

# Stabilizing Effects of a Particulate Demineralized Bone Matrix in the L4- Interbody Space with and without PEEK Cage – A Literature Review and Preliminary Results of a Cadaveric Biomechanical Study

Kingsley R. Chin, M.D., *Charles E. Schmidt College of Medicine at Florida Atlantic University  
Institute for Modern and Innovative Surgery (iMIS), 1100 W. Oakland Park Blvd. Suite #3, Fort Lauderdale, FL, 33311*

Carl A.R. Bruce, M.D., *Department of Surgery, Radiology, Anaesthesia & Intensive Care, University of the West Indies, Mona Campus, Kingston, Jamaica*

Vanessa Cumming, M.B. B.S., *LES Society, 300 E. Oakland Park Blvd. Suite 502, Fort Lauderdale, FL, 33334*

Neil R. Crawford, Ph.D., *Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ*



**Corresponding Author: Kingsley R. Chin, M.D.**

*Affiliate Associate Professor of Clinical Biomedical Sciences, Charles E. Schmidt College of Medicine at Florida Atlantic University  
Attending Spine Surgeon, Institute for Modern & Innovative Surgery (iMIS), 1100 W. Oakland Park Blvd. Suite #3, Fort Lauderdale, FL, 33311.  
Tel: 617-697-5442 Fax: 877-647-7874 Email: kingsleychin@gmail.com*

## Introduction

A fusion procedure has become one of the most common means of treating spinal morbidities such as trauma, deformity, and degenerative disc diseases. In recent times the spinal fusion technique has been augmented with the use of autogenous bone grafting, but with the added complication of donor site morbidity and graft volume limitations, the pseudoarthrosis rates still range between 5 and 43%<sup>(1)</sup>. Host risk factors such as smoking, osteoporosis, and diabetes have also been implicated in increasing the rates of pseudoarthrosis in patients with spinal fusion. More recently newer techniques, including the use of internal fixation devices, have been developed to increase fusion rates<sup>(2,3)</sup>. Despite these newer techniques, however, pseudoarthrosis rates remain persistently high<sup>(4-6)</sup>. The consequences of pseudoarthroses include poor clinical outcomes and substantial medical expense. This has led to the development of newer techniques, osteosynthetic devices, and biological strategies to provide an alternative to autogenous bone grafting and to enhance and stimulate fusion.

## Review

### *The need for demineralized bone matrix*

The biological processes involved in bone regeneration require three elements. These are: an osteogenic potential capable of directly providing cells to new bone being formed, osteoinductive factors able to cause the osteoblastic differentiation of osteoprogenitor stem cells, and osteoconductive scaffold facilitating neovascularization and supporting the ingrowth of bone. The ideal bone graft material possesses all of these three properties along with an optimal biological reaction and without risk of disease transmission. Autogenous bone grafts possess each of these three essential properties, and are thus considered the first choice for graft material in patients undergoing spinal fusion<sup>(7)</sup>.

The autograft is not without complications. Autografts are associated with significant harvest site pain<sup>(8-14)</sup> persisting into the postoperative period. The invasiveness of an autogenous bone graft procedure is another concern.

Allografts provide another option for the stimulation of fusion in the human spine; but provide minimal growth factors stimulating new bone growth, have exemplified poor incorporation, and adjacent tissue reactions are reported in some prospective studies<sup>(15-19)</sup>. There are, however, other lower level evidence studies reporting acceptable rates of fusion when compared with autografts<sup>(20-25)</sup>.

In an attempt to increase fusion rates and avoid significant morbidity associated with acquiring a graft, many bone substitutes have been developed. None of the existing bone substitutes exhibit all three of the

principal elements in their present stages, however, some bone graft substitutes have shown some usefulness in basic and clinical studies. Research in progress in molecular biology has revealed new technologies for bone regeneration. Chiefly, with the improvements in regional gene therapy as well as in osteoinductive proteins and osteoconductive carrier matrices, spinal fusion procedures are progressing into a new era of osteobiological technology.

Herewith we aim to present a review some of the biologic properties of a particulate form of demineralized bone matrix (DBM) (DBMPure, SpineFrontier Inc., Beverly MA, USA), its usefulness, and discuss its limitations as have been determined thus far. All cadaveric specimens are received without any protected health information attached, so IRB approval is not required for cadaveric studies in the USA.

### *Demineralized bone matrix*

Demineralized bone matrices (DBMs) are created by the acid excretion of allograft bone. The consequence is a loss of most of the mineralized component of bone, but they do give rise to type I collagen and noncollagenous proteins, including growth factors. This means that DBMs will lack structural strength but possess osteoconductivity and osteoinductive properties. The osteoinductive ability in DBMs to stimulate bone regeneration is dependent upon the activity of the bone morphogenic proteins (BMPs). DBM derived from human tissues is most likely to induce osteoinductive properties of bone and enhance fusion and bone growth<sup>(26-30)</sup>. These materials include the osteoinductive proteins of human bone and have the potential to aid with fusion.

DBM may provide a very useful substitute to bone grafts promoting bony fusion because of the presence of growth factors making this substance easier to absorb<sup>(31-34)</sup>. The particulate form of DBM is known to be easier to work with as it is easily packed into defect sites in bone without the need for operative planning or shaping prior to use<sup>(35)</sup>.

Earlier studies of DBM and its usefulness have reported somewhat conflicting evidence of its usefulness in the clinical realm. An et al<sup>(19)</sup> reported that an allograft-DBM matrix yielded a higher rate of collapse and pseudoarthrosis in a prospective trial of allograft-DBM matrix versus autograft in anterior cervical spine fusion; while lower level evidence data report equal or similar performance of DBM used alone or to augment autografts in spinal fusion trials in the lumbar spine or with scoliosis<sup>(9, 23, 36-39)</sup>.

As aforementioned, DBMPure is created by the acid excretion of allograft bone. It is prepared as a micro- or macro-particle powder to be used as a packing material inside hollow metal cages, around PEEK cages, or on

its own to fill disc or other space in the spine. Each of these uses present challenges to the efficacy of DBM in clinical practice.

When DBM is used to pack metal cages in situ there are concerns about introducing metal particulate effects from corrosion debris and phagocytosable particulate wear leading to particle-induced osteolysis after arthrodesis using metal implants and DBM. These effects, such as increased inflammatory response (cytokine mediated or increased expression of tumor necrosis factor- $\alpha$ ), increased osteoclastic activity, or cellular apoptosis, are described in animal models<sup>(40-42)</sup> and in clinical review of patients presenting with spinal implant related pain<sup>(41)</sup>. Another challenge when using DBM packed inside a metal cage is the lack of compression from bone to assist stimulating new bone growth. Bone necessitates compression to promote neovascularization and bone growth.

DBM packing around PEEK cages is also practiced to assist fusion with interbody use. Stress shielding is of concern with PEEK cages surrounded with DBM, but less so than DBM packing within the cage.

In our work, packing DBMPure around an Extraforaminal Lumbar Interbody Fusion Technology PEEK cage (ELIFT, SpineFrontier Inc.) after discectomy resulted in close results in range of motion as with the ELIFT alone post discectomy<sup>(43)</sup>. As such conclusions made in the aforementioned study suggest that the addition of DBMPure around a PEEK cage does not provide any additional stability during biomechanical flexibility testing. In our early studies of size of DBMPure particles and their ability to clump together to form a supporting base, we found no differences in stability when comparing the micro- and macro-particle sizes at 50% fill of the L4-L5 disc height<sup>(43)</sup>.

The use of DBMPure alone to fill intervertebral space after discectomy was also examined in the abovementioned study. The effects of DBMPure at 100% fill of the disc space after discectomy were biomechanically similar to the discectomy state<sup>(43)</sup>. The biomechanical data garnered demonstrated a loss of height with DBMPure packing alone and significantly increased range of motion during testing conditions. The experimenters also noted a pasty consistency of the DBMPure materials used, leading to a type of "toothpaste effect". To control this effect, plastic wrap was employed to limit the amount of DBMPure used during the experiment and help restrain and monitor the true fill effects based on real percentages of the disc space available for filling.

## Conclusion

There remain many challenges to bone formation in spinal fusion as the indications and surgical practices continue to expand<sup>(44)</sup>. We predict that

the weaknesses of DBMPure may be overcome by efforts to increase the consistency of the product, thus allowing hardening of the paste allowing it to fill disc space more rigidly. At this time it seems the biomechanical advantage of DBMPure in spinal fusion rests with its use in conjunction with PEEK interbodies and not alone at its current incarnation.

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