

Technical Notes & Surgical Techniques

Can the use of a novel bone graft delivery system significantly increase the volume of bone graft material in a lumbar in situ cage, beyond volumes normally achieved via standard cage filling methodology? Results from a cadaveric pilot study.



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ABSTRACT

Lateral lumbar interbody fusion (LLIF) is an interbody fusion technique which approaches the spine via the transpoas route. Although such an approach eliminates many of the known complications associated with traditional fusion, it does not allow for the harvesting of local bone. Therefore, alternative strategies must be employed in order to ensure high rates of successful arthrodesis. One such strategy is to increase the volume of bone graft material (BGM) within the cage, thereby improving the environment for osteogenesis and subsequent fusion. In this study, we tested the hypothesis that the use of a novel bone graft delivery system would lead to significantly higher volumes of intra-cage BGM, compared to traditional cage filling methodology. The senior author performed a LLIF on a cadaveric spine in a traditional manner, which included hand-packing the cages with BGM and then inserting them into prepared disc spaces. A CT scan was performed and all BGM cage volumes were calculated. Next, attempts were made to inject additional quantities of BGM into the in situ cages, via the delivery system. A second CT was performed and new cage volumes of BGM were calculated. Results demonstrated significantly higher cage volumes of BGM after the use of the bone graft delivery system ($p = 0.014$), compared to those volumes achieved with standard cage packing methodology. This first-of-its-kind study suggests the use of a novel bone graft delivery system will significantly increase cage volumes of BGM which potentially may lead to increase rates of arthrodesis and improved clinical outcomes.

1. Introduction

Chronic low back pain (LBP), with or without associated lower extremity pain, is a major cause of world-wide morbidity [1,2], significantly affecting over 60% of all people at some point in their lives [3]. Most LBP can be successfully managed with conservative care; however, for those cases refractory to such care, lumbar arthrodesis (fusion) has become a standard surgical option [4].

Although there continues to be considerable controversy with regard to which fusion technique is best for what spinal disorder, it is generally accepted that the achievement of a solid interosseous fusion is the cornerstone for successful clinical outcomes [5].

Currently, there are four mainstream fusion techniques which

include posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF), anterior lumbar interbody fusion (ALIF) and transforaminal lumbar interbody fusion (TLIF). Unfortunately, all of these techniques have been associated with well described complications. For example, TLIF and PLIF are associated with intraoperative nerve root injury and subsequent chronic radicular pain [6]; standalone posterolateral fusion is associated with a high rate of nonunion (pseudoarthrosis) [7]; and ALIF is associated with vascular injury [8], superior hypogastric plexus injury and retrograde ejaculation [9].

In hopes of avoiding such complications, alternate fusion techniques have been developed which include lateral lumbar interbody fusion (LLIF), also known as extreme lateral interbody fusion (XLIF Nuvasive®), XLIF, or direct lumbar interbody fusion (DLIF,

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Medtronic®).

Developed in the late 1990s by Pimenta [10], LLIF has been gaining popularity, particularly subsequent to the 2006 publication by Ozgur et al., which reported encouraging clinical outcomes, without the typical mainstream fusion complications [11].

Unlike the contemporary fusion techniques, LLIF employs a novel transposas approach to the spine which completely bypasses the great vessels, superior hypogastric plexus, traversing nerve roots, and exiting nerve roots, thereby eliminating the chance for intraoperative injury of those structures [9]. However, one disadvantage of this approach is that there is no local autogenous bone (autograft) to harvest and use as bone graft material (BGM). To compensate for this missing important source autograft, which is considered the gold standard BGM [12,13], the surgeon must either harvest autograft from the iliac crest or use bone graft alternatives, both of which have been associated with known complications. Specifically, the harvesting of iliac crest autograft (ICAG) has been associated with postoperative infection [14], the development of chronic harvest site pain [15], and injury to the lateral femoral cutaneous nerve [14]. In order to achieve similar rates of successful arthrodesis, many bone graft alternatives must be combined with biologics. Recombinant human bone morphogenetic protein-2 (rhBMP-2), has been particularly successful at increasing rates of successful fusion. However, it has also been associated with complications, such as pathological osteolysis, heterotopic bone formation, unexplained postoperative radiculopathy, and an increased risk for the development of cancer [16–21]. Therefore, researchers continue the search for novel BGMs and/or surgical techniques that could substitute for local bone, yet not have the aforementioned complications.

It is well-established that in order to achieve a successful interosseous fusion, a sufficient volume of BGM must be placed between the two bones being fused. Failure to do so has been shown to decrease the success of fusion and negatively affect clinical outcomes [22]. Therefore, it seems reasonable to assume that increasing the volume of BGM in and around the cage [cage volume] will lead to increased rates of successful fusion, which in turn will lead to improved clinical outcomes. Surprisingly, with regard to interbody fusion, it appears that this simple concept has not been tested in human or animal.

The objective of this pilot study was to test the hypothesis that the use of a novel in situ cage filling system will significantly increase the cage volume of BGM, as compared to traditional hand-packing cage filling procedures.

2. Materials and methods

2.1. Part 1

Using an adult cadaveric lumbar spine specimen which was stripped of paravertebral muscle the senior author performed an abbreviated LLIF on the top four lumbar discs (L1–L4) at a private cadaver laboratory.

From a standard transposas approach, a square-shaped annulotomy was made on the lateral aspect of each disc, followed by a standard nucleotomy and endplate decortication. A cage specifically designed for LLIF (InFill® V2 Lateral Interbody Fusion Device) was, in typical fashion, hand-packed with BGM made from a combination of demineralized bone matrix (DBM) and contrast material (OmniPaque®).

A specially designed insertion tool was next attached to the delivery port on the lateral margin of the cage, and then the cage was carefully inserted through the annular window and into the center portion of the prepared disc space [Fig. 1]. After the cage was in place, the insertion tool was removed and general observations were made with regard to the cage filling and insertion process. Subsequently, the same procedure and observations were repeated at the other three levels.

The specimen was transported to a local imaging facility where a comprehensive thin-sliced computed tomographic (CT) scan (0.6 mm cuts) with 3D reconstruction was completed. The subsequent images



Fig. 1. Cage insertion process. As the interbody cage is being slid into the prepared disc space, any additional bone graft material above or below the margins of the cage is scraped off. Therefore, it is impossible to fill the cage endplate interval via traditional cage filling methodology.

were assessed by a board-certified neuroradiologist who was instructed to calculate the pre-injection cage volume of BGM at each level by simply finding the product of its height, width, and length. Such measurements were easily made with the PACS imaging software. The senior author and DMG were also required to make qualitative observations with regard to the success of cage filling.

2.2. Part 2

After pulling the specimen out of the CT scanner, a special BGM injection tool was carefully inserted through the annular window of the disc and connected to the delivery port of the in situ cage, which still contained the BGM from part I of the study.

Next, a specially designed syringe was hand loaded with the same BGM that was used in the first part of the study and then attached to the extra-spinal end of the injection tool. In attempts to inject more BGM into the cage, the metal plunger was slowly and steadily depressed until significant resistance was met. Next, the syringe was detached from the injection tool which in turn was removed from the disc space. General observations were made and recorded regarding the bone graft injection procedure. The same procedure and observations were repeated at the other three levels.

The specimen was once again returned to the imaging facility where another post-injection CT scan was performed using the same parameters as before. The new images were interpreted by the same board-certified neuroradiologist, and new post injection cage volumes of BGM were calculated at all levels using the previous described methodology. Again, the senior author and DMG make qualitative observations with regard to the success of cage filling.

2.3. Statistical analysis

The pre- and post-injection cage volume data were analyzed by a biostatistician who employed a two-sided paired *t*-test, at 95% level of confidence. A standard open-source statistical program platform, R, was used to perform this analysis.

Table 1
Pre- vs post-injection bone graft material volume results.

Level	Pre-injection vol. (cc)	Post-injection vol. (cc)	Change in vol. (cc)	Percent change in vol. (%)
L1/L2	3.038	5.115	2.077	60.4
L2/L3	3.136	5.376	2.240	71.4
L3/L4	3.584	4.836	1.252	35.0
L4/L5	3.528	6.851	3.323	94.2

3. Results

No technical difficulties were encountered with either the cage insertion or injection procedures. Specifically, the cages were easily inserted through the annular windows and into the interbody spaces during part 1 of the experiment without incident. Of interest was the observation that during the cage insertion process, all additional BGM packed above or below the cage margins was scraped off as it passed through the narrow annular window, thereby reducing the volume of BGM [Fig. 1]. During the cage injection procedure of part 2, BGM flowed steadily out of syringe, through the insertion tool, and into the intra-cage space without apparent blockage, leakage, or incident.

Statistical analysis of the pre- versus post-injection cage volume data demonstrated a significant ($p = 0.014$, paired t -test) increase in the cage volume following the injection of additional BGM into the in situ cages, as compared to those volumes achieved via the traditional cage filling technique [Table 1].

General observations reveal a striking absence of BGM between the upper and lower cage margins and the adjacent vertebral endplates, a space called the cage-endplate-interval, (CEI) following the traditional cage hand-packing procedure employed in part 1 of the study. [Fig. 2] However, following the injection phase of the study (part 2), BGM filled the CEI at all levels to various increased the overall cage volumes of the BGM [Fig. 3].

4. Discussion

Lateral lumbar interbody fusion has been gaining popularity in the surgical community because of its reported good clinical outcomes, without the typical mainstream fusion complications [1,9]. However, its transpoas approach does not allow for the harvest of local bone to use as autograft. As a substitute, surgeons may choose to use ICAG;

however, its harvesting has been associated with significant complications and morbidity [14,15]. Another popular workaround to achieve good rates of successful fusion is to use a biologic like rhBMP-2 in combination with a bone graft enhancer, such as DBM. However, rhBMP-2 continues to be controversial because of its well-described complications [2–7].

Therefore, researchers continue the search for novel bone graft alternatives and/or surgical techniques which could potentially increase rates of successful fusion without the complications associated with ICAG and rhBMP-2.

One basic factor for the success of any type of fusion is the need for an adequate volume of BGM between the osseous surfaces that are being fused. DiGiovanni et al. clearly demonstrated this principle in their recent ankle and hindfoot fusion study [22]. During that study, a board-certified musculoskeletal radiologist first reviewed 379 post-operative CT images and then classified them as either having a sufficient volume of BGM in the joint space, or not. Next, he reviewed the 24 week follow-up CT images from those same patients and then classified them as either having a solid fusion or not. The results indicated that only 21% of the patients from the insufficient BGM volume group demonstrated successful fusion at the follow-up, compared to 81% of the patients from the sufficient BGM volume group ($p < 0.001$) [22]. In another example, Martin et al. used a rabbit PLF model to demonstrate that a 50% reduction of BGM in the intertransverse beds, significantly reduced the rate of successful fusion from 70% down to 33% [11].

Although it seems logical that these results would apply to lumbar interbody fusion, surprisingly, a thorough search in the English language through CINAHL Complete, MEDLINE Complete, DynaMed, The Cochrane Library, and PubMed failed to elucidate a single investigation reporting the relationships between the success of interbody fusion and the volume of BGM in the intervertebral disc space. Therefore, we believed it was important to design and execute a study specific to interbody fusion which investigated this relationship, and this current pilot study is the beginning of that journey.

One technical problem inherent to LLIF results from a mismatch between the cage and vertebral endplates surfaces. Specifically, the upper and lower cage margins are flat, yet their adjacent vertebral endplates are typically concave and/or pitted with developmental or degenerative defects. This mismatch creates significant gaps between the cage and the endplate, a space called the CEI, which cannot be filled with BGM via traditional cage filling technology. This is because, as

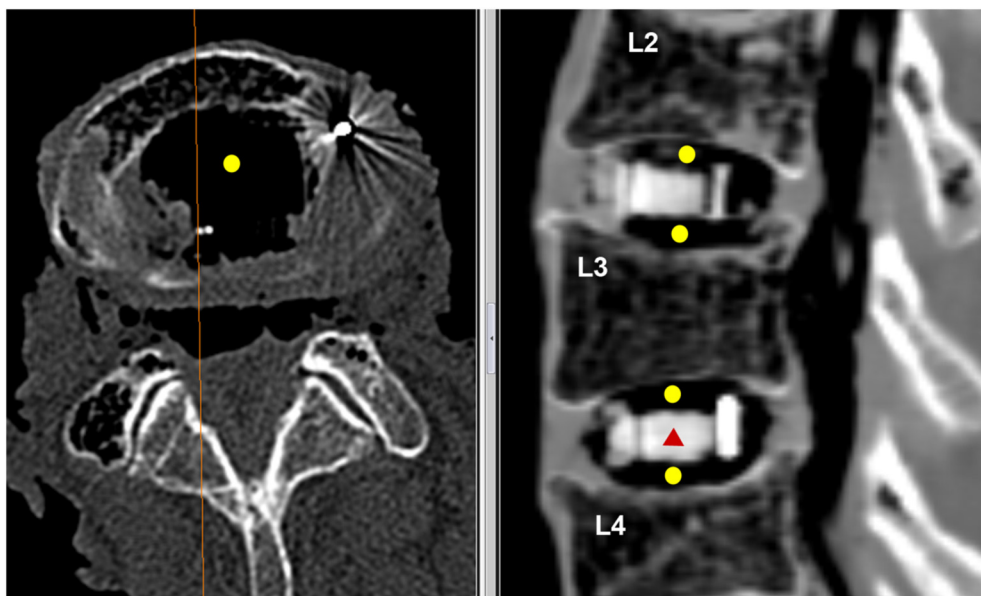


Fig. 2. CT example of the cage endplate interval: pre-injection. These images represent cut through the right paracentral zone, just below the inferior endplate of L3. Note the regions above and below the intra-cage space, which is filled with bone graft material (red triangle), are devoid of bone graft material (yellow circles). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

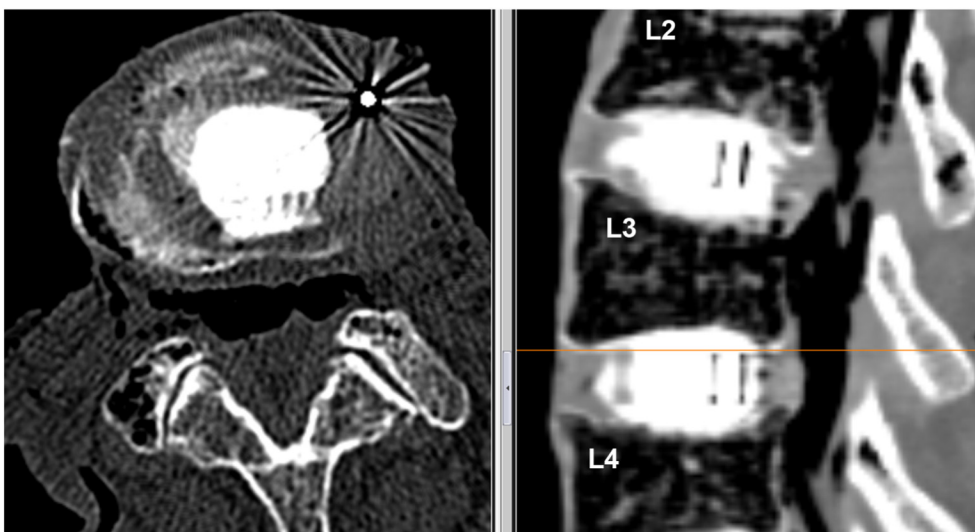


Fig. 3. CT example of the cage endplate interval: post-injection. These images represent an identical cut to that of Fig. 2, only following the injection of bone graft material into the in situ cage. Note there was substantial filling of the cage endplate interval.

noted in our study, any BGM packed above and/or below the cage margins gets scraped off during the cage insertion process [Fig. 1] and cannot be recovered via traditional cage-packing methodology.

By employing a novel bone graft delivery system, we demonstrated that it was possible to fill the CEI after the cage had already been inserted which led to a significant overall increase in the cage volume of BGM compared to traditional cage filling methodology [Fig. 4].

It is our hypothesis that by increasing the volume of BGM material within the cage during LLIF, the surgeon will achieve a significant increase in the rate of successful interbody fusion, as well as subsequent improved clinical outcomes, as compared to LLIFs performed via traditional cage filling methodology.

One obvious shortcoming of this pilot study stems from the fact that the cadaveric spine section used in this study was stripped of all paravertebral musculature. Therefore, the specimen lacked the normal axial load forces and intradiscal pressures that are inherent in the living. It is still unknown how this new bone graft delivery system will

function in a living human spine. Furthermore, because of our limited funding, we were unable to use a larger sample size which would have increased the statistical power of the study. Therefore, caution should be used when interpreting our outcomes.

There are other in situ cage filling technologies that have recently come onto the market since the development of the patent-pending InFill® V2 Lateral Interbody Fusion Device. However, no group, including the manufacturers, have published any type of study describing the usefulness or efficacy of their products. Therefore, it's impossible to know or compare their products to the InFill® V2 Lateral Interbody Fusion Device. Our study is the first of its kind and it is hoped that its publication will stimulate other research on this important topic. We now plan on proceeding with the next phase of the study, which will test the hypothesis that the addition of extra volumes of BGM will in fact lead to higher rates of successful interbody fusion.

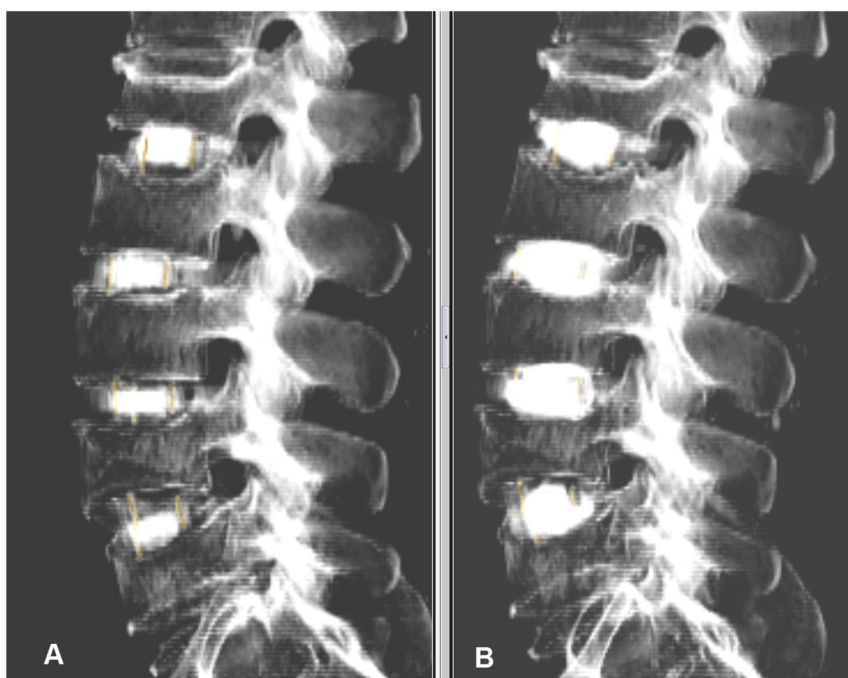


Fig. 4. Three-dimensional reconstructed CT: pre- vs. post-injection images. Image A demonstrates only modest filling of the cage with bone graft material after traditional cage packing techniques. Image B demonstrates a more robust filling following injection of additional bone graft material to the in situ cages via the novel bone graft delivery system.

5. Conclusions

The results of this first-of-its-kind cadaveric study demonstrated that it was possible to increase the volume of BGM during LLIF, to cages already in situ, beyond those volumes achieved with traditional cage packing methodology. We would speculate that this increased volume of BGM will lead to increased rates of successful fusion and improved clinical outcomes, without the need for the use of ICAG or potentially-dangerous biologics.

Conflicts of interest

The authors declare there are no competing financial interests.

Study funding

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