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Basic Science

A pictorial classification atlas of cement extravasation with vertebral augmentation

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Abstract

BACKGROUND CONTEXT: Minimally invasive procedures for the treatment of vertebral compression fractures (VCFs) have been in use since the mid-1980s. A mixture of liquid monomer and powder is introduced through a needle into one or both pedicles, and it polymerizes within the vertebral body in an exothermic chemical reaction. The interaction between cement and the fractured vertebral body determines whether and how the cement stabilizes the fragments, alters morphology, and extravasates. The cement is intended to remain within the vertebral body. However, some studies have reported cement leakage in more than 80% of the procedures. Although cement leakage can have no or minimal clinical consequences, adverse events, such as paraplegia, spinal cord and nerve root compression, cement pulmonary embolisms, or death, can occur. The details of how the cement infiltrates a vertebral body or extravasates out of the body are poorly understood and may help to identify strategies to reduce complications and improve clinical efficacy.

PURPOSE: Apply novel techniques to demonstrate the cement spread inside vertebrae as well as the points and pattern of cement extravastation.

STUDY DESIGN: Ex vivo assessment of vertebral augmentation procedures.

METHODS: Vertebrae from six fresh whole human cadaver spines were used to create 24 specimens of three vertebrae each. The specimens were placed in a pneumatic testing system, designed to create controlled anterior wedge compression fractures. Unipedicular augmentation was performed on the central vertebra of 24 specimens using polymethylmethacrylate/barium sulfate Vertebroplastic cements (DePuy Spine, Raynham, MA, USA). The volume of cement injected into each vertebra was recorded. Fine-cut computed tomography (CT) scans of all segments were obtained (Brilliance 64; Philips Medical Imaging, Amsterdam, The Netherlands). Using multiplanar reconstructions and volume compositing three-dimensional imaging (Osirix, www.osirix-viewer.com), each specimen was carefully assessed for cement extravasation. Specimens were then immersed in a 50% sodium hypochlorite solution until all overlying soft tissues were removed, leaving the bone and cement intact. The specimens were dried and visually examined and photographed to assess cement extravasation and fracture patterns. Specimens were cut in the axial or sagittal plains to assess the gross morphology of cement infiltration and extravasation. Finally, 25-mm block sections were removed from selected specimens and imaged at 14-μm resolution using a GE Locus-SP micro-CT system (GE Healthcare, London, Ontario, Canada).

RESULTS: Infiltration was characterized by an intimate capture of trabecular bone within the cement, forming an irregular border at the perimeter of the cement that is determined by the morphology of the trabeculae and marrow spaces. Extravasation of the cement was assessed as ‘‘any’’ if any small or large amount of extravastation was detected and was also assessed as severe if a large amount of extravasation was found. Out of the 23 levels studied, some extravasation was visibly apparent in all levels. A wide spectrum of filling patterns, leakage points, and interdigitation of the cement was observed and appeared to be determined by the interaction of the cement with the trabecular morphology. The results support the fact that the cement generally advances through the vertebrae with relatively regular and easily identifiable borders.

FDA device/drug status: not applicable.

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CONCLUSIONS: Using a cadaver VCF model, this study demonstrated the exact filling and extravastation patterns of bone cement inside and out of fractured vertebrae. These data enhance our understanding of the vertebral augmentation and extravastation mechanics.

Keywords: Vertebral augmentation; Infiltration; Extravasation; High-resolution imaging

Introduction

Minimally invasive procedures for the treatment of vertebral compression fractures have been in use since the mid-1980s [1]. Percutaneous vertebroplasty was designed as a pain relief procedure based on the hypothesis that the injected cement would provide support and stability to a fractured vertebra compromised by previous osteolytic destruction, such as osteoporosis or metastases. This surgical procedure generally involves the percutaneous image-guided navigation of an 11- to 13-gauge needle through one or both the pedicles into the vertebral body and the insertion of bone cement into the damaged vertebral body. The cement is introduced as a paste-like mixture of powder and monomer that polymerizes within the vertebral body in an exothermic chemical reaction. It is generally accepted that the cement should remain within the boundaries defined by the external surfaces of the vertebrae that existed before fracture.

The procedure is reported to provide pain relief in up to 90% of patients [2–4]. However, complications can arise and are mainly the result of extravertebral leakage of bone cement. A wide range of leakage rates have been reported, with some studies reporting leakage in more than 80% of the procedures [5–8]. Most cement extravasations are asymptomatic [7] but span a range of clinical consequences up to severe outcomes, such as paraplegia [9,10], spinal cord and nerve root compression [7,10–12], cement pulmonary embolisms [13–16], and possible death [17]. Minimizing the incidence and severity of extravasation requires an understanding of the factors that determine whether and how the cement extravasates.

There are three categories of factors that may influence cement flow within and out of a vertebral body [18]: (1) bone- and fracture-related parameters; (2) cement properties; and (3) injection method (volume, speed, pressure, needle placement). Some of these parameters have already been studied, and a general description of different types of extravasation has been published [11]. The interaction of cement with the structure of the vertebral body and details of how cement extravasates from the vertebral body are poorly understood.

The goals of the present study were to document the cement spread inside the vertebrae as well as the points and pattern of leakage of cement from the vertebra. These details may help to define strategies to improve delivery of cement into a vertebra and reduce extravasation outside of vertebrae.

Material and methods

Six fresh whole human cadaver spines were purchased through the anatomical gift program of the University of Texas, Southwest (Dallas, TX, USA). All vertebrae from the sixth thoracic vertebra to the sacrum were used for testing. Spines were kept in a refrigerated state of 2°C before testing. Fine-cut computed tomography (CT) scans (1-mm slices) of the whole intact spines were obtained (Brilliance 64; Philips Medical Imaging, Amsterdam, The Netherlands). Before the CT examinations, small metal markers were placed in every fourth disc space to aid with identification of levels. Each spine was cut into four, three-vertebrae segments, using measurements from the CT scans to section through the intervertebral disc spaces while preserving vertebral body integrity.

Specimens were prepared for creation of vertebral fractures by scraping remaining disc material from the end plates at either end of each specimen and mounting plexiglass plates to each end using polymethylmethacrylate bone cement (CMW; DePuy, Blackpool, Lancashire, UK).

The mounted specimens were placed in a pneumatic testing system, designed to create controlled anterior wedge compression fractures using compressive loads applied anterior and posterior to the specimen [19]. 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 commercial load cell, and the peak compressive load was recorded. After creating the fractures, specimens were refrigerated at 2°C until the day of augmentation.

For the augmentation procedure, each segment was clamped to a radiolucent plate. Two senior spine surgeons performed a unipedicular augmentation on the central vertebra of all specimens. All augmentations were done using the same method commonly practiced in clinical treatment. Parameters including cement volume, speed of injection, and needle placement were implemented in all specimens based on the surgeon's clinical experience, using the same operative technique. Segments were treated using radiopaque polymethylmethacrylate Vertebroplastic cements (DePuy Spine, Raynham, MA, USA). The volume of cement injected was determined by the surgeons based on the standard clinical practice of monitoring of sagittal and coronal plain fluoroscopic images obtained with a digital C-Arm system (Vision; Ziehm, Inc., Riverside, CA, USA). Pressure of cement filling was controlled using the injection system (DePuy Spine). Cement insertion was discontinued when cement appeared to propagate toward the posterior wall, outside the vertebral body, or when the vertebra was sufficiently filled with cement based on the clinical experience of the surgeons. The volume of cement injected into each vertebra was recorded. Anteroposterior and lateral fluoroscopic images were recorded before and immediately after augmentation.

Specimens were then stacked and loaded into 4-inch–diameter, plastic cylindrical tubes. Cylinders were filled with plain water and capped several hours before the CT scans with intermittent vacuum applied to remove air from the specimens. Fine-cut CT scans (1-mm slices) of all segments were then obtained (Brilliance 64).

Using multiplanar reconstructions and volume compositing three-dimensional imaging (Osirix, www.osirix-viewer.com), each specimen was carefully assessed for cement extravasation. For the purpose of this study, extravasation was defined as the presence of cement external to the perceived outer osseous boundaries of the vertebral body. In the event of a displaced fracture fragment or very irregular surface morphology, subjectivity is required in applying this definition. A new classification system was created to assess cement extravasation by addressing both the clinical relevance of the location of extravasation and the potential significance of the extravasation. Four categories of cement extravasation were created and ranked based on their perceived potential for harm. Each category is further described by three severity scores: none, moderate, and severe (Table 1). Extravasation was assessed as "moderate" if any amount of cement was perceived to protrude external to the outer osseous boundaries of the vertebra, but the depth of the protrusion was small (<2 mm). Classification of severe was established after reviewing all the specimens and was used to identify the extrusions that appeared most severe relative to all of the extrusions studied. Cases classified as severe had cement that protruded more than a few millimeters out of the external surface of the vertebrae, had a thin irregular strut of cement that was perceived to have passed several millimeters out of the vertebral body through a blood vessel, or where a substantial volume of cement was outside the external boundaries of the vertebra (typically in the disc space). In addition, the volume of each vertebral body and the volume of the cement in each body were measured (three-dimensional region-of-interest volume measurements using Osirix).

Table 1
Classification of extravasation

Category	Description	Severity
A	Cortical defect extravasation	None Moderate Severe
B	End plate extravasation	None Moderate Severe
C	Segmental vein extravasation	None Moderate Severe
D	Canal extravasation	None Moderate Severe

Specimens were then immersed in a 50% sodium hypochlorite solution until all overlying soft tissues were removed, leaving the bone and cement intact. The specimens were dried and visually examined to better assess details of cement extravasation and relationship with fracture patterns. Finally, 25-mm cubic block sections were removed from selected specimens and imaged at 14-μm resolution using a GE Locus-SP micro-CT system (GE Healthcare, London, Ontario, Canada).

Results

A total of 24 three-body specimens were prepared and tested from the six spines. One specimen was not injected for lack of any evidence of a fracture, and one was not injected because the specimen was crushed to a state that augmentation would not be attempted in clinical practice. In one specimen, two vertebrae were found to be fractured, and both were injected. Eleven specimens were injected in each of the Vertebroplastic and Confidence groups. The volume of cement injected averaged 8.9±3.4 cc, and the percent of vertebral body volume filled by cement averaged 33±12%. Some amount of extravasation was visibly apparent in all 23 levels.

The filling pattern of cement is demonstrated in Fig. 1. In six of the treated levels (26%), cement leaked into the spinal canal. In 13 specimens (57%), cement leaked through the fracture line (Fig. 2), and in 20 levels (87%), cement leaked through the vertebral end plate (Fig. 3). The most common type of extravasation classified as severe was through the small vessels surrounding the vertebra where extravasation was apparent in 19 levels (83%). These extravasations were noticed more commonly in the vessels passing through the anterior wall of the vertebra (Figs. 4 and 5). Table 2 summarizes the location of cement extravasation based on the classification system suggested by our observations (Table 1). Comparisons between extravasations as seen from clinical CT examinations, micro-CT imaging, and photographs of the specimen after all soft tissues were removed are provided in Figs. 6 and 7. Wide variability in infiltration and extravasation was observed in the basivertebral region (Fig. 8), with some specimens showing cement at the base of the foramen that did not fill what appeared to be a clear path out of the foramen, with other specimens having cement just reaching or slightly protruding through the posterior border of the foramen and a few specimens with gross extravasation out of the foramen.

Discussion

This study details the filling pattern of bone cement within fracture vertebrae and extravasation out of the

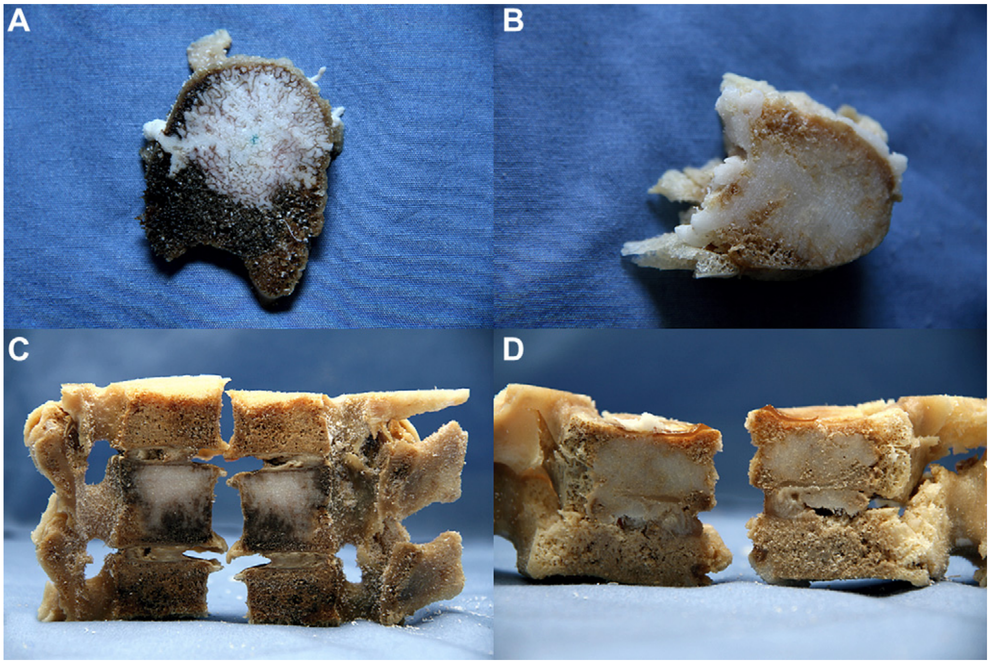

Fig. 1. Photographs of posttreatment vertebra showing filling pattern of cement within the vertebra. (A) and (B) show vertebrae after block sectioning in the axial plane; (C) and (D) show vertebrae after block sectioning in the midsagittal plane. Note the interdigitation of cement through the intervertebral structures (A) and the small extravasations out of the lateral walls.

bodies, using a cadaver-based vertebral compression fracture model. These data enhance our understanding of the vertebral augmentation cement infiltration and extravasation processes. From the CT images and photographs of postaugmentation vertebrae, it is possible to clearly visualize the leakage locations and patterns of cement extravasations. This article is the first step in addressing the hypothesis that an improved understanding of how cement fills vertebral bodies and extravasates out of the vertebral body may help to identify new strategies to improve the efficacy of vertebral augmentation procedures.

Based on the observed patterns of leakage, a cement extravasation classification system is suggested. It is hypothesized that this classification system may prove to relate to the potential clinical significance of each type of extravasation. Extravasation into the spinal canal may be

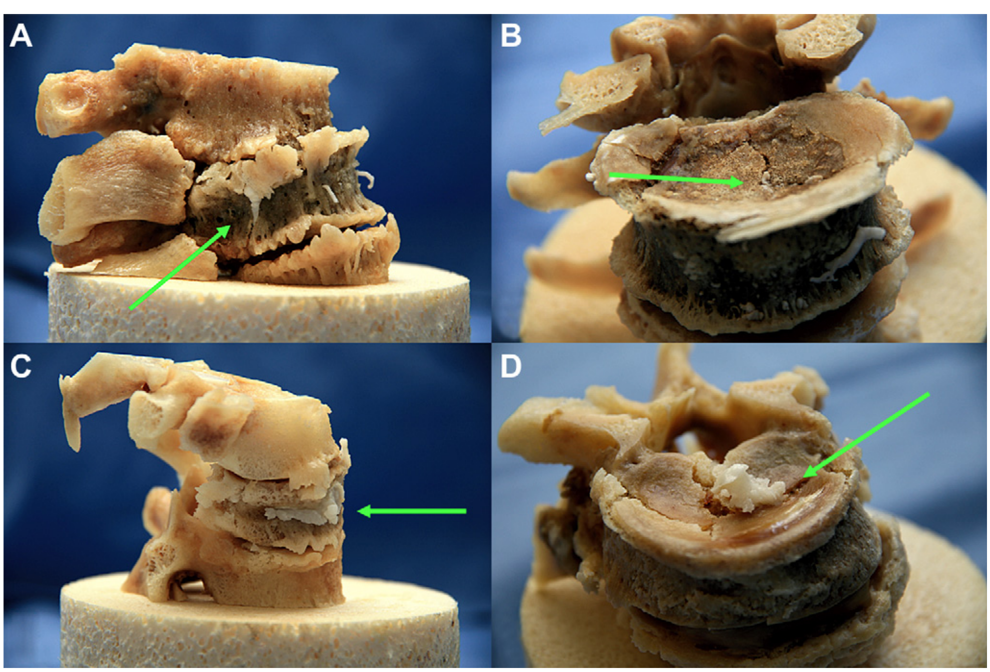

Fig. 2. Cement leakage out of fracture lines (green arrows) in the lateral cortex (A and C) and through the end plates (B and D).

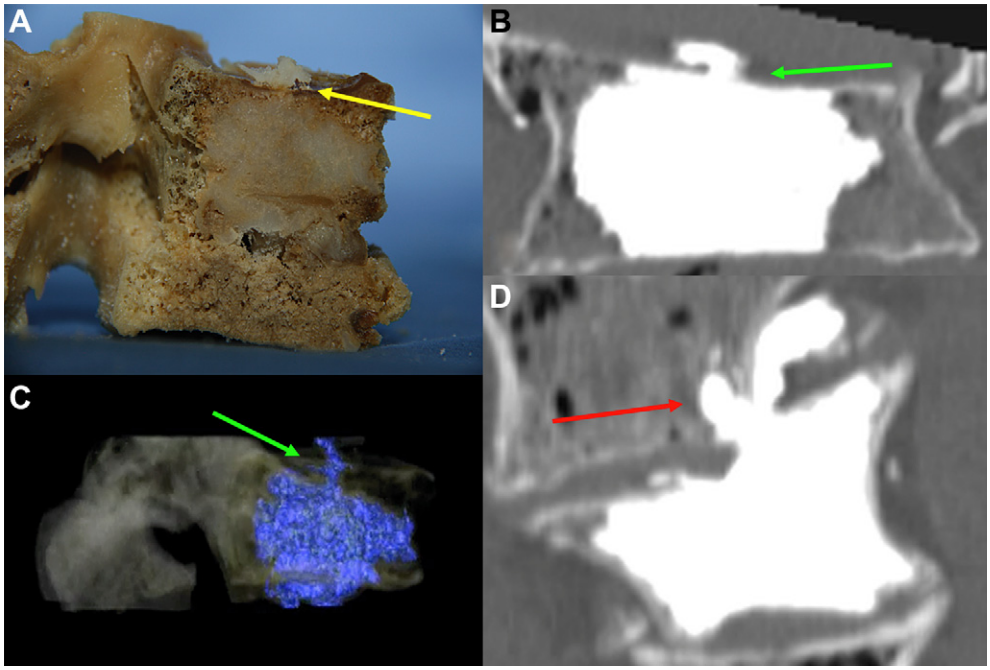

Fig. 3. Cement leakage through the endplates. (A) Photograph of leakage (yellow arrow) through the end plates. (B) Computed tomography (CT) image of leakage into the disc space (green arrow). (C) Three-dimensional reconstruction of cement-filling pattern and leakage (green arrow). (D) CT coronal image of cement leakage through the end plate into the adjacent vertebra (red arrow).

of particular clinical concern. For this reason, most surgeons will stop injecting as the cement is perceived near the posterior vertebral wall. In our study, only 26% of the levels demonstrated cement leakage to the spinal canal, and in most cases, the extravasation was only a small (<1 mm) protrusion of cement outside of the external osseous borders of the vertebral body. However, this frequency of leakage was significantly higher than what was perceived by the surgeons at the time of the augmentation through fluoroscopy, who believed in all cases that they had stopped the injection before any cement had extravasated. These data support that despite the attention currently paid

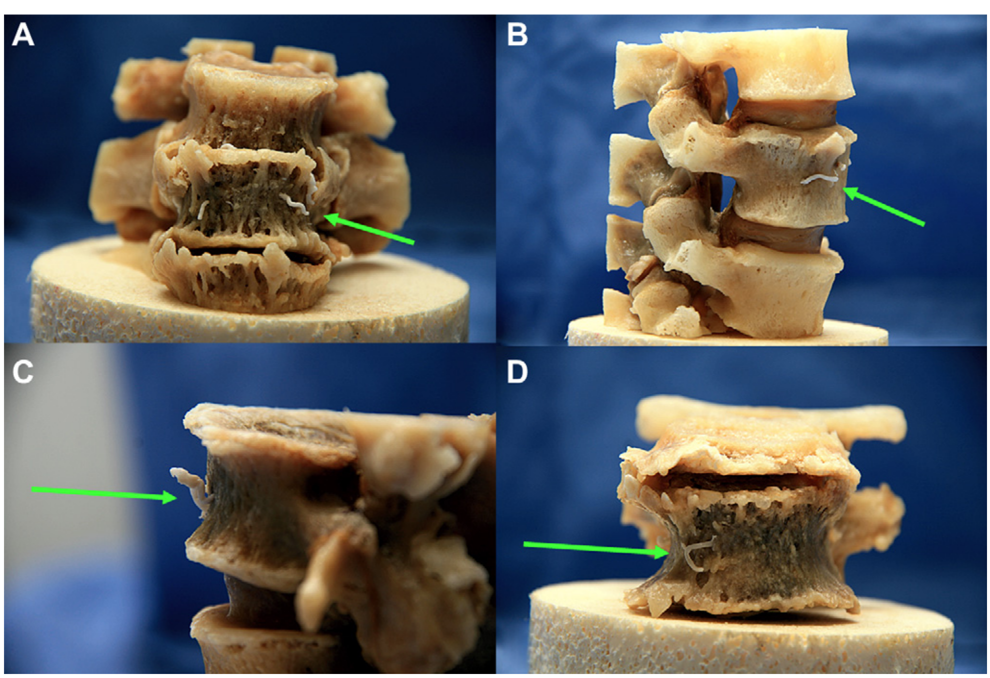

Fig. 4. Cement leakage through small vessels surrounding the vertebra (green arrows).

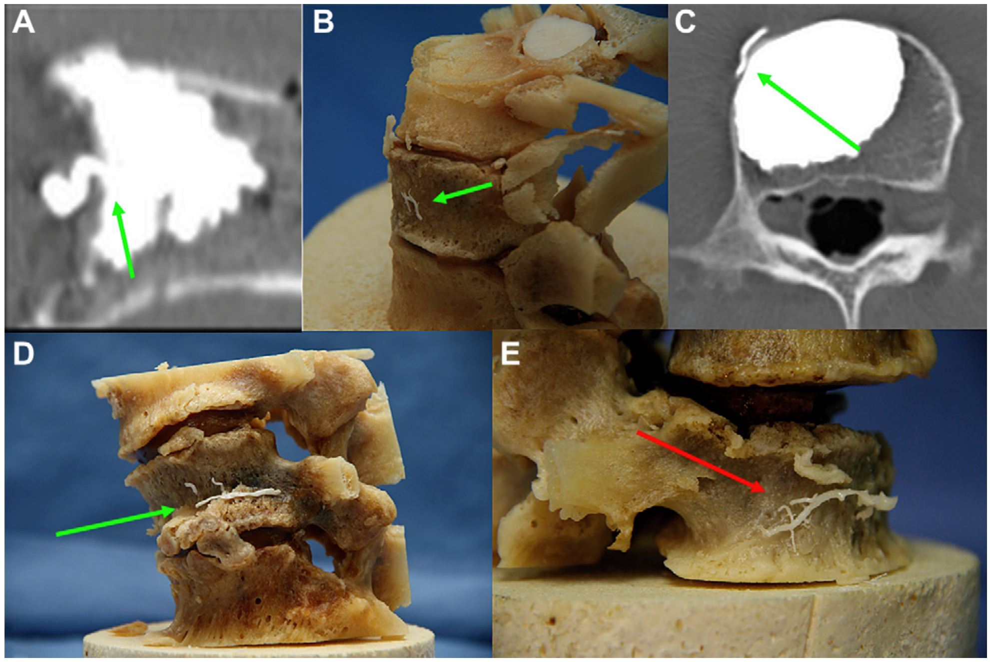

Fig. 5. Computed tomography and still images of cement leakage into the surrounding vessels (green arrows). Note the smaller vessels conjoining the larger vessel filled with extravasated cement (red arrow).

to the posterior vertebral wall, there is still leakage. Nevertheless, this small percentage and the minor nature of the leakage may suggest that the current safety measures are sufficient. Cement extravasation through the end plates was observed in 86% of the levels, most of which was minor. There are insufficient data in the literature to determine if the amount or type of extravasations observed would have any clinical significance.

A clinically rare but life-threatening complication might be cement emboli. The probable mechanism by which cement may reach remote areas of the body, such as the lungs, would be leakage through small vessels around the vertebra. It is known that cement leakage through small vessels can reach remote regions of the body and cause damage. It is likely that this is particularly true if the cement is in a relatively low-viscosity state when it extravasates. In this study, 78% of the levels demonstrated leakage through small vessels (Figs. 4 and 5). These data support the notion that not enough attention is paid to anterior small vessel leakage. It is our opinion that the clinician should monitor all vertebral walls for cement extravasation through the small vessels to avoid possible life-threatening risk to the patient.

As previously noted, there are three categories of factors that may influence cement flow within and out of a vertebral body [18]: (1) bone- and fracture-related parameters; (2) cement properties; (3) injection method. Bone- and fracture-related parameters may play a dominant role in explaining variations between patients; because of the wide range of indications for vertebral augmentation, the procedure is applied to a wide range of bone densities and porosities and a wide range of fracture morphologies. Based on the micro-CT examinations of the present study, the cement appeared to infiltrate the trabecular bone in regions with thick closely spaced trabeculae, the same as in regions with thin

Table 2
Cement extravasation grading

Segment number	A—cortical defect	B—end plate	C—segmental vein	D—canal
1	None	Moderate	None	Severe
2	Moderate	Severe	Moderate	Severe
3	None	Moderate	Severe	None
4	None	None	Severe	None
5	Severe	Severe	None	None
6	Moderate	Severe	Severe	None
7	None	Moderate	Severe	Moderate
8	Severe	Severe	Severe	None
9	None	Severe	Severe	None
10	Moderate	Moderate	Severe	None
11	Severe	Severe	Severe	None
12	None	Severe	Severe	None
13	Severe	Severe	Severe	Severe
14	Severe	Severe	Severe	Moderate
15	None	Severe	None	None
16	Severe	Severe	Severe	Moderate
17	Severe	Severe	Moderate	None
18	Severe	Moderate	Severe	None
19	None	None	Severe	None
20	Moderate	Severe	Severe	None
21	None	None	Moderate	None
22	None	Moderate	Severe	None
23	Severe	Severe	Severe	None
Overall (%)				
None	10/23 (43)	3/23 (13)	4/23 (17)	17/23 (74)
Moderate	4/23 (17)	6/23 (26)	2/23 (9)	3/23 (13)
Severe	9/23 (39)	14/23 (61)	17/23 (74)	3/23 (13)
Total (%)	13/23 (57)	20/23 (87)	19/23 (83)	6/23 (26)

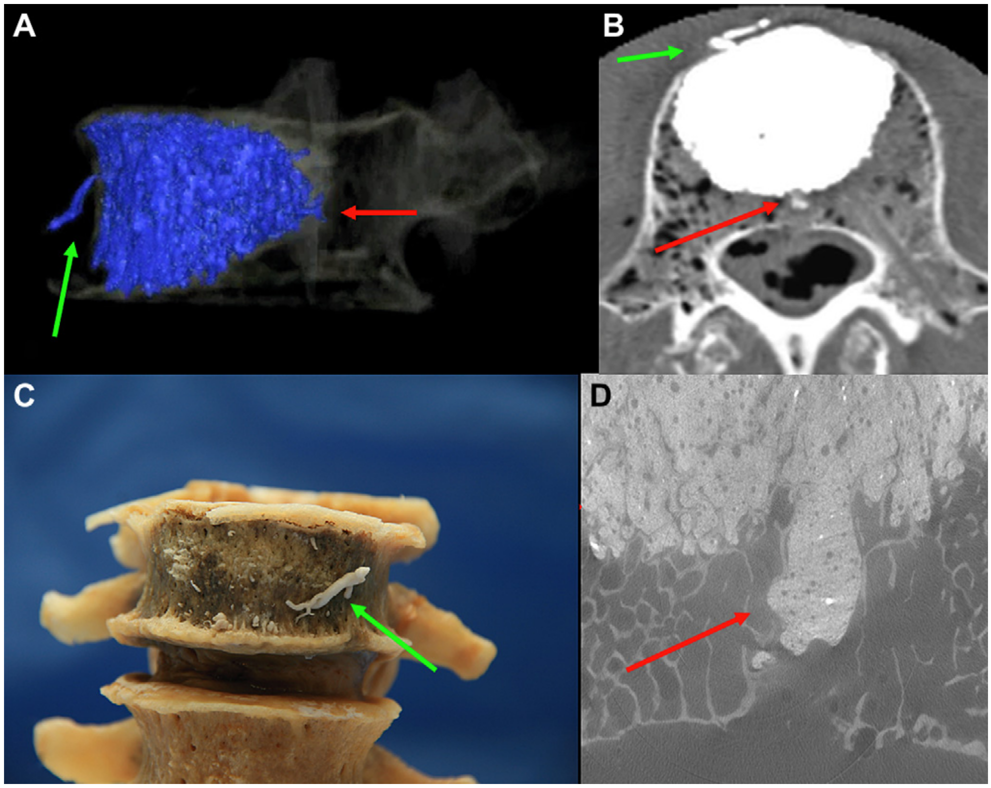

Fig. 6. (A) Computed tomography (CT) three-dimensional reconstruction of cement-filling pattern, (B) axial cut CT, (C) still image, (D) and micro-CT of the same segment. Note the cement leakage to the surrounding vessels (green arrows). The red arrows demonstrate the cement within the basivertebral foramen. Note that the cement did not extravasate out of the foramen (red arrow—D).

sparsely spaced trabeculae. With respect to the cement injection method, simple syringes or high-pressure injectors are well-accepted injection methods. This study used high-pressure injection systems in both groups and, therefore, the study neither helps to understand if alternative injection methods might help to minimize extravasation nor helps to provide nay evidence for the potential efficacy of pressurized vessels, use of curettes, or other technical variations.

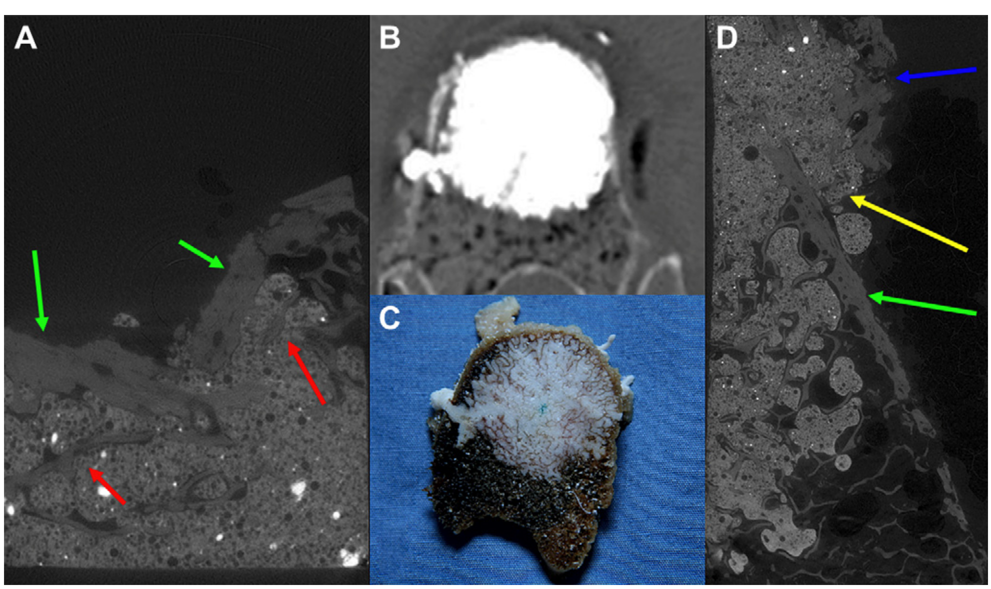

Fig. 7. (A and D) Micro–computed tomography (CT) images, (B) CT axial cut, (C) and still axial cut images of the same segment. (A) Cement interdigitates through broken fragments (red arrows), holding both fragments and cortexes close together (green arrows). (B and C) Note the interdigitation of cement through the trabecular bone and the leakage through the external cortex. (D) Cement leakage (yellow arrow) through a fractured cortex (green and blue arrows). Note the displacement of the fractured cortex (blue arrow) by the cement.

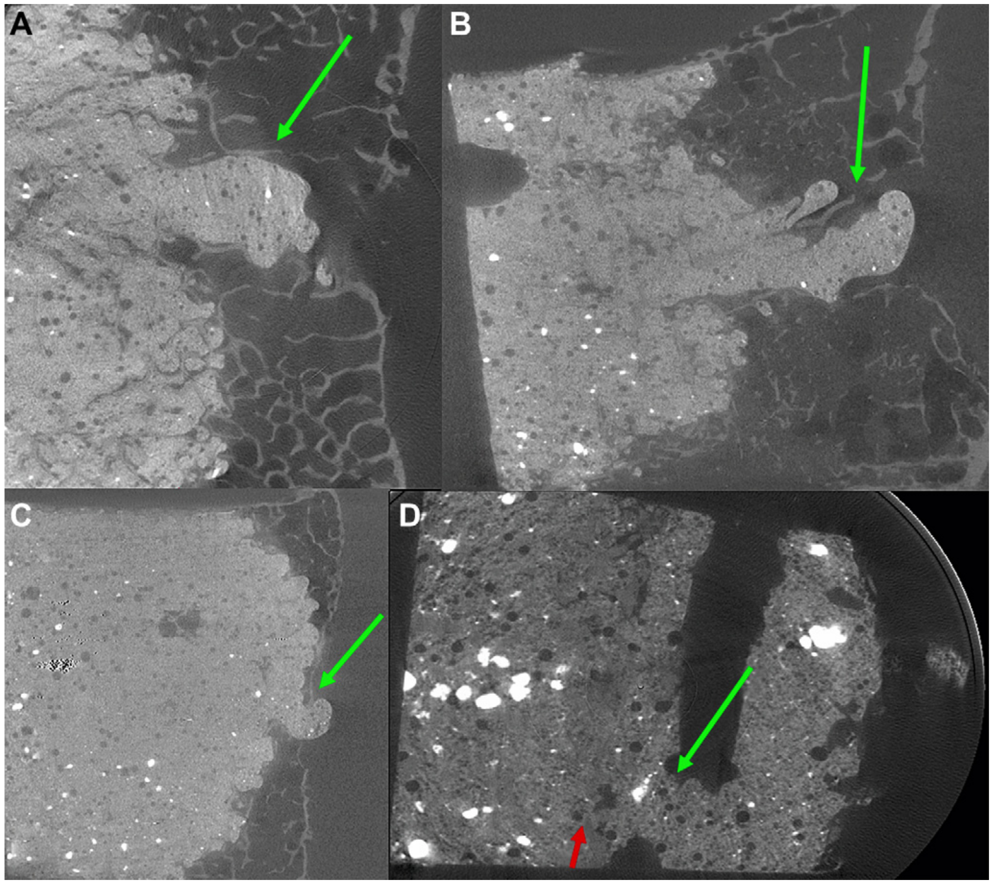

Fig. 8. Micro–computed tomography (CT) images of the basivertebral foramen showing different stages of cement extravasation. (A) Cement within the foramen without extravasating. (B) Cement reaching the edge without protruding. (C) Small amount of cement protruding. (D) Cement leakage through the foramen. Red arrow shows the estimated point of extravasated cement.

The volume of cement inserted to the vertebral body has been shown to correlate with the amount of extravertebral leakage [20]. In the present study, as in clinical practice in the operating suite, the volume of cement was determined by the training and experience of the surgeon and was based on his or her visual assessment of fluoroscopic images during the procedure.

With respect to cement properties, it has been suggested that the cement should spread through the vertebral body in a controlled manner that appears fluoroscopically as a ''uniformly expanding cloud'' and not as ''fingers of a glove,'' which might represent the uncontrolled spread through lower resistance paths in the bone [21]. The viscosity of the cement, which is a measure of the resistance of a fluid to deformation by stress and the resistance to flow, correlates deeply with its leakage potential. The viscosity is represented in SI unit, which is the Pascal second. Pascal second expresses the ratio between the pressure applied to a fluid and the induced shear rate. High-viscosity material means that the fluid is thicker and more resistant to flow, thus requiring greater pressure to be applied to produce a given shear rate. Baroud et al. [21] recently stated that cements with higher viscosity spread more uniformly than cements with lower viscosity, thus, significantly reducing the risk of leakage.

This study does not directly address the clinical consequences of cement leakage, which can vary from no apparent clinical symptoms to severe consequences, such as paraplegia [9,10], spinal cord and nerve root compression [7,10–12], cement pulmonary embolisms [13–16], and possible death [17]. However, by demonstrating and understanding the exact points of extravasation, additional background is available to help understand the complications that might arise.

Similarly, the present study does not directly address the controversial mechanism of how injecting an exothermic cement into a vertebral body might provide the observed analgesic effect. It has been proposed that the mechanical support of fractured vertebrae contributes to the reduction of segmental motion within the damaged vertebra, thus reducing pain [22–25]. Another hypothesis is that the exothermic chemical reaction during polymerization causes thermal destruction of surrounding interosseous nerve fibers [26].

In this study, a cadaver model had been used. Because of the need of complete vertebrae for augmentation, segments of three vertebrae were used. This model preserves the integrity of the middle vertebra. As compared with the alternative model of testing isolated vertebrae, the primary advantage of this model is that fractures were created with loads through intact disc spaces, and the postfracture disc spaces were thereby a closer representation of conditions that exist in clinical applications. The use of the pneumatic device to create the controlled anterior wedge compression fracture allowed the preservation of the posterior vertebral wall in most cases, thus enabling the use of the vertebroplasty surgical method.

This study has several limitations. We did not systematically control for all the variables that might influence cement infiltration and extravasation. This would be a valuable experiment to complete, but given the number of variables that might have a significant effect, and the high likelihood of interaction between variables (eg, needle position and fracture type/location), this experiment would require a very large sample size. The design of a large systematic study to optimize these variables would benefit from the data collected in the present study. The actual correlation of a cadaver to the actual living bone has never, to the best of the authors' knowledge, been validated scientifically in terms of resistance to cement injection and leakage. In living patients, the circulatory system is pressurized; however, the average pressure in the venous system, which is the major small-vessel leakage point, is usually very low. Still the effect of such venous pressure is not demonstrated in the present study. The severity of the compression fractures created by the use of the pneumatic device was not always the same for all vertebrae. In some, a very subtle indication of vertebral fracture was noticed, whereas some were so severely fractured they could not be treated using the vertebroplasty methods (these vertebrae were excluded from the study). Although the cement injection was done by two experienced spinal surgeons, the decision regarding the amount of cement to be injected relied solely on the surgeon's opinion and experience using continuous fluoroscopy (as done in clinical practice). The amount of cement injected may have been more than that typically used by some clinicians. The time of injection process and the reasons for injection termination could not be recorded under this experimental model.

In summary, this study provides new insight into cement infiltration and extravasations. Cement extravasation through the posterior aspect of the vertebra occurred despite stopping the injection before cement was fluoroscopically perceived to be close to this region. Much of the extravasations through the lateral and anterior aspects of the vertebrae were through small vessels, and these extravasations may be difficult to detect fluoroscopically or with thick-section CT examinations. Further study is needed to determine if factors such as needle positioning can help to prevent extravasations. In particular, needle position with respect to fracture lines and foramen may strongly influence extravasations.

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