The biomechanical effectiveness of prophylactic vertebroplasty: a dynamic cadaveric study

Laboratory investigation

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Object. The purpose of the study was to investigate the segmental effects of prophylactic vertebroplasty under increasingly demanding loading conditions and to assess the effect of altered cement properties on the construct biomechanics.

Methods. Twelve human cadaveric 3-vertebral functional spinal units (T12–L2) were prepared such that the intact L-1 vertebra was prophylactically augmented with cements of differing elastic moduli (100, 50, 25, and 12.5% modulus of the base cement). These specimens were subjected to quasistatic subfailure compression pre- and postaugmentation to 50% of the predicted failure strength and then cyclic loading in a fatigue rig (115,000 cycles) to characterize the high-stress, short-cycle fatigue properties of the construct. Loading was increased incrementally in proportion to body weight to a maximum of 3.5 × body weight. Quantitative computed tomography assessment was conducted pre- and postaugmentation and following cyclic testing to assess vertebral condition, cement placement, and fracture classification.

Results. Adjacent and periaugmentation fractures were induced in the prophylactically augmented segments. However, it appeared that these fractures mainly occurred when the specimens were subjected to loads beyond those that may commonly occur during most normal physiological activities.

Conclusions. Lowering the elastic modulus of the cement appeared to have no significant effect on the frequency or severity of the induced fracture within the vertebral segment. (DOI: 10.3171/SPI/2008/8/5/442)

KEY WORDS • osteoporosis • percutaneous vertebroplasty • vertebral compression fracture

The pathogenesis of osteoporosis has been well documented and is characterized by abnormal homeostasis between bone deposition and resorption. One of the recognized complications is VCF within the spinal column, which may lead to pain and progressive deformity for the individual. The current load on the health service provision in treating these fractures is significant, with direct socioeconomic annual costs estimated at $440 million and $750 million (US dollars) in the European Union and the US, respectively. Initially, conservative treatment strategies are often implemented, including a period of bed rest and analgesic medication together with pharmacological treatments for osteoporosis that may reduce the risk of further fracture. However, for a significant proportion of patients these interventions may be ineffective, and surgical options may then be considered to reduce pain and prevent or correct deformity. The scope for open invasive therapies, however, is often limited by the fragile nature of osteoporotic bone and the anesthetic risk to the patient.

The minimally invasive procedure of PVP was initially performed by Galibert et al. in 1987 for the prophylactic treatment of a vertebra that was at risk for fracture secondary to a hemangioma. Over the past decade, PVP has been adopted as a recognized treatment for painful osteoporotic vertebral compression fractures and involves the injection of cement into the VB with the aim of offering stabilization and structural support to the fracture site. Retrospective and short-term prospective outcomes have been almost universally good, with rapid reduction in pain.

Abbreviations used in this paper: BMD = bone mineral density; CMC = carboxymethylcellulose; CT = computed tomography; PMMA = polymethylmethacrylate; PVP = percutaneous vertebroplasty; SD = standard deviation; VB = vertebral body; VCF = vertebral compression fracture.
within 1–2 days following intervention. There is, however, a risk of cement extravasation (30–67%) that could lead to cement embolism or spinal cord compression in a small proportion of patients. Evidence has also emerged that suggests there may be an associated risk of accelerated adjacent VB failure in patients who have undergone PVP augmentation. These complications have the potential to limit the procedure to the most pressing cases, and with an increase in the prevalence of osteoporotic vertebral fractures due to a growing elderly population, there is a need to optimize the vertebroplasty procedure and develop preventative strategies for this patient population.

One strategy recently proposed is the prophylactic reinforcement of the VB by using minimal quantities of cement to improve failure strength while simultaneously minimizing the complication rate. The hypothetical advantages of prophylactic PVP are associated with the retention of the original VB height, and thus spinal alignment, while the kyphotic angle is maintained. This ensures that the flexion moment is not increased as is the case following the development of a VCF. This increased moment is thought to be a factor in the fracture of the vertebra adjacent to an augmented one in which the kyphotic angle has not been restored. Current biomechanical knowledge of prophylactic vertebroplasty, however, is limited mainly to static testing of a single vertebra and finite element analysis and there is now a growing need to elucidate the dynamic mechanical behavior of prophylactic augmentation and the subsequent segmental effects before its clinical use can be recommended.

The mechanical properties of the bone cement used in the vertebroplasty procedure are thought to play a key role in the clinical outcome of the treatment. Vertebral augmentation with a conventional PMMA bone cement of high elastic modulus may transfer a greater proportion of the load through the central augmented trabecular structure than would occur naturally. This results in an altered load distribution in which the pillar of cement in the VB causes a reduced deflection in the neighboring endplate, but an exaggerated deformation of the endplate in the adjacent VB which may contribute to an accelerated rate of fracture. These current limitations in the vertebroplasty procedure may also extend to its use in a prophylactic treatment regimen, and may require further optimization of current cements such that regional spine biomechanics are not altered in a manner that increases the risk of adjacent fracture. The purpose of this study was to assess the behavior of prophylactic PVP in a 3–vertebral segment unit using both static and dynamic simulations with particular analysis of adjacent VB failure. In addition, the vertebroplasty cement modulus was modified to investigate its biomechanical effects as part of a prophylactic treatment scenario.

Materials and Methods

Preparation of Cadaveric Specimens

The experimental protocol followed the flow diagram outlined in Fig. 1. Twelve spines were harvested from 6 male and 6 female cadavers (mean age at death 72.4 ± 13.6 years [± SD]). The specimens were acquired from the Leeds Tissue Bank (Leeds General Infirmary) with ethics committee approval (Leeds East Research Ethics Committee, St. James University Hospital, Leeds [06/Q1206/149]).

All specimens underwent gross examination and plain lateral radiography to exclude previous fracture (1 exposure, 70 kV). Each of the 12 spines was dissected free of soft-tissue attachments. Three-vertebral segment units were prepared by disarticulation at the cranial T11–12 intervertebral disc and the caudal intervertebral disc of L2–3. Care was taken to preserve all major ligaments including the capsular attachments of the zygapophysial joints. Posterior elements were retained in all specimens, and the integrity of the spinal canal was not compromized.

The VB dimensions were obtained using digital calipers accurate to 0.01 mm (Mitutoyo MTI Corp.). A rod was passed through the spinal canal of the segmental units and clamped against the anterior margin to maintain sagittal and coronal alignment and also as a reference point from which to locate the dimensions of the superior endplate of the cranial VB (T-12). The cranial T-12 endplate and caudal L-2 endplate were then secured within simulator fixtures by using PMMA bone cement, with the load axis located in the mid-point of the T-12 VB. The segmental units were wrapped in saline-soaked gauze, sealed in plastic bags, and stored at −20°C until 24 hours prior to the day of augmentation and testing, at which time they were thawed at room temperature (20°C). The specimens were then assigned to 1 of 4 groups in which cement of different moduli was injected into the middle vertebra. Initial quantitative CT scans (PQ 2000, Picker) with the aid of image transfer software (e-film version 1.5.3) were obtained in all 3–vertebral segment units. Spatial resolution was set at 2 mm (65 mA, 140 kV). The largest circular region of interest of trabecular bone taken from the middle of the L-1 vertebra was selected from which an average Hounsfield Unit of bone cement was derived from previous experiments. In which a viscous solution was added to PMMA cement. Initial laboratory experiments confirmed the elastic modulus of Vertebralplastic cement (DePuy CMW) by axial compression in a material testing
machine (AGS-10kNG, Shimadzu Corp.) at 5 mm/minute, with measurements defined according to International Organization for Standardization (ISO) 5833. Subsequent modification of the mechanical properties of Vertebroplastic cement was performed by dissolving CMC in sterile water to form a 7% aqueous solution, which was then added to the cement formulation in incremental quantities (wt/wt). The following 4 groups of modified Vertebroplastic/CMC were chosen: the unmodified cement (100%) and formulations of cement such that the moduli were 50, 25, and 12.5% of the original modulus value (Fig. 2).

Vertebroplasty Procedure

Augmentation of the L-1 VBs was achieved using a unilateral transpedicular approach with a 13-gauge bone biopsy needle advanced to the anterior third of the VB. Modified vertebroplastic cement was mixed following the manufacturer’s recommendations and injected using a V-Max cement delivery system (DePuy CMW). The defined end point of the procedure was an estimated 20% volume fill based on the gross dimensions (height × endplate surface area) obtained from the quantitative CT images. All augmented vertebrae were wrapped in saline-soaked gauze, placed in sealed plastic bags, and floated in a water bath at 37°C for 24 hours to simulate physiological conditions and to allow adequate time for cement curing. The quantitative CT scans were then obtained to evaluate cement placement.

Mechanical Testing

All specimens underwent repeated quasi-static loading before and after augmentation to characterize the stiffness of the segment. The 3–vertebral segment unit was placed between 2 custom-made steel endplates, constrained to prevent lateral translation, and inserted into the materials testing machine attached to a personal computer running a compression program (version 1.84, R.D.P. Howden, Ltd.) to control the experimental conditions. A steel ball was placed between an indentation in the upper endplate and the cross-head of the machine such that load was applied at a single point through the central axis of the specimen. Compression was applied in stroke control at 1 mm/minute with force and displacement data recorded at 10 Hz. The test was terminated at 50% of the predicted failure load of L-1 for each 3–vertebral segment unit. Prediction of failure load was determined using quantitative CT images by the previously described method in which a high level of correlation was observed between the actual failure load and the product of caudal endplate area and BMD for nonaugmented vertebrae. The stiffness of the 3-VB construct was defined as the gradient of the load-displacement curve over a 0.6-mm section ending at 50% of the predicted failure load. This criterion was used because this region was repeatedly found to be the most linear.

Following augmentation, all 12 specimens underwent dynamic compression at 1 Hz in a fatigue rig (Simulation Solutions, Ltd.) (Fig. 3). The segmental units were subjected to an incremental cyclic loading regimen proportional to the body weight of the cadaver: 80,000 cycles from 1 × to 2 × body weight; 15,000 cycles from 1.25 × to 2.5 × body weight; 10,000 cycles from 1.5 × to 3 × body weight; and 10,000 cycles from 1.75 × to 3.5 × body weight. Force-displacement data were collected for every 100th cycle, and the stiffness of the segment was derived from the complete loading protocol. The quantitative CT scans were obtained postsimulation to assess the vertebrae for periaugmentation and adjacent fractures. The fracture was described using the classification for thoracic and lumbar injuries.

Results

No significant difference was found in the stiffness of the 3–vertebral segment unit pre- or postaugmentation (t = 0.0048, p = 0.987; paired t-test) (Fig. 4). The 12 T12–L2 specimens were successfully loaded to within 95% of the required demand profile at the maximum and minimum loads. Linear displacement plots for each modulus of cement (Fig. 5) indicated that in 10 of the specimens there was little evidence of adjacent or periaugmentation fracture within the first 80,000 cycles of testing at 1–2 × body weight. However, two 3–vertebral segment units (25% E: Specimen 2 and 12.5% E: Specimen 2 [where E denotes the elastic modulus]) exhibited a sharp increase in subsidence within the first 7000 cycles. These were subsequently shown to have fractures at all 3 levels (Table 1). Three
additional 3–vertebral segment units (100% E: Specimen 2, 50% E: Specimen 2, 25% E: Specimen 3) demonstrated a rapid decrease in overall height following the application of more demanding load profiles, corresponding to adjacent or periaugmentation fractures and an average linear displacement at the test termination of 17.1 ± 5.2 mm. An additional two 3–vertebral segment units showed step changes in behavior midway through loading: Specimen 1 (50% E) during 1.5–3 × body weight loading, and Specimen 1 (12.5% E) during 1.25–2.5 × body weight loading. These specimens were found to have an L-2 adjacent fracture and an L-1 periaugmentation fracture, respectively, with an average linear displacement of 17.9 ± 4.9 mm at the end of testing. In those specimens that had no evidence of fracture, the average linear displacement at the termination of testing was 9.9 ± 1.9 mm.

During testing, all 3–vertebral segment units demonstrated a reduction in the overall segment height and a corresponding increase in stiffness (Pearson r = 0.88–0.99). Predicted failure strength of the L-1 vertebra gave a poor correlation with the level of subsidence measured at the end of testing (Spearman r = −0.40, p = 0.20). A poor correlation was also noted between BMD and subsidence (Spearman r = −0.24, p = 0.45). Altering the modulus of cement was found to have a poor correlation with the reduction in overall segment height (Spearman r = 0.09, p = 0.79).

The fracture severity characterized from quantitative CT images postsimulation is shown in Table 1. A typical fracture pattern (postaugmentation and postsimulation) can be seen in Fig. 6. Twelve fractures were observed in 7 specimens (7 were split and 5 were compression fractures). Analysis of quantitative CT data showed that 5 of the fractures occurred in the L-1 VB around the cement augmentation and vertebral endplate and 7 fractures were located in the adjacent VBs (3 T-12 fractures and 4 L-2 fractures). There was a strong positive correlation observed between fracture severity and subsidence at the end of the loading regimen (Spearman r = 0.77, p = 0.004).

A poor correlation was found between the fracture severity and the predicted failure load (Spearman r = −0.10, p = 0.75) and cement modulus (Spearman r = 0.15, p = 0.62). Quantitative CT images used to quantify measurements of disc height before and after simulation revealed an average total disc height loss of 7.9 ± 1.2 mm (± SD).

**Discussion**

Prophylactic vertebroplasty is currently not a recommended therapy for patients with osteoporosis who are at risk of developing a compression fracture; however, its use has been documented in tumors of the VB. Due to the demographic shifts occurring in western populations, there is now a growing interest in developing vertebroplasty as a preventative treatment, with the underlying aim of strengthening the vertebrae at risk of fracture and hence preventing pain, deformity, and possible neurological deficit. Initial investigations have demonstrated that cement augmentation in prophylactic PVP increases the failure strength of intact osteoporotic vertebrae over the predicted failure load and restores vertebral stiffness. However, further biomechanical testing and preclinical trials are required prior to clinical recommendation. The objectives of this study were 2-fold: 1) to examine the effects of prophylactic vertebroplasty on a 3–vertebral segment unit, and 2) to assess the effect of altering the mechanical properties of the cement used in vertebroplasty.

There have been several experimental studies in which the authors have used multilevel spinal units in vertebro-
Although few appear to have investigated the segmental effects of prophylactic vertebral augmentation under cyclic loading,\(^\text{17}\) it is possible to envisage prophylactic vertebroplasty being indicated in active patients with osteoporosis and in patients with a history of a compression fracture; hence, the dynamic loading protocol in this study was designed to represent various activity demands for this cohort. Loads representing normal physiological motion did not appear to induce fracture in the majority of specimens tested, a finding that concurs with previous studies that found only small amounts of height loss within the first 80,000 cycles of loading.\(^\text{47}\) Here, prophylactic augmentation may act to stabilize the treated VB and does not appear to adversely affect the construct biomechanics. Early fracture in 2 specimens (25% E: Specimen 2 and 12.5% E: Specimen 2) may have been initiated by microfractures and regional weaknesses that were present in the adjacent vertebrae prior to testing. However, these were not detectable with the quantitative CT scan resolution available, and the BMD values for these vertebrae, as well as the cement volume and distribution, were normal within the data set.

Incremental increases in applied load, which were used to represent more strenuous physical activity, showed progressive levels of subsidence that could be characterized into the following 3 groups: 1) sudden and large height loss at the start of the loading regimen; 2) step changes in subsidence during a loading cycle; and 3) small decreases in segmental height at the start of a loading regimen followed by a steady state of subsidence.

Specimens with sudden or step changes in height loss were confirmed to have either adjacent or periaugmentation fractures or both, with a strong positive correlation between subsidence at the end of testing and fracture severity. There was no evidence of fracture in the specimens that demonstrated a small but continuous state of subsidence throughout the entire loading profile. The absence of correlation between the height loss of the 3–vertebral segment unit and BMD or the predicted failure load suggests that, under more demanding activities, prophylactic augmentation may not act to prevent fracture in the augmented VB and that adjacent fractures may also be induced due to an altered load distribution within the segment. Huber et al.,\(^\text{17}\) however, suggested that prophylactic treatment of a VB did appear to prevent fracture during dynamic loading, al-

### TABLE 1

<table>
<thead>
<tr>
<th>Specimen No.†</th>
<th>T-12</th>
<th>L-1</th>
<th>L-2</th>
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<tr>
<td>100% E cement</td>
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<tr>
<td>1</td>
<td>—</td>
<td>—</td>
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<td>2</td>
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<td>A2.2</td>
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</tr>
<tr>
<td>3</td>
<td>—</td>
<td>—</td>
<td>A1.2.3</td>
</tr>
</tbody>
</table>

| 50% E cement   |      |     |     |
| 1              | —    | —   | —   |
| 2              | —    | A2.3| —   |
| 3              | —    | —   | —   |

| 25% E cement   |      |     |     |
| 1              | —    | —   | —   |
| 2              | A2.3 | A2.3| A1.2.1 |
| 3              | A1.2.3 | — | — |

| 12.5% E cement |      |     |     |
| 1              | —    | A2.2| —   |
| 2              | A1.2.1 | A2.2| A1.1 |
| 3              | —    | —   | —   |

* — = not applicable.
† The E denotes elastic modulus.
‡ Fracture classification according to the scheme of Magerl et al. Impaction fractures are classified as A1. Further definitions: A1.1 = endplate impaction; A1.2 = wedge impaction fracture; A1.2.1 = superior wedge impaction fracture; A1.2.2 = lateral wedge impaction fracture; A1.2.3 = inferior wedge impaction fracture; A1.3 = VB collapse. Split fractures are classified as A2. Further definitions: A2.1 = sagittal split fracture; A2.2 = coronal split fracture; A2.3 = pincer fracture.

Fig. 5. Linear displacement plots for the modulus of cement tested: 100% (A), 50% (B), 25% (C), and 12.5% (D) E cement. BW = body weight.
though fractures in this study were generated when higher loads (approaching 1500 N) were introduced, which represents \(2\text{–}3 \times \) body weight in an elderly population.

Previous studies have postulated that cement with a lower modulus may reduce the change in load distribution through the spinal unit and hence reduce the risk of adjacent VB failure.\(^{1,44}\) In this study, however, reducing the elastic modulus of conventional PMMA cement with various ratios of CMC gel appeared to have no significant effect on the construct biomechanics. In all categories of modified cement that we tested, the quasistatic stiffness of the specimens did not significantly change after augmentation, indicating that cement augmentation may not have a deleterious effect on the load-carrying behavior of the intervertebral discs. During cyclic loading, the different types of cement were found to have no significant correlation with either the fracture severity or the level of subsidence observed throughout the incremental loading regimen. This is in agreement with previous finite element studies, which found that reducing the elastic modulus of the cement had no significant effect on the incidence of adjacent vertebral failure.\(^{43}\) If a modified material is to be a viable solution for improving the vertebroplasty procedure, further studies are required to reduce the elastic modulus while the other existing properties of these injectable cements (for instance compressive strength, toughness, and flow properties) are maintained.\(^{24}\) Recently developed calcium phosphate cements have also been proposed as an alternative to PMMA, as they are biocompatible, injectable, and have a nonexothermic curing phase. Their osteoconductive effects may be limited in patients with osteoporosis, however, as bone turnover is degraded, and instability, secondary to biodegradation, is a possible hazard if support of the anterior column is not maintained.\(^{39}\) In addition, there are concerns with the mechanical robustness of these current cements. In particular, previous studies have shown that the failure loads in calcium phosphate–augmented constructs are not as high as those observed for PMMA-injected vertebrae.\(^{16,26}\) Wilke et al.\(^{47}\) also showed that there may be evidence of inferior fatigue performance of calcium phosphate cement within augmented VBs.

The use of a dynamic loading profile to represent activity over a longer period of time than static compressive loading protocols with multilevel segments\(^{3,34,48}\) presents a significant challenge in analyzing and interpreting data from these tests due to the complex temporal aspects of the outcome measures. Previous dynamic studies on multilevel segments have either prefilled the adjacent vertebrae\(^{21,47}\) or encased the adjacent levels to restrict motion,\(^{17}\) which may reduce the fracture threshold of the treated vertebrae.\(^{3,34}\) Leaving the adjacent VBs untreated, however, is more representative of the segmental effects of prophylactic PVP in vivo but could obscure results of the treated vertebrae.\(^{47}\) This study has also demonstrated that the actual loading profile plays a dominant role in determining the outcome of prophylactic vertebroplasty. Different vertebroplasty studies have implemented different loading regimens with varying outcomes.\(^{15,17,21,28,47}\) Consideration is required in designing future studies with dynamic simulations that represent the physiological situation and load demands that are applied in vivo.

This biomechanical evaluation has limitations that are common in most in vitro cadaveric studies, such as a limited number of specimens, significant quality variations in the biological tissue, and the inability to study long-term treatment effects due to degradation and the associated effects on the biomechanical behavior of specimens.\(^{46}\) In addition, the application of a single axial compressive load used in this investigation does not completely address how progressive vertebral collapse occurs in vivo, although it does allow a meaningful comparison to be made between study groups. Augmented vertebrae will be subjected to a complex spectrum of spinal loads, which are dependent on patient-related factors and lifestyle, and further biomechanical studies and clinical trials are now required to evaluate the potential role of these mechanical challenges in the outcomes of the interventions.

Conclusions

This work begins to elucidate the mechanical nature of vertebroplasty as a preventative treatment for vertebral compression fractures in osteoporotic bone. In particular, it starts to develop an understanding of the segmental effects
of prophylactic vertebroplasty under a dynamic load simulation, which is an important step toward developing an efficacious treatment suitable for clinical evaluation and in defining the risks and benefits for this procedure. In the majority of cases, there was no evidence of adjacent or periaugmentation fractures under loads representing normal physiological activities, although more demanding loading conditions appeared to induce fractures. Lowering the elastic modulus of the cement appeared to have no significant effect on the frequency or severity of the induced fracture within the vertebral segment. Research is now required to allow us to discern the importance of the cement properties on the stabilization of the vertebral construct and to assess the use of prophylactic vertebroplasty adjacent to a vertebra that has already been fractured and augmented with cement.

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