# Percutaneous Vertebral Augmentation

D Togawa, M Kayanja, I Lieberman

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## Abstract

Over 700,000 osteoporotic compression fractures occur each year in the United States. These vertebral fractures are associated with significant morbidity and mortality and represent a tremendous personal and societal burden. Percutaneous vertebroplasty (PVP) involves the injection of polymethylmethacrylate to strengthen a vertebra. This minimally invasive method, which has been adopted by practitioners since 1980s to treat symptomatic compression fracture is reported to provide quick pain relief in 90% of patients, with only infrequent, mostly minor complications. Kyphoplasty (KP) is an extension of PVP that uses an inflatable bone tamp to restore the vertebral body toward its original height while creating a cavity to be filled with bone cement. Reported results indicate that KP is a safe procedure associated with a lower risk of cement leak that not only yields quick pain relief, like PVP, but also restores vertebral height, potentially decreasing kyphosis and improving pulmonary mechanics as well.

## VERTEBRAL AUGMENTATION PERCUTANEOUS VERTEBROPLASTY BACKGROUND

Percutaneous vertebral augmentation (vertebroplasty, PVP) was first reported by Galibert et al in 1984 and initially involved the augmentation of the vertebral body with PMMA to treat a hemangioma [1] . Percutaneous vertebroplasty was reportedly not performed in the United States until 1993 [2] . Originally targeted for osteolytic metastasis, myeloma, and hemangioma, PVP resulted in early appreciable pain relief and a low complication rate [1, 3] . Its indications subsequently expanded to osteoporotic vertebral collapse with chronic pain, further to include treatment of asymptomatic vertebral collapse and even prophylactic intervention for at-risk vertebral bodies [4] . Nevertheless, the treatment of acute fractures in ambulatory patients and prophylactic treatment remains controversial [5] . In fact, vertebral augmentation itself is somewhat controversial, with questions concerning a lack of defined indications, expected complications, outcome measures, and the need for long-term follow-up data [6] .

An open question in PVP is the mechanism of pain relief. The most intuitive explanation involves simple mechanical stabilization of the fracture. However, another possibility is the analgesic result from local chemical, vascular, or thermal effects of PMMA on nerve endings in surrounding tissue [7, 8] . Supporting this concept is the lack of correlation between cement volume and pain relief [9, 10] . Further evidence against an effect resulting solely from mechanical stabilization is the fact that PVP typically does not restore lost vertebral body height and therefore does not correct altered biomechanics [5, 11] .

## TECHNIQUE

Injection of opacified PMMA is performed via a transpedicular or paravertebral approach under continuous fluoroscopic guidance to obtain adequate filling and to avoid PMMA leakage. For complex or high-risk cases, CT and fluoroscopic guidance are sometimes combined [5, 12] . In routine cases, PVP can be performed under local anesthesia with slight sedation in less than an hour, [1] although general anesthesia is sometimes required because pain may intensify during cement injection [7] . Preceding PMMA injection, intraosseous venography is often used to determine the filling pattern and identify sites of potential PMMA leakage (outline the venous drainage pattern, confirm needle

placement within the bony trabeculae, and delineate fractures in the bony cortex). However, others have dispensed with routine venography [11].

Contraindications to vertebroplasty include; coagulopathy, absence of facilities to perform emergency decompressive surgery in the event of a complication, and extreme vertebral collapse (>65% to 70% reduction in vertebral height) [7].

## RESULTS

From 1985 to January 2005, there were 407 paper related to vertebroplasty published in peer reviewed journals. Vertebroplasty data from over 1,000 patients have been reported in several case series [3, 5, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. The longest reported follow-up is three years, although the first paper on vertebroplasty was published in 1987. Reportedly, pain has been reduced in 70%-90% of patients. There have been no reported cement failures, and only two reported cases of fracture progression in the treated vertebral bodies (caused by inadequate cement fill). Barr et al. reported the results of 47 patients treated with vertebroplasty with an average follow up of 18 months [5]. The report outlines marked to complete pain relief in only 63% of patients with osteoporotic vertebral compression fractures.

Vertebroplasty, however, does not address the spinal deformity. Also, this technique requires a forcefull cement injection using low viscosity cement thus increasing the risk of cement leaks through the fracture clefts or the venous sinuses. Evans et al. reported their retrospective results of 245 cases with an average follow-up of 7 months. In this study pain score was significantly decreased and the ability to perform activities of daily living was significantly improved following vertebroplasty [17]. Alvarez et al. determined the factors affecting the outcome of PVP through a retrospective review of 260 cases . Their results showed that the presence of two or less symptomatic vertebrae (p<0.03), the American Society of Anesthesiologists status I (p<0.001), the presence of signal changes on magnetic resonance images (p<0.001, highest odds ratio), and the collapse of the vertebral body less than 70% (p<0.001) are the predictable factors for favorable post-operative outcome. These results suggest that appropriate patient selection is essential for achieving clinical success.

## COMPLICATIONS

The principal risk of PVP, which involves the forced injection of low-viscosity PMMA cement into the closed space of the collapsed vertebral body, is cement extravasation. Extravasation rates are as high as 65% when used to treat osteoporotic fractures [3, 19]. The likelihood is greater when using cement with a liquid rather than paste consistency, or with higher PMMA volume [16]. However, in most settings, the majority of extravasations have no clinical relevance, at least in the short term [11].

The consequence of an extravasation depends on its location. In epidural or foraminal extravasation, nerve root compression and radiculopathy is the major risk. This occurred in 11 of 274 patients (4%) treated by Deramond [12]. Three of those patients required surgical nerve root decompression. Others have been described a 5 % rate of radiculopathy as well [9, 26]. Extravasation into perivertebral veins can cause cement embolism to the lungs; deaths attributed to cement embolism have been documented. However, 2 reported deaths attributed to pulmonary embolism were felt to be unrelated to the procedure; no cement material was detected by chest x-ray of the first patient [7, 27], and the second pulmonary embolism arose from deep venous lower extremity thrombosis [12]. On the other hand, extravasation into adjacent disks or paravertebral tissue, although common, generally produces no patient symptoms and carries little clinical significance; many such extravasations can be avoided by careful needle positioning [12].

Other operative and long-term complications of PVP are specific to PMMA as a filler [4, 11, 28]. The physician may work with PMMA in large batches in order to keep it liquid and to extend the working time for vertebroplasty. However, its high polymerization temperature (86°C to 107°C within cement core) can damage adjacent tissue, including the spinal cord and nerve roots [29], leading to an inflammatory reaction and transitory exacerbation of pain [7]. When injecting PMMA monomer, physician vigilance and caution is required. Absorption of PMMA monomer during the injection can induce hypotension by virtue of its cardiotoxic and arrythmogenic properties . Keeping in mind that placing a material in the spine affords proximity and access to the chest and the heart, vertebral augmentation with PMMA demands meticulous attention to technique.

Overall, the risk of complications that carry clinical significance following PVP for osteoporotic vertebral fracture is felt to be 1% to 3%, and most potential complications can be avoided with good technique [12].

## KYPHOPLASTY
## BACKGROUND

Kyphoplasty is an advanced surgical technique having evolved from a marriage of vertebroplasty with balloon angioplasty. It has a number of potential advantages, including lower risk of cement extravasation and better restoration of vertebral body height. A cannula is introduced into the vertebral body, via a transpedicular or extrapedicular route, followed by insertion of an inflatable bone tamp, which when deployed, reduces the compression fracture and restores the vertebral body toward its original height. This then creates a cavity to be filled with bone cement. The cement augmentation can now be completed with more control into the low-pressure environment of the preformed cavity with viscous, partially cured cement. Using a cannula for bone filler with a steel stylet as a plunger enables the operator to apply cement at considerably higher viscosity than is possible with injection through a 5-cc syringe and 11 gauge needle. Both the higher cement viscosity and controlled fill reduce the risk of cement extravasation. Filling is performed under continuous lateral fluoroscopic guidance similar to vertebroplasty. The procedure can be performed under general anesthesia or local with intravenous sedation; most of the patients are able to return home the same day of procedure.

## TECHNIQUE

With the patient under general or local anesthesia in prone position on a radiolucent spinal frame, two C-arms are positioned for antero-posterior and lateral fluoroscopic images. Once positioned the C-arms or patient are not moved to ensure repeatable images throughout the case. Two 3-mm incisions are made at the vertebral level, parallel to the pedicles in both planes. Then a guide wire or biopsy needle is advanced into the vertebral body via a transpedicular or extrapedicular approach, depending on fracture configuration and patient's anatomy. The guide wire is then exchanged for the working cannula using a series of obturators. Once the working cannula is positioned the surgeon reams out a corridor to accommodate the inflatable bone tamp (IBT) and positions IBT under the collapsed endplate. To deploy the IBT, inflation proceeds slowly under fluoroscopy until maximum fracture reduction is achieved or the balloon reaches a cortical wall. At this point the surgeon deflates and removes the IBT, mixes the cement, pre-fills the cement cannulae and allows the cement to partially cure in the cement cannulae. Partially cured PMMA is then slowly extruded into the vertebral body through each pedicle under continuous lateral fluoroscopic guidance. This technique permits a controlled fill. In most instances, the volume of cement can slightly exceed that of the bone cavity to interdigitate filler from the central bolus with the surrounding bone. Once filling is complete and the cement has hardened the surgeon removes the cannula and closes the 3mm incisions.

## RESULTS

In our ongoing Institutional Review Board approved study [30], [31], [32], over 900 consecutive kyphoplasty procedures were performed in over 300 patients between April 1999 and February 2004. The mean age was 69 years (range 35-89). The mean duration of symptoms was 7 months. Outcome data was obtained by administering the Short Form-36 health survey (SF-36), and visual analog scale (VAS) for pain rating, additionally the patients underwent detailed neurological and radiographical examinations pre- and postoperatively. Peri-operative and clinical follow-up revealed that the procedure was well tolerated with improvement in pain and early mobilization. The levels treated ranged from T3 to L5 with 47% of the vertebrae at thoraco-lumbar junction. Length of stay ranged from 0.5 day to 9 days (mean 1.1 day). In our experience there were no clinically significant cement leaks and no peri-operative complications attributable to the inflatable bone tamp or tools. SF-36 data pre- and post-operative are available on over 230 patients (72%) with follow-up ranging from 1 week to 59 months (mean 14 months). SF-36 scores improved in every category, statistically significant in all but the General Health modality. Physical function improved from 22.0 to 36.0 ($p \leq 0.0001$). Role physical improved from 9.3 to 27.3 ($p \leq 0.0001$). Bodily pain improved from 22.4 to 41.9 ($p \leq 0.0001$). Vitality improved from 31.4 to 40.7 ($p \leq 0.0001$). Social function improved from 37.7 to 61.2 ($p \leq 0.0001$). Role emotional improved from 54.8 to 65.5 ($p=0.030$). Mental health improved from 63.1 to 68.0 ($p<0.001$). General health was unchanged from 51.3 to 49.2 ($p=0.067$). The VAS scores improved from a preoperative level of 7.0 to an initial postoperative level of 3.2 ($p<0.0001$). At last follow-up examination, the value remained unchanged at 3.4 ($p<0.0001$).

Ledlie et al. reported functional and radiographic outcomes in the first 96 kyphoplasty patients with 133 fractures [33]. Their follow-up period was minimum 12 months and the mean patient age at the time of surgery was 76 years (51-93). With regard to pain as rated by the patient using a 10-point VAS, the mean score was decreased to 1.4 at the 1-year

follow-up, while the mean preoperative VAS score was 8.6. Ambulatory status was also improved postoperatively. Over 90% of the patients (27/29, with 1 year follow-up) were ambulatory at 1 year, while only 35% of the patients (28/79) were ambulatory preoperatively.

Phillips et al. also reported their early radiographic and clinical results of kyphoplasty [34]. In this study 29 patients with 61 fractures between T6 to L5 were evaluated. The mean age of these 29 patients was 70 years. Their clinical information including pain relief, improvement in activity, and satisfaction with the surgical procedure as well as their sagittal spinal alignment on the standing radiographs were assessed and followed up to 1 year. Average pain scores were significantly decreased to 2.6 and 0.6, at 1-week and 1-year, respectively, while average pain score was 8.6 preoperatively.

In addition to good clinical results, height restoration by kyphoplasty has been reported in several studies. Our initial results showed height restoration in 70% of 70 fractured vertebrae treated with kyphoplasty. In patients in whom the vertebral fractures were reduced by kyphoplasty, vertebral height was increased by a mean of 46.8%.

Garfin et al. reported in a prospective multi-center series that the average anterior and midline height were 83+/-14 % and 76+/-14 % before treatment respectively, that were increased to 99+/-13 % and 92+/-11 % after the treatment respectively. In vertebral bodies with 15% or more of the estimated height lost, the average anterior and midline height were 68+/-12 % and 64+/-13 % before treatment respectively, that improved to 84+/-14 % and 90+/-12 % after the treatment respectively [35].

Ledlie et al. reported from radiographic measures anterior and midline points of the fractured vertebrae using the two nearest normal vertebrae as reference points [33]. At 1 year, the anterior vertebral height was 85% of the predicted height and midline height was 89%, while their preoperative heights were 66% and 65%, respectively.

Phillips et al. also reported that local kyphosis improved by a mean of 14 degrees in patients with reducible fractures [34].

## COMPLICATIONS

To date, there is no case report that document serious neurological complications after Kyphoplasty with the exception of a few cases related to inappropriate cement injection and needle placement in the early phase [35]. In our

series of patients [30, 31], cement extravasation was seen in less than 10% of cases. No problems were identified clinically as a result of these extravasations immediately after surgery or at final follow up. In one patient a myocardial infarction occurred as a result of fluid overload during the procedure.

In a separate prospective multi-center series reported by Garfin et al., there were six major complications out of six hundred cases associated with the kyphoplasty procedure. Four of these were neurologic complications (0.75%) [36]. These were directly attributable to surgeon error and breach of technique.

To date no reports of primary or secondary infection of the cement mantle have been published. In our series of over 300 patients we had no primary infections. We did however encounter one hematogenous infection 2 years after the kyphoplasty in a patient receiving multiple blood and platelet transfusions for Waldenstroms macroglobulinemia.

Ledlie et al. reported that asymptomatic cement leaks were noted in 9% of vertebral bodies treated, but no device or procedure related complications were reported [33].

Phillips et al. reported that asymptomatic cement leaks were observed in 6 of 61 vertebral fractures (9.8%) . In this series as well there were no clinical consequences attributable to the bone tamp or cement deposition.

## MECHANISM OF PAIN RELIEF

The etiology of pain after an osteoporotic or an osteolytic vertebral collapse is multi variate (biomechanical, physiological, or neurogenic). Although a number of reports describing clinical results of vertebral augmentation reveal good pain relief, the mechanism of this relief remains unclear. The most intuitive explanation involves simple mechanical stabilization of the fracture; the cement stabilizes the vertebral bodies and offloads the facet joints. However, another explanation is that analgesia results from local chemical, vascular, or thermal effects of PMMA on nerve ending in surrounding tissue. Supporting this concept is the lack of correlation between cement volume and pain relief. Further evidence against an effect resulting solely from mechanical stabilization is the fact that percutaneous vertebroplasty typically does not restore lost vertebral body height and therefore does not correct altered biomechanics. Another potential mechanism of pain relief involves the normalization of strains through the centrum and away from the cortices of the vertebral body. It has been shown that with osteoporosis the centrum of the vertebral body becomes

deficient and the axial load is transmitted to the vertebral body walls. By augmenting the centrum with or without a sagittal realignment the force transmission may now be normalized [37]. The contribution of metabolic bone disease such as osteomalacia to the pain remains unclear.

## BIOMECHANICS

The ability for organ systems to compensate for changes diminishes as humans age. The skeletal system and spinal column also become more vulnerable to fractures with increased age. There is a significant decrease in vertebral body strength with aging, resulting from the loss of cancellous bone support [38, 39]. The compressive strength of any bone is dependent on numerous factors, including the species, site, health status, and quality of bone. The compressive strength of normal human cancellous bone shows great variation but typically resists 5 megapascals (MPa) or 725 pounds of load per square inch (psi) [40]. Osteoporotic vertebral bone would exhibit compressive strength in the lower region of this range (<2 MPa, or 290 psi), whereas younger, healthier, or cancellous bone from other sites may exhibit compressive strength in the upper region of this range. Carter and Hayes showed a strong correlation between bone density and the strength of cancellous bone [41]. The compressive strength of trabecular bone increases approximately with the square of its density. Therefore, doubling the density of a given bone will result in a fourfold increase in compressive strength. In contrast, if the density of the bone were decreased by 50%, the remaining compressive strength would be only 25% of original value [42]. Bell also reported a direct correlation between bone loss and strength, noting that a decrease of 25% in the osseous structure resulted in a 50% decrease in vertebral strength [38]. Rockoff et al further characterized the effects of age on loss of bone strength, by analyzing the cancellous or trabecular bone's ability to compensate for applied forces [43]. The cancellous vertebral body bone carries approximately 55% of axial loads in the adult spine, under the age of 40, but this percentage declines to only 35% after the age of 40. These changes in bone density are directly responsible for the 4% annual incidence of VCFs in post-menopausal women (primary osteoporosis) [44]. These fractures can result in functional limitations such as decrease in the gait velocity, an increase in muscle fatigue, and additional falls.

The thoracic and thoraco-lumbar regions of the spine have a natural kyphotic curvature. This curvature biomechanically places the ventral thoracic spine at an increased risk for developing compression fractures as a consequence of axial loads [45, 46, 47]. The kyphotic curvature concentrates the applied axial load on the ventral portion of the vertebral body. These axial loads cause all points ventral to the vertebral body (instantaneous axis of rotation (IAR)) to come closer together, while simultaneously all points dorsal to the IAR are spread apart [48]. If the failure point of the vertebral body is exceeded, a compression fracture occurs. In younger patients, significant forces are required to create a fracture, which are typically acquired after high energy trauma. However, as the vertebral body is weakened by osteoporosis, the amount of energy required to initiate a fracture is significantly decreased. Once a VCF occurs, the transmission of forces through the vertebral column is altered. A VCF reduces the load carrying capacity of the anterior column, and causes the IAR to migrates dorsally to the region with intact supporting structures [49]. The dorsal migration of the IAR causes the previous mechanical advantage of a longer lever arm from which the posterior ligaments and muscles acted to maintain sagittal balance, to be shortened. The posterior displacement of the IAR simultaneously causes the distance from the ventrally located center of gravity to the IAR to be greater, which places additional distraction on the posterior columns and compression on the anterior columns [47, 49]. Kayanja et al. investigated the distribution of anterior cortical strain at, above and below an experimentally created index VCF to determine the vertebral body at risk of secondary fracture [37]. In this study seventeen human cadaveric thoracic vertebrae were divided into multilevel segments composed of 3 vertebrae (T1-3, T4-6, T7-9, and T10-12). Measurements of anterior cortical shear strain, applied moments and applied flexion angle were made in compression and flexion. The results showed that the shear strain distribution was independent of the location of the multilevel segment level in the spine, and was highest at the apex of a thoracic index VCF. The vertebra above the index VCF had increased anterior cortical shear strain and was therefore at greatest risk of secondary fracture. These results suggest that restoration of sagittal alignment, minimizes strain on the vulnerable vertebral levels above an index VCF, preventing subsequent vertebral fractures. Kayanja et al. also determined the effects of load (compression and flexion) on the adjacent levels (above and below) an augmented VCF [50]. Six upper thoracic segments (T1-T5) and six lower thoracic segments (T8-T12) were biomechanically tested creating VCF that were subsequently augmented in the intermediate vertebrae T3 and T10. Multilevel segment stiffness and

adjacent vertebral strain at superior and inferior levels were measured before and after the vertebral augmentation. The results showed that VCF and augmentation reduced compressive and bending stiffness in vertebral segment, while the adjacent vertebral strain increased. The augmentation also caused a greater amount of strain on the inferior adjacent level compared to the superior level. These results suggested that cement augmentation reduces stiffness while increasing adjacent level strain primarily on the inferior adjacent vertebra and this alteration in strain distribution probably spares the superior adjacent vertebra from fracture.

## FILLER MATERIALS

The filling materials used for vertebral augmentation require good biocompatibility, good biomechanical strength and stiffness, and good radiopacity for the fluoroscopically guided procedures .

Polymethylmethacrylate has been the material most commonly used during vertebral augmentation procedures . As of April 2004 the FDA did approve the labeling of certain brands of PMMA for the treatment of pathological fractures of the vertebral body due to osteoporosis and tumor using a kyphoplasty technique [51]. PMMA is reportedly bioinert and shows good biocompatibility over long-term follow-up. Several inherent advantages to PMMA include familiarity for orthopaedic surgeons, ease of handling, good biomechanical strength and stiffness, and cost effectiveness. Several disadvantages, on the other hand, include; no biologic potential to remodel or integrate into the surrounding bone, no direct bone apposition, excessive inherent stiffness, high polymerization temperature, and potential monomer toxicity. Although good clinical results have been reported in several series of both vertebroplasty and kyphoplasty procedures [3, 19, 30, 31, 32, 33, 34, 35, 52], it is still unclear whether some component of the pain relief is secondary to the mechanical stabilization, chemical toxicity, or thermal necrosis of surrounding tissues and nerve ends. The concern regarding thermal bone necrosis is still theoretical as to date, there has been no obvious evidence to support this [53, 54].

Calcium phosphate cement offers the potential for resorption of the cement over time and replacement with new bone as a biological method to restore vertebral body mass and avoid any potential thermal effects of PMMA . This material is also expected to work as an optimum carrier for osteoinductive proteins . Preclinical animal studies and human pilot studies have shown that these calcium phosphate cements are highly osteoconductive and undergo gradual remodeling with time . There are only a few published manuscripts reporting histologic data with calcium phosphate cement in vertebroplasty model [60, 61, 62]. In general the cement undergoes resorption and remodeling, that was apparent as fragmentation with vascular invasion and bone ingrowth into the material. The reports also described evidence of osteoclastic resorption of the cement and direct bone apposition in a pattern that suggested remodeling similar to that of normal bone. Turner et al. tested both PMMA and calcium phosphate cement (BoneSource ®, Stryker Orthopaedics, Mahwah, NJ) in a canine vertebral body defect. In their study, both materials were well integrated histologically, but calcium phosphate underwent resorption and remodeling, and demonstrated excellent biocompatibility and osteoconductivity [61]. Takikawa et al. also reported greater than 80% direct apposition to cancellous bone in post-operative osteopenic sheep vertebrae at 3, 6, 12, and 24 months [62]. A number of hydroxyapatite and calcium phosphate cements also have been biomechanically tested in vitro , most are able to restore mechanical integrity to the vertebral body [64, 65, 66].

Calcium sulfate, more commonly known as plaster of Paris, has a long clinical history for use as a bone graft substitute in various skeletal sites. This material is injectable, osteoconductive, and cures with a limited exothermic reaction . Calcium sulfate paste has also been reported to significantly augment pull-out strength when used for augmentation of pedicle screw fixation [67]. However, this material is rapidly resorbed [68, 69, 70], it might not be able to support spinal alignment while it is remodeling, therefore it would likely be inappropriate for use in a vertebral augmentation procedure.

These calcium phosphate and sulfate cements have some problems including their low viscosity, handling characteristics different from those of PMMA, and high cost. These products are true cements, that is ions in suspension. As such they exhibit thixotropic properties in that when pressurized in a confined space such as a delivery tube, the suspension dewaters leaving chalk that cannot advance through a tube or even percolate through the interstices of the bone. Many synthetic bone substitute cements are currently being developed but none are yet readily available for use in the spine.

Composite materials (acrylic cements in conjunction with

ceramics) are bioactive, highly radiopaque, and feature excellent mechanical properties . One such material, Cortoss ® (terpolymer resin reinforced with combeite glass-ceramic particles, Orthovita, Malvern, PA) is currently undergoing clinical trials for vertebroplasty and kyphoplasty in the United States and has been reported to be a potential alternative to PMMA. Cortoss was approved for vertebroplasty in Europe in January 2003 based on the results of a prospective clinical trial conducted in Europe . Its osteoconductivity has been proven in several animal models , but no human histology has been reported to date.

## BIOPSY RESULTS

A diagnostic bone biopsy can be easily performed during a Kyphoplasty procedure and does not affect the safety of the procedure if done appropriately. We histologically evaluated 178 biopsies obtained from 142 patients during 246 kyphoplasty procedures. These showed partially necrotic fragments of bone as well as areas of fibrosis and variable stages of woven bone suggesting ongoing fracture healing . The specimens obtained from 30 patients (21%) showed marked increased osteoid in undecalcified sections. These thickened osteoid seams may suggest possible mineralization defect (osteomalacia). Osteoid can be increased either because of increased bone remodeling activity, or because of a mineralization defect. Tetracycline labeling is the only way to distinguish between these two diagnoses. Careful administration of tetracycline labels may help identify any correlation between vertebral fracture and osteomalacia. Also in this series, the biopsies of 4 patients provided a definite diagnosis of plasma cell dyscrasia, in otherwise unsuspected or unknown spinal lesions. These findings suggest that a biopsy is useful for all initial vertebral augmentation cases to rule out any occult lesions.

## HISTOLOGY OF VERTEBRAL AUGMENTATION

In spite of reported good clinical results, several aspects of the vertebral augmentation procedure are controversial, including the optimum methods of mixing and depositing the cement, the potential importance of a foreign body reaction at the cement-bone interface, efficacy of bone tamp usage, the use of relatively high concentrations of radiopaque agents and antibiotics in the cement, and the clinical indications for the procedure. We were able to study histologically four vertebral bodies from two cases 1 month and 2 years after cement augmentation, after a surgical corpectomy and at an autopsy [54] . In this study the histology of vertebrae treated using the kyphoplasty technique revealed a dense cancellous shell around the cement mantle.

This suggests that the tamping had displaced bone, essentially autografting the space around the cement. Bone immediately around the cement did not show extensive necrosis. However, foreign body giant cells contained material consistent with cement particles and/or barium sulfate. Particles were also identified within vascular spaces.

In a baboon vertebral augmentation study, the same histologic features were observed in the vertebrae treated with both vertebroplasty and kyphoplasty [53] . There was evidence of a foreign body reaction to PMMA and a few necrotic segments of bone present in both the vertebroplasty and kyphoplasty vertebrae. It was not clear however whether the necrosis was caused by PMMA polymerization process or bone tamping procedures. Further histologic evaluation may help clarify the safety and efficacy of vertebral augmentation.

## ADJACENT AND REMOTE FRACTURES

One theoretical issue continuously raised by spine practitioners regards the incidence of remote and adjacent level vertebral compression fractures after an index vertebral compression fracture has been augmented by either vertebroplasty or kyphoplasty. Keller et al. investigated the biomechanics of age-related spinal deformity using a sagittal plane biomechanical model and showed that postural forces were responsible for initiation and propagation of osteoporotic spinal deformity in the elderly [71] . Kayanja et al. reported their results of biomechanical tests for cadaveric thoracic wedge compression fractures and showed that anterior cortical strain was maximum at the apex of a thoracic kyphotic curve and the vertebral body immediately above it had the next highest strain with an increased risk of secondary fracture [37] . Moreover, Hasserius et al. reported a Swedish cohort, in a 10 year population based study of 598 individuals and suggested a prevalent vertebral deformity could predict both increased mortality and increased fracture incidence during the following decade in both men and women . Left untreated the incidence of subsequent vertebral fracture after an index fracture is reported in other studies as approximately 20% [44, 72] .

There was no consistent rate of subsequent fracture after vertebroplasty. From the vertebroplasty literature, one study reported a 52% rate of remote or adjacent level fractures after vertebroplasty [22] . A second study reported a 12% rate of remote (one thirds) and adjacent (two thirds) level fractures [73] .

From the kyphoplasty literature, Harrop et al. reported that

the incidence of post-Kyphoplasty vertebral compression fracture in the primary osteoporotic patients was 11.25 % (9 fractures / 80 patients), while the incidence in the steroid induced osteoporotic patients was 48.6 % (17 fractures / 35 patients) [74]. The above results imply that the intervention, kyphoplasty, in primary osteoporotic patients does not increase the rate of remote or adjacent level fractures compared to the published natural history reports. These results also imply that the secondary osteoporotic patients are in fact at increased risk compared to primary osteoporotic patients for subsequent vertebral compression fractures although there is no natural history bench mark to which we can compare this rate. Fribourg et al. also reported the results of retrospective review of charts and radiographs of patients who underwent kyphoplasty . Among 38 patients with 47 treated levels, 10 patients sustained 17 subsequent fractures in this study (9; at adjacent above, 4 at adjacent below, 4 at remote levels). While this report is informative, 40 % (15 cases) of the patients in this series had known oncologic diseases and 7 cases were steroid use patients with known increased risk for subsequent fractures.

## CONCLUSIONS

Osteoporotic VCFs pose a significant clinical problem including spinal deformity, pain, reduced pulmonary function and mobility, as well as an overall increase in mortality in the elderly. Traditional medical and surgical options in many cases prove inadequate.

PVP is a relatively non-invasive technique that has gained increased acceptance over the last decade in the treatment of symptomatic osteoporotic vertebral fractures. The available clinical studies describe pain relief achieved in greater than 90% of symptomatic osteoporotic fractures, with only infrequent, mostly minor, complications. Some of the drawbacks of PVP, stem from the use of PMMA, because of its toxicity and poor handling characteristics, rather than from the procedure itself.

Kyphoplasty is a modification of PVP that may add a margin of safety by virtue of a lower observed incidence of cement leakage. Kyphoplasty has been shown to be worthwhile in acute vertebral fractures to predictably restore vertebral height and to facilitate a controlled fill of the vertebral body. Favorable outcomes in early trials appear to imply that kyphoplasty permits early mobilization, which has the potential to decrease mortality. Considering the greater mortality that is associated with osteoporotic compression fractures, early mobilization in these patients is of prime importance.

The next logical step beyond treatment of evident vertebral fractures is prophylactic augmentation. Prevention of osteoporotic vertebral fractures with a combination of pharmacologics and timely reinforcement of at-risk osteoporotic vertebrae is the ultimate goal aside from prevention of osteoporosis itself. It is here that new osteoconductive synthetic composites will figure more prominently as an emerging alternative to cement. Advances in minimally invasive surgical techniques, imaging, and synthetic engineering are rapidly changing the treatment protocols available for osteoporotic compression fracture.

## CORRESPONDENCE TO

Daisuke Togawa, MD, PhD Cleveland Clinic Spine Institute, A-41 9500 Euclid Avenue, Cleveland, Ohio 44195, USA. Phone: +1-216-444-5987 Facsimile: +1-206-350-8578 E-mail: Daisuke@Togawa.MD, or DaisukeTogawa@aol.com

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## Author Information

**Daisuke Togawa, M.D., Ph.D.**
Cleveland Clinic Spine Institute

**Mark M. Kayanja, M.D., Ph.D.**
Cleveland Clinic Spine Institute

**Isador H. Lieberman, M.D, M.B.A., F.R.C.S.(C)**
Cleveland Clinic Spine Institute