A Cadaver Study to Compare Vertebral Augmentation With a High-viscosity Cement to Augmentation With Conventional Lower-viscosity Cement

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Study Design: Comparison of extravasations in fractured cadaver vertebrae augmented with commercial low-viscosity versus high-viscosity cements.

Objective: Use of high-resolution, 3-dimensional (3D) imaging to test the hypothesis that high-viscosity cements can reduce the type and severity of extravasations after vertebral augmentation procedures.

Summary of Background Data: Cement extravasations are one of the primary complications of vertebral augmentation procedures. There is some evidence that high-viscosity cements might reduce extravasations, but additional data are needed to confirm the early findings.

Methods: A range of vertebral fractures were created in fresh human cadavers. One group was then augmented with a low-viscosity polymethylmethacrylate (PMMA)-based cement and the other group injected with high-viscosity PMMA-based cement. High-resolution computerized tomography exams were obtained, and extravasations were assessed using 3D volume renderings. The type and severity of extravasations were recorded and analyzed.

Results: The proportion of vertebrae with any type of extravasation through the posterior wall to the spinal canal, into small vessels laterally or anteriorly, through the endplates, or anywhere around the body was not significantly different between the high-viscosity and low-viscosity groups. There was significantly less severe extravasation through the endplates ($P = 0.02$), and a trend toward less severe extravasation through vessels ($P = 0.06$) with the high versus low-viscosity cements.

Conclusions: In agreement with previous research, high-viscosity PMMA-based cement may help to reduce the more severe forms of extravasations after vertebral augmentation procedures in newly fractured vertebrae.

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Cement viscosity is 1 option that a clinician must select when planning a vertebral augmentation procedure. Early reports support that higher viscosity cement can reduce extravasations, and improve infiltration and height restoration.[1–3] However, additional data to confirm or refute previous results are needed to help clinicians select the optimum cement for augmentation procedures.

The goal of this study was to compare a high-viscosity bone cement system to standard viscosity polymethylmethacrylate (PMMA) cement based on high-resolution, 3-dimensional (3D) computerized tomography (CT) assessment of extravertebral leakage and interdigitation into osteoporotic/fractured bone.

MATERIALS AND METHODS

Six fresh, whole human cadaver spines were obtained through the willed body program of the University of Texas, Southwest, Dallas, TX (3 male, 3 female, average age 74 ± 5.3 y, all white). Vertebrae from the sixth thoracic vertebra to the sacrum were used for testing. The spines were kept in a refrigerated state of 2°C before testing. Fine cut CT scans (1-mm slices) were obtained of each whole, intact spine (Brilliance 64, Philips Medical Imaging, Amsterdam). A hydroxyapatite phantom (CIRS, Norfolk, VA) was included in each scan to enable quantitative assessment of bone density. Each spine was then cut through the intervertebral disc spaces into 4, 3-vertebrae segments, guided by measurements from the CT scans. The center vertebra in the final specimens was: 2-T6, 4-T7, 1-T8, 5-T10, 1-T12, 5-L1, 1-L3, 5-L4.

Specimens were prepared for fracture creation by scraping remaining disc material from the cranial-most and caudal-most endplates, and then attaching the specimens onto 6.4-mm thick plexiglass plates using PMMA bone cement (CMW DePuy, Johnson and Johnson). The mounted specimens were mounted in a pneumatic testing system, designed to create controlled anterior wedge compression fractures using compressive loads applied anterior and posterior to the specimen.[4] The anterior loads were applied at a greater distance from the specimen than the posterior loads to create a superimposed anterior bending moment. Loads were monitored during the testing using a load cell (AMTI, Watertown, MA), and the peak compressive load was recorded. After creating the fracture, specimens were refrigerated at 2°C until the augmentation procedure.

Senior spine surgeons performed unipedicular vertebroplasty on the central vertebra of all specimens. Segments were randomly divided into 2 equal groups. The first group was augmented using vertebroplastic radiopaque resinous material (DePuy Spine Johnson & Johnson) containing PMMA and barium sulfate. The second group was augmented using the confidence system (DePuy Spine, Raynham, MA). As in their clinical practice, the surgeons used the rationale that the more fill the better short of extravasation. This theoretically offers the optimal potential benefits of the procedure, including fracture reduction and maximal surface area of stabilization. Cement was injected with fluoroscopic monitoring (Vision, Ziehm Inc., Riverside, CA) until visible extravasation outside the vertebral body was observed, cement was approaching the posterior cortex, or there was complete fill of the superior endplate. The volume of cement at which this occurred was variable with each augmentation procedure, and depended on the size of the vertebral body and the degree of fracture compression.

Specimens were then loaded into cylindrical vessels, each containing all of the segments in the group. Cylinders were filled with plain water several hours before the CT scans with intermittent vacuum applied to remove air from the specimens and simulate an in vivo environment. Fine cut CT scans (0.9-mm thick slices spaced 0.45 mm apart, 0.35-mm pixel size) of all segments were then obtained (Brilliance 64, Philips Medical Imaging, Amsterdam). Using multiplanar reconstructions and 3D volume compositing imaging (Osirix[5]), the CT scans were used to carefully assess every surface of each vertebra for cement extravasation (Fig. 1). Extravasation was assessed using 4 categories of cement extravasation (Table 1). Each category is further described by 3 severity scores, none, moderate, and severe (Table 1). These severity scores were based on a recent paper by Georgy,[3] where mild extravasation was considered as clear cement visible protruding 1 to 2 mm out of the vertebra, moderate was considered as cement protruding >3 mm from the vertebra, and severe was identified as unusually extensive extravasations (eg >6 mm protrusions, multiple protrusions from 1 surface, broad-based extrusions, etc.). In addition, the 3D volume of each vertebral body and the volume of the cement contained within each body were measured (Osirix[5]).

RESULTS

A total of 24 three-body segments were prepared and tested from the 6 spines. Two specimens were not injected; 1 for lack of any evidence of a fracture and the other because the specimen was crushed beyond anatomically recognizable features. Data for 11 vertebrae were obtained for each of the vertebroplastic and confidence groups.

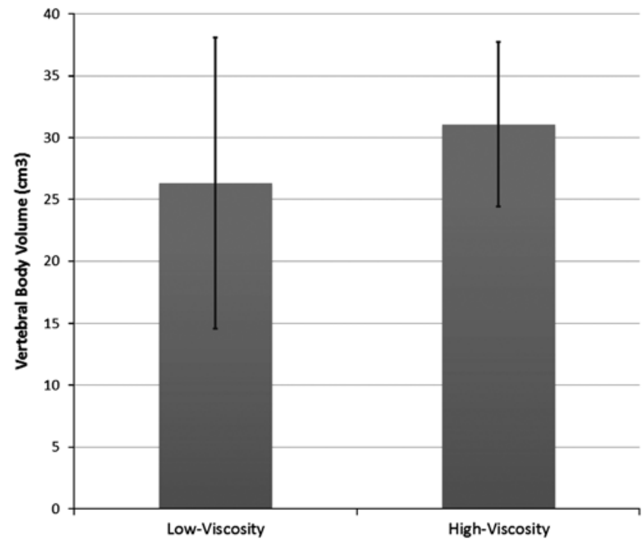

FIGURE 1. Vertebral body volume calculated from computerized tomography exams. The error bars show ±1 standard deviation.

There were no significant differences between the high-viscosity and low-viscosity groups with respect to average bone density ($P = 0.35$), or the fracture patterns. On the basis of analysis of the postinjection CT exams, there was no difference in the average volume of the vertebral bodies ($P = 0.23$, Fig. 1), the average volume of cement injected ($P = 0.76$, Fig. 2), or the percent of vertebral body that was filled with cement ($P = 0.36$, Fig. 3). Extravasation data were analyzed in 2 ways: (1) as "any" including any small or large amount of extravasation; (2) as "severe" by including on large amounts of extravasation as per the extravasation classification system (Table 1). Figure 4 provides an example of a 3D reconstruction from CT of a vertebroplastic specimen that was assessed to have severe posterior and severe endplate extravasation. Table 2 provides

TABLE 1. Details of the System Used to Classify the Location and Severity of Extravasations

Category	Description	Severity
A	Cortical defect extravasation	1-None 2-Moderate 3-Severe
B	End plate extravasation	1-None 2-Moderate 3-Severe
C	Segmental vessel extravasation	1-None 2-Moderate 3-Severe
D	Canal extravasation	1-None 2-Moderate 3-Severe

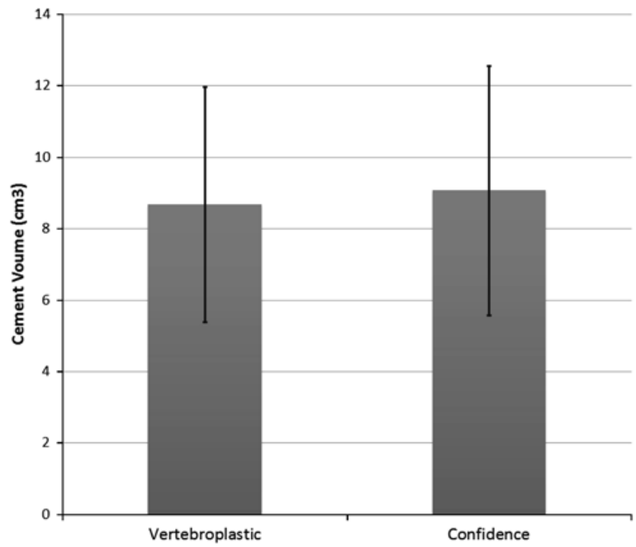

FIGURE 2. Volume of cement injected into the vertebral bodies. The error bars show ±1 standard deviation.

the results for the assessment of "any" extravasation. The proportion of cases with any extravasation through the posterior wall to the spinal canal, into small vessels laterally or anteriorly, through the endplates, or anywhere around the body was not significantly different between the high-viscosity and low-viscosity groups. The *P*-values for tests of proportions are also provided in Table 2, both for a 1-sided and 2-sided test of proportions. With respect to the analysis of only severe cases of extravasation, Table 3 provides the results. There was significantly less severe extravasation through the endplates ($P = 0.02$), and a trend toward less severe extravasation through vessels ($P = 0.06$) with the confidence cement compared with the vertebroplastic cement.

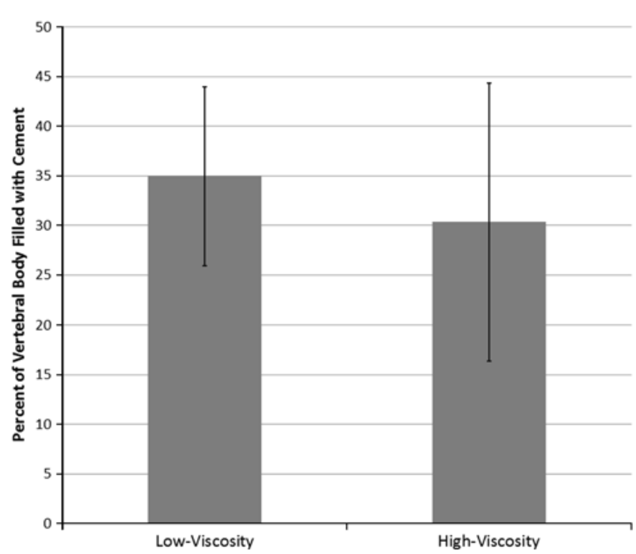

FIGURE 3. Percent of the vertebral body filled with cement. The error bars show ±1 standard deviation.

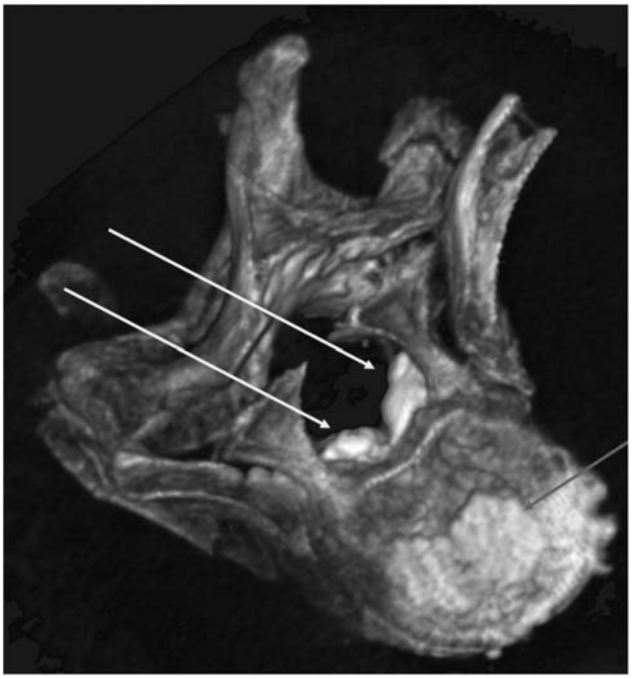

FIGURE 4. A volume compositing 3 dimensional reconstruction (Osirix[5]) from the computerized tomography exam of a vertebroplastic specimen that was assessed as having severe posterior (white arrows) and severe endplate extravasation (darker arrow). The cement appears white in this reconstruction with the bone appearing in shades of gray reflecting low (darker) to high (brighter) bone densities.

Both the low-viscosity and high-viscosity cements infiltrated the marrow spaces and interdigitated well with the trabecular bone. Close apposition of the cement to the trabecular bone was evident in the CT exams (Fig. 5A, B). No obvious differences were discerned between the groups with respect to spread through the vertebral body or interdigitation with trabecular bone, although interdigitiation was only subjectively assessed.

DISCUSSION

Minimally invasive procedures for the treatment of vertebral compression fractures have been in use since the mid-1980s.[6] Percutaneous vertebroplasty was intended to be a pain-relief procedure based on the hypothesis that the injected cement would provide support and stability

TABLE 2. Proportion of Cases With Different Types of Extravasations

	Cortical	Endplate	Vessel	Canal	Any
High-viscosity	55	55	73	9	91
Low-viscosity	58	75	67	17	83
Pval 1 tail	0.44	0.15	0.38	0.30	0.30
Pval 2 tail	0.89	0.30	0.75	0.59	0.59

These data are for assessments that considered any amount of extravasation. The significance levels for tests of proportions are provided, both for 1-tailed, and 2-tailed tests (Stata Ver 11).

TABLE 3. Proportion of Cases With Different Types of Severe Extravasations

	Cortical	Endplate	Vessel	Canal	Any Severe
High-viscosity	27	18	18	9	45
Low-viscosity	50	58	50	8	83
Pval 1 tail	0.13	0.02	0.06	0.47	0.03
Pval 2 tail	0.27	0.05	0.11	0.95	0.06

In contrast to the data in Table 1, these data are for only those cases with severe extravasation. The significance levels for tests of proportions are provided, both for 1-tailed, and 2-tailed tests (Stata Ver 11).

to a fractured vertebra. The procedure may also be used with the goal of restoring height or reducing kyphosis in a fractured vertebra. The procedure is reported to provide pain relief in up to 90% of cases.[7–9] The exact mechanism of how this procedure provides the observed analgesic effect is controversial and likely dependent on patient selection, as is evident in recent studies showing that some patients have similar outcomes whether or not PMMA cement was actually injected into the vertebral body.[10,11] It has been proposed that the procedure may provide mechanical support that contributes to reduction or elimination of micromotion between fractured fragments of the vertebra, thereby reducing pain.[12–15] Another proposed theory is the exothermic chemical reaction that occurs within the vertebral body, which causes thermal damage to surrounding interosseous nerve fibers.[12] Despite marginal understanding of the mechanism of action, percutaneous vertebroplasty is generally considered to be a safe and effective treatment option for vertebral compression fractures. Although efficacy has been reported in many studies, vertebral augmentation has also been associated with both minor and major complications.[16]

Extravertebral bone cement leakage has been the most common complication reported with percutaneous vertebroplasty. Cement extravasation can be directly correlated to the severity of the fracture and the volume of cement injected; clinical studies have shown leakage as high as 73%,[17–19] however, most cement extravasations are asymptomatic.[18] Clinical outcomes of cement leakage vary between leakage with no apparent clinical symptoms to severe outcomes such as paraplegia,[20–22] spinal cord and nerve root compression,[18,20,23,24] cement pulmonary embolisms,[4,25–27] and possible death.[28]

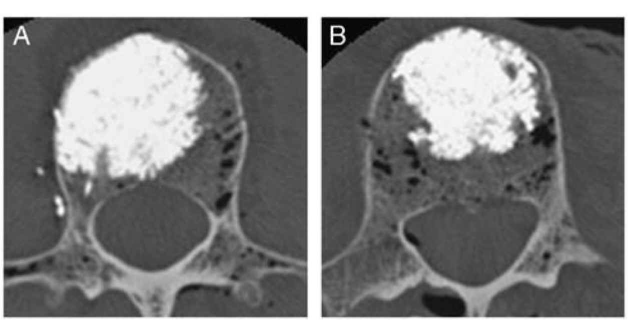

FIGURE 5. Example axial sections from computerized tomography exams taken after injecting fractured vertebral bodies with conventional low-viscosity cement (A) or with high-viscosity cement (B).

There are 3 factors that may influence the cement flow into and out of the vertebral body: bone and fracture-related parameters, cement properties, and injection methods.[29] Although fracture morphology is impossible to control and the method of injection has been standardized, the cement properties may be manipulated to ultimately decrease the complication rate. In terms of cement properties, the cement should spread within the vertebral body in a controlled manner, as a "uniformly expanding cloud," as opposed to "fingers of a glove," which represents the uncontrolled spread through lower resistance paths in the bone.[30]

It has recently been shown that cement with higher viscosity spreads more uniformly than cements with lower viscosity and thereby, reduces the risk of leakage.[30] A reduction in extravasation with the confidence cement is hypothesized to be achieved by reaching maximum viscosity at a quicker rate and remaining at this higher viscosity for a longer duration compared with lower viscosity PMMA cement. In a recent study by Georgy,[3] patients with vertebral augmentation performed using high-viscosity cement without first creating a cavity with a balloon had similar rates of leakage compared with that of kyphoplasty, a procedure documented to have less leakage rates compared with the standard vertebroplasty.

As this study was aimed to investigate cement distribution and extravasation in fractured vertebral bodies, the volume of cement injected was intended to represent the upper-end of what might be used clinically. The amount injected averaged over 8 mL, which is higher than in some recent publications.[1,3,31] In particular, Anselmetti et al[1] injected between 1 and 3.5 mL in their study of the confidence cement, and reported a much lower rate of extravastation. There is limited clinical evidence to help justify the optimal amount of cement to inject. The amount of cement injected may depend on the philosophy of the clinician. In this study, the clinician's goals include filling enough of the vertebral body to achieve height restoration and also to capture all fracture fragments, because "loose" fracture fragments may be a continued source of postoperative pain. It is likely that a larger volume of injected cement would be more likely to capture "loose" fragments, but this was not specifically tested. A trade-off may be that a larger volume of injected cement is also more likely to result in extravasations. A goal of this study was to compare extravasation rates, so the use of a larger volume of cement (approximately 1/3 of the vertebral body volume filled, very similar to fill reported by Mousavi et al[32]) is more likely to facilitate detection of differences. The amount injected in this study, is consistent with the amounts described in previous studies.[2,17,33] In our cadaveric study, although small extravasations were seen in the same proportions with both high-viscosity and low-viscosity cement, severe extravasations were more common for the low-viscosity cement. These severe extravasations were seen through foramen in the lateral and anterior walls of the vertebral bodies and through the endplates. By controlling severe extravasations, one can hypothesize that both the minor and major complications associated with vertebroplasty in a clinical environment would be decreased.

Limitations of our study include those inherent to a cadaveric study and those specific to our methods. Although attempts were made during this study to recreate the clinical scenario of a vertebral compression fracture, cadavers do not have the same structure properties, such as soft tissue support and vascular qualities, found in vivo. Therefore, we cannot describe the clinical significance of a decrease in extravasation in the live patient scenario. Although a density phantom was included in the CT exams, the densities were only used to assure equal densities in the high-viscosity and low-viscosity groups. A normative database was not available for the density phantom that was used so the T or Z scores were not known. However, given the age at death of the cadaveric sources of vertebrae, it was assumed that they were all osteoporotic. Another limitation of this study is the small sample size. The statistical power for the comparison of canal extrusions is only 0.03. A sample size of 394 per group is needed to determine if an extravasation rate of 9% is not different than 17% with a power of 0.9 (Stata, Ver 11, College Station). Finally, another challenge in this study was recreating similar fracture patterns in each cadaver. We attempted to generate consistent fractures by using the same controlled loading for each specimen. However, a wide range of fracture types were created. Subjectively, this was due to the presence and extent of anterior osteophytes and the wide range of densities. Even though this could be considered a limitation, it could also represent strength of the study, as a wide range of fracture patterns occur in clinical practice. Despite these limitations, cadaver studies are still an important preliminary stepping stone in research and this study provides a solid base for future controlled prospective studies.

In agreement with previous research,[1–3] this cadaver study also supports that vertebral augmentation through higher viscosity cement produces less severe extravasation compared with standard vertebroplasty cement. Although future clinical studies are indicated, one may extrapolate from this study that by reducing the amount of severe extravasation in vivo, the complication rate associated with this procedure would also decrease, thus making vertebroplasty a safer, more effective procedure.

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