbar interbody fusion; RCT, randomized control trial; TCP, tricalcium phosphate; TLIF, transforminal lumbar interbody fusion; VBM, viable bone matrix; VCBM, viable cell bone matrix; XLIF, extreme lateral interbody fusion.

⁴CFR Code of Federal Regulations (CFR) 1270 (Human tissue intended for transplantation), and 1271 (Human cells, tissues and tissue-based products) are federal regulations relating to the procurement and processing of human-derived tissues. Claims: grafting with component to provide the required osteoconduction, osteogenesis, and osteoinduction necessary for successful bone grafting

FDA510(k) cleared. 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent to a legally marketed device that is not subject to premarket approval. 501(k) documentation for individual products is available via FDA online database (<http://www.accessdata.fda.gov>). FDA premarket approval, typically investigation; HDE, humanitarian device exemption, FDA-approved under an HDE; IND, investigational new drug application.

processes, and the donor bone itself contribute to differences among the products. Unlike for clinical use, for purposes of testing in rats, the products are not mixed with autograft bone. Clinically these allografts are not used in isolation; bone from the surgical dissection is morselized and mixed with allograft bone graft extenders of DBM-based or CBM products. Autograft potentially compensates for allograft products' debility.

In conclusion, there is no definitive clinical evidence that viable cellular allografts promote increased fusion compared with regular allograft DBM-based products. The claimed advantage of osteoinductive and osteogenic properties remains theoretical. The CBM allografts are available at an increased cost compared with other allografts, and more research is needed to justify each product's use instead of standard allografts.

CONCLUSION

Use of bone grafting techniques performed in surgical procedures for spinal fusion have been reported since the beginning of the 20th century.⁹⁴ Novel instrumentation and surgical techniques are designed and inspired by advances in grafting technologies. The history of allografts dates back many decades and has greatly evolved since Urist's first observation on how bone demineralization impacts the incorporation at the graft-host interface. The advancements in allograft products have purposely been designed to facilitate surgical procedures for fracture healing and spinal fusion. Allografts vary in size, shape, consistency, strength, viable cellular components, and many other properties. For the past decades, with a clinical history of use of allografts and DBM bases, diverse materials and composites have been continually combined with various materials and allograft forms to improve material properties, and further developed as novel grafting options.⁴ Once bone allografts in various forms are approved or cleared by the responsible agency of the intended market country, they are rapidly adopted into specific surgical application. However, graft-contributing complications may still occur, and sometimes systematically with the use of a particular form or product. The target allograft then moves from bedside to "bench" for reevaluation. In the application process for approval, grafts' safety is evaluated, yet the osteoinductive and conductive

effectiveness burden may not have been investigated, which likely has unintended consequences.

As discussed in this paper, there is a great unmet need for improvement in allografts. The ideal bone graft provides a biocompatible scaffold that promotes osteoconduction, osteoinduction, and osteogenesis. Allografts predominantly contain osteoconductive and some osteoinductive potential. However, with the advancement of viable cellular allografts, there is the theoretical addition of osteogenesis. Allografts with blood-derived augmentation (either with BMAC or PRP) were not directly discussed in this paper because this subject is the primary focus of another article in submission. With time and technologic advantages in stem cells and differentiation factors, more products will be developed to enrich the bone graft-to-fusion process and increase the rapidity and success rate of bone healing after spinal fusion procedures.

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Corrections

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In this article, the author's name Andrew J. Tronits was misspelled and should have appeared as Andrew J. Trontis.
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