Spine

SPINE Volume 39, Number 4, pp E231-E239

RANDOMIZED TRIAL

Is Kiva Implant Advantageous to Balloon Kyphoplasty in Treating Osteolytic Metastasis to the Spine? Comparison of 2 Percutaneous Minimal Invasive Spine Techniques

A Prospective Randomized Controlled Short-Term Study

Korovessis Panagiotis, MD, PhD, Vardakastanis Konstantinos, MsC, MD, Vitsas Vasilios, MD, and Syrimpeis Vasilios, MD

Study Design. Prospective, parallel-group, controlled, comparative randomized study.

Objective. To compare cement leakage rate and efficacy for vertebral body restoration of balloon kyphoplasty (BK) *versus* Kiva novel implant with polymethylmethacrylate (PMMA) for treating osteolytic vertebral body metastasis.

Summary of Background Data. Minimally invasively vertebral augmentation techniques with PMMA are mostly performed for treating osteoporotic compression fractures. The Kiva implant with PMMA offers better vertebral body restoration and less PMMA leakage than BK in osteoporotic fractures. No previous study compared leakage rate and efficacy for vertebral body restoration in traditional BK and Kiva with PMMA in osteolytic vertebral body metastases.

Methods. This study examined 23 patients (71 ± 13 yr) with 41 osteolytic vertebral bodies, who received Kiva with low viscosity PMMA and 24 patients (70 ± 11 yr) with 43 vertebral body osteolyses, who were reinforced with BK and high viscosity PMMA. All osteolyses were graded as Tomita 1 to 3. Anterior vertebral body height ratio (AVBHr), posterior vertebral body height ratio (PVBHr), and middle vertebral body height ratio (MVBHr), Gardner kyphotic deformity, PMMA leakage and were measured and compared between the groups. Visual analogue scale and Oswestry Disability Index were used for functional outcome evaluation.

Results. No patient survived after 3 months. Asymptomatic PMMA leakage occurred in 4 (9.3%) vertebrae in the BK group solely (2 to the spinal canal, in Tomita grade 3 osteolysis) Anterior, posterior and middle vertebral body height ratio, Gardner angle improved insignificantly in both groups. Visual anlogue scale and Oswestry Disability Index improved postoperatively similarly in both groups ($P < 0.001$).

Conclusion. BK and Kiva provided equally significant spinal pain relief in patients with cancer with osteolytic metastasis. The absence of cement leakage in the Kiva group and absence of neurological complication in the BK group leakages reflects the safety of both augmentation techniques even in significant osteolysis. The lack of cement leakage in the Kiva cases, although low viscosity PMMA was used, increases this implant safety in augmenting severely destructed thoracolumbar vertebrae and sacrum from osteolytic metastasis.

Key words: metastatic, osteolytic, fractures, Kiva, polymethylmethacrylate, balloon kyphoplasty, leakage.

Level of Evidence: 1

Spine 2014;39:E231–E239

Patients who experience osteolytic spinal metastases are subjected to significant mortality and morbidity and claim for intractable axial pain, which is mostly of mechanical origin.[1–7] Epidural spine compression and/or nerve root compression may furthermore increase pain severity and deteriorate neurological function.[8–10]

Because of the fragility and comorbidities associated with patients with cancer, the surgical risk is high and open surgery is reserved only for cases with neurological involvement. Spine surgery for vertebral osteolytic metastasis is often demanding and thus management of symptomatic metastatic spine disease is fundamentally palliative. Spinal surgical staging[11,12] is needed to map the extent of local disease. The Tomita *et al*[12] staging system accommodates lesions at multiple levels and is more applicable to spinal metastases.

The most common diagnoses for surgical management of spinal metastases are neurological compression, spinal

From the Department of Orthopaedic Surgery, General Hospital "Agios Andreas," Patras, Greece.

Acknowledgment date: June 20, 2013. First revision date: September 4, 2013. Second revision date: October 16, 2013. Acceptance date: October 25, 2013.

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work.

No relevant financial activities outside the submitted work.

Address correspondence and reprint requests to Panagiotis Korovessis, MD, PhD, Department of Orthopaedic Surgery, General Hospital of Patras, GR-26224 Patras, Greece; E-mail: korovess@otenet.gr

DOI: 10.1097/BRS.0000000000000112

instability, including pathological vertebral fracture, and unrelenting pain.

Historically, laminectomy was used to manage spinal metastases, however, because the location of metastasis is usually anterior, such a decompression destabilizes the spine and may deteriorate the already impaired neurological function.[13,14] In contrary, although most metastatic lesions are anteriorly based, this does not necessarily dictate an anterior approach for decompression, particularly in patients with increased morbidity and lung involvement (*e.g.*, lung cancer, lung metastases, *etc.*). Resection of isolated vertebral metastasis is indicated in few kinds of tumors (thyroid cancer, hypernephroma, *etc.*). Thus, most patients who are treated surgically for metastatic disease undergo intralesional tumor resection to provide neurological decompression and local stabilization. Decompressive surgery followed by radiotherapy was shown to be superior to those following radiotherapy alone,[14,15] but it is technically demanding and is associated with a high rate of morbidity.

Besides traditional open procedures to treat spinal metastasis, the minimal invasive spine (MIS) procedures, vertebroplasty (VP), and balloon kyphoplasty (BK), were introduced to restore and stabilize vertebral osteoporotic fractures and osteolytic metastases.[16,17] These MIS procedures have been shown to be efficacious, providing rapid pain relief, reduced need for pain medication, improvement of functional disability, and enhanced health-related quality of life.

However, several complications have been associated with VP and BK. Bone cement leakage, particularly to the spinal canal, is 1 disastrous complication associated with VP and less commonly with BK.[18–21] Bone cement leakage becomes a highly potential complication in the presence of severe vertebral body destruction from osteolytic metastases.

There is only level III evidence[4,22] that BK and Kiva are well-tolerated, relatively safe, and effective techniques to provide early pain relief and improved functional outcomes in patients with painful neoplastic spinal fractures. BK also provided long-term benefits in terms of pain and disability.[16,23–29]

A systematic review[21] identified that only about 2% of BK outcome data had been collected in patients with metastatic vertebral fractures. Furthermore, these data were frequently collected in small number metastatic lesions in mixed case series where osteoporosis was the dominant indication with short-term follow-up.[21] Kiva implant is a novel minimal invasively percutaneous vertebral augmentation technique that has been recently introduced and successfully used to reduce cement leakage in osteoporotic and metastatic vertebral fractures.[22]

Mention should be made to the fact that, at this time, there is an evident lack of studies comparing BK with other noninvasive interventions (*e.g.*, Kiva) in the treatment of symptomatic osteolytic spinal disease.

The null hypotheses of this study were that (1) both Kiva and BK can immediately postoperatively equally restore sagittal vertebral body heights and Gardner segmental kyphotic deformity; (2) intraoperative cement leakage rate in BK is similar to that in Kiva when treating osteolytic vertebral body metastasis; and (3) immediately postoperative short-term functional outcomes (pain, Oswestry Disability Index [ODI]) after vertebral augmentation are similar in both BK and Kiva groups.

MATERIALS AND METHODS

We performed a prospective, parallel-group, controlled comparative randomized study (Figure 1) in patients with vertebral metastatic osteolyses, who randomly received in the same period 2 different vertebral MIS augmentation techniques, in 1 institution by the same senior orthopedic spine surgeon.

Patient Selection

In the authors' institution, which is a tertiary regional spine center, 50 consecutive patients with end stage disease with evidence (history, imaging evidences, and biopsy) for painful osteolytic vertebral metastases in 1 to 5 vertebral bodies, were randomized to receive either percutaneous BK or Kiva with polymethylmethacrylate (PMMA) as "stand alone" "palliative" surgery in the period from March 2010 and March 2012 (Figure 1). In addition to vertebral metastases, all patients showed metastases in the axial skeleton and visceral metastases. Exclusion criteria were: significant spinal deformity (*e.g.*, idiopathic, adult scoliosis), previous spinal operation, spinal infection, spinal canal compromise due to epidural disease associated/not with neurological impairment, vertebral osteolysis Tomita grade[12] more than 3 (high potential for cement leakage), radiculopathy, Tomita prognostic[12]

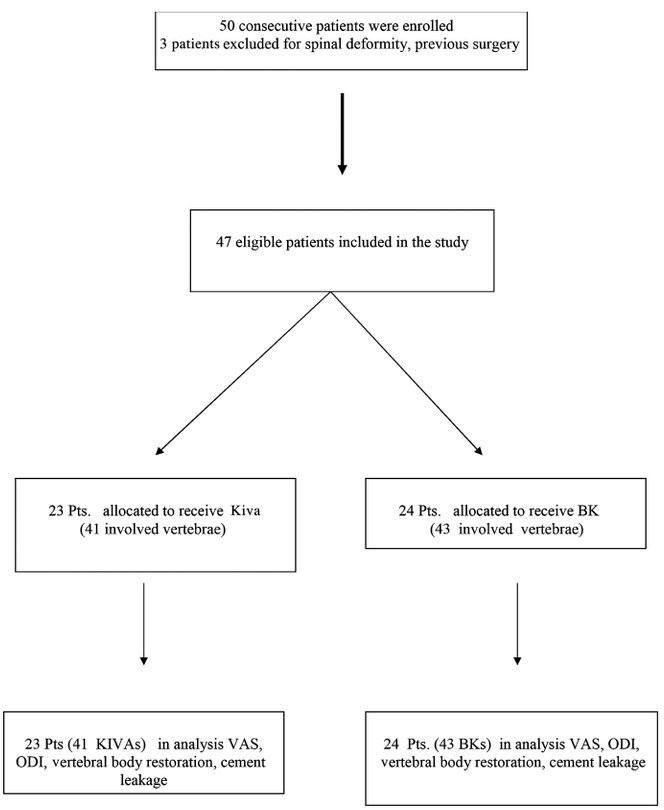

Figure 1. Patient allocation flow chart. VAS indicates visual analogue scale; ODI, Oswestry Disability Index; BK, balloon kyphoplasty.

score less than 6, and/or uncorrected coagulopathy. Not the erosion of the posterior vertebral body wall, but the simultaneous infiltration of the posterior vertebral body cortex by the tumor with extension into the spinal canal was contraindication for vertebral augmentation. Patients, who were treated combined with vertebral augmentation plus spinal instrumentation for significant angular deformity caused by metastasis (>75%) were excluded. Thus, patients with significant vertebral wedge deformities due to osteolytic vertebral fractures were not included in this study. Patients were included in this prospective series if they have experienced: severe back pain refractory or potential of further vertebral deformation and danger for neurological lesion caused by vertebral lesions secondary to osteolytic metastases.

From the 50 consecutive patients, who were initially enrolled for this study (Figure 1), 3 patients, were excluded for meeting the above-mentioned exclusion criteria. Forty-seven patients with similar anthropometric characteristics were eligible and finally included in the study.

On admission, all patients underwent digital anteroposterior and lateral radiograph of the whole spine. The patients, who were enrolled in this study had history of malignancy (colon, breast, and lung) and evidence for osteolytic spinal metastasis and underwent whole body technetium bone scintigraphy, head and spinal spiral computed tomographic (CT) scan to disclose all possible areas of metastasis and to detect further asymptomatic lesions.

Twenty-three patients (10 males, 13 females), aged 71 ± 13 years, with 41 osteolytic vertebral body metastasis, were allocated to received Kiva and 24 patients (11 males, 13 females), aged 70 ± 11 years with 43 osteolytic vertebral body metastasis, were allocated to receive BK. Eighty-four vertebral and sacral osteolyses were included (67 vertebral body and 9 sacral) (Figure 2, 3). All procedures in 84 vertebrae were performed in a total of 47 sessions.

The diagnosis of bone metastasis had been definitively secured intraoperatively with transpedicular bone biopsy (Balex; Taeyeon Medical Co, Ltd, Incheon, Korea). The primary tumor for the Kiva group patients was lung carcinoma in 6 cases, colon carcinoma in 9 cases, and breast carcinoma in 8 cases. For the BK-group patients, lung carcinoma was the cause of metastasis in 7 cases, colon carcinoma in 9 cases, and breast carcinoma in 8 cases. CT scans of the fractured

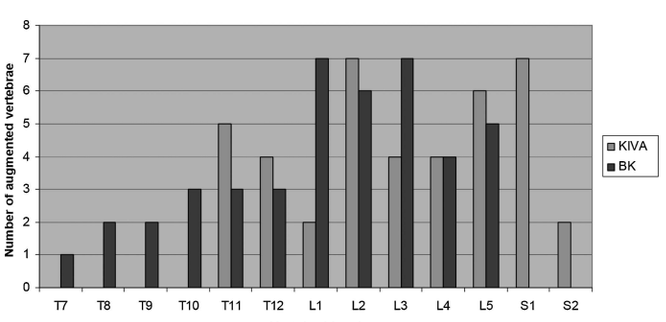

Figure 2. Spinal level distribution of osteolytic metastasis plotted as Kiva *vs*. balloon kyphoplasty. BK indicates balloon kyphoplasty.

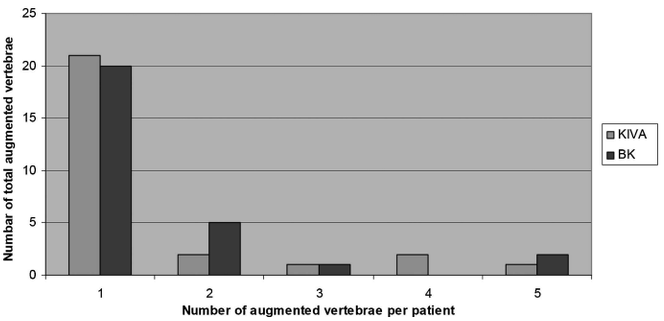

Figure 3. Number of levels augmented by each technique (Kiva *vs*. balloon kyphoplasty). BK indicates balloon kyphoplasty.

vertebra/-e was/were digitally (E-film; Merge Healthcare, Chicago, IL) evaluated by 2 experienced orthopedic radiologists and graded according to Tomita *et al*[12] for vertebral body wall integrity.

Radiographical and functional outcome was evaluated 1 month postoperatively in all patients. On admission the Tomita *et al*[12] prognostic score was recorded in all patients. For the Kiva-group patients the preoperative Tomita prognostic score was 6.95 ± 0.88 (range, 6–8), whereas in the BK group it averaged 7.04 ± 0.88 (range, 6–8). All patients were neurological intact on admission. Because the aim of this study was to compare the immediate effects and surgical complications of vertebral augmentation between Kiva and BK, no longer follow-up observation was performed.

Patient-Related Outcome Measures

Outcomes were assessed prior to surgery, and 1 month postoperatively. Back pain was assessed using a 10-point visual analogue scale (VAS) where a score of zero indicated "no pain" and a score of 10 indicated "severe pain".[10] Functional capacity was assessed using the ODI.[30]

Radiographical Parameters

Radiographical evaluation including standing anteroposterior and lateral plain roentgenograms of the spine plus CT scans with sagittal 2-dimensional reconstruction of augmented vertebrae were performed preoperatively and 1 month after surgery. The CT scan was performed in a multidetector spiral CT 16 row (Light Speed Pro 16; GE, Milwaukee, WI). The slice thickness was 2.5 mm with a bone algorithm. Magnetic resonance imaging was performed in about 50% of the cases magnetic resonance imaging (Signa 1.5 T; GE) scanning included T1 and T2 sequences; 0.2 mg/kg body weight paramagnetic contrast agent (Magnevist; Schering, Berlin, Germany) was used.

Changes in anterior vertebral body height, posterior vertebral body height, and middle vertebral body height and degree of segmental vertebral kyphosis angle were measured in lateral radiographs by caliper in the digital system (E-film; Merge Healthcare). The anterior, posterior and midvertebral height ratio were defined as the distance between the upper and lower endplates at the anterior and posterior vertebral wall and in the center of the vertebra, respectively (Figure 4).

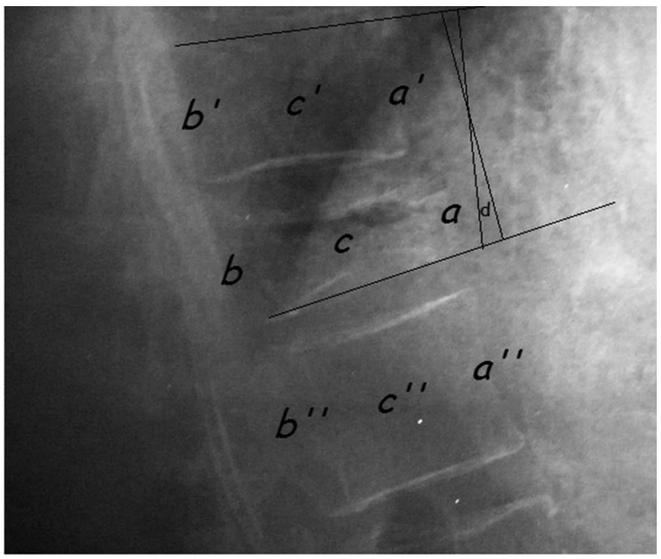

Figure 4. Radiological measurements. **a**, AVBHr = a/[(a′ + a′′)/2]. **b**, PVBHr = b/[(b′ + b′′)/2]. **c**, MVBHr = c/[(c′ + c′′)/2]. **d**, Gardner angle. AVBHr indicates anterior vertebral body height ratio; PVBHr, posterior vertebral body height ratio; MVBHr, middle vertebral body height ratio.

The "normal" heights for the anterior vertebral wall and mid-vertebral region were considered as the sum of the measurement of the corresponding heights of the adjacent superior and inferior nearest nonfractured vertebrae divided by 2. Two independent assessors evaluated radiological changes pre- to postoperation. Cement leakages were evaluated on plain postoperative roentgenograms and detailed CT scans.

Interventions

All surgical procedures were done with informed consent from the patients. The patients were placed in the prone position on a AcroMed frame (DePuy Spine Inc., Raynham, MA). Both Kiva and BK augmentations were performed under biplane fluoroscopy in the operating theater and under general anesthesia and continuous neuromonitoring. Biopsy was routinely obtained from all affected vertebrae, in all patients even when the diagnosis was preoperatively known, prior to augmentation with either BK or Kiva. The spine surgeon, who performed all surgical procedures, was unaware of the augmentation method to be used and only at the operation table was he informed about the method to be used, resulted from randomization. The hospital stay was 24 hours. Patients were mobilized as soon as they tolerated with a light body brace.

Kiva Procedure

Kiva is a relatively novel percutaneous unilateral vertebral augmentation implant (Kiva VCF Treatment System; Benvenue Medical, Santa Clara, CA) (Figure 5).[22] The Kiva System is a single-use device in which an external delivery handle is used to deploy the Kiva implant over a nitinol coil guidewire.

The coil is first advanced through the deployment cannula and into the cancellous portion of the vertebral body using an external handle. The Kiva implant, which comprises PEEK-OPTIMA (Invibio Inc., West Conshohocken, PA) and loaded with 15% barium sulfate to enhance visibility under fluoroscopy, is incrementally advanced over the coil to form a nesting, cylindrical column with an *in situ* outer diameter of 20 mm. Kiva implant should be delivered between anterior and middle third of the vertebral body. Up to 4 loops of the implant may be inserted into the vertebral body for a maximum coil stack height of 12 mm, which re-elevates the endplate, thereby providing the desired vertebral fracture reduction. After the coil is retracted, low viscosity radiopaque PMMA cement (Tecres, Verona, Italy) is injected through the lumen of the polyetheretherketone (PEEK) implant, thereby interlocking the implant to the cancellous bone of the through the osteolysis destructed vertebral body. The manufacturer's instructions are that PMMA should be injected unilaterally close to the anterior two-thirds of the vertebral body through a 1.1-mm thick, 14-cm long delivery needle directly into the PEEK implant. PEEK implant after its implantation, forms a nesting, cylindrical column and through the internal small holes enables low viscosity PMMA to flow into the hollow PEEK cylindrical column and not outside.

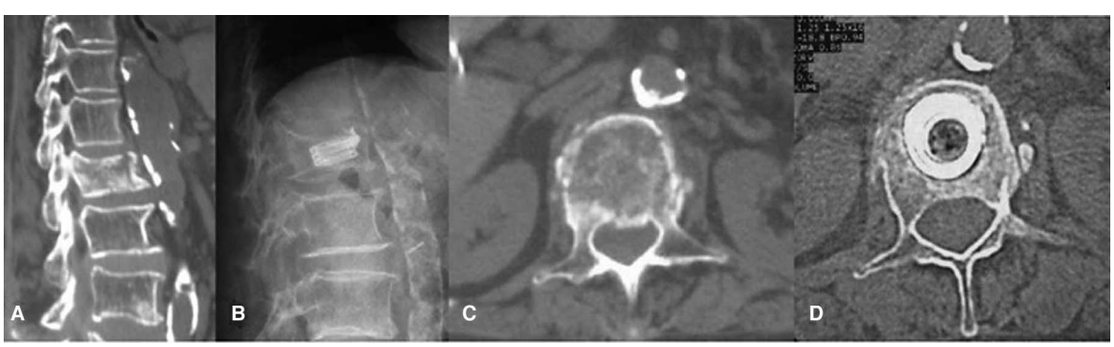

Figure 5. A, Lateral CT scan of 77-year-old female with colon cancer, severe distraction of L1 vertebral body. **B**, Lateral roentgenogram after Kiva with PMMA. **C**, Preoperative axial CT at L1 disclosing violation at posterior wall. **D**, Postoperative axial CT disclosing excellent PMMA containment and PEEK-PMMA column construction between anterior and middle column. PMMA indicates polymethylmethacrylate; PEEK, polyetheretherketone; CT, computed tomography.

Balloon Kyphoplasty Procedure

The Balex (Taeyeon Medical Co, Ltd) device and technique is very similar to the traditional BK (Kyphon; Medtronic, Inc., Sunnyvale, CA) (Figure 6). K-wires of 2-mm diameter are inserted through both pedicles of the damaged vertebra). Then, a cannula was inserted into the pedicle with cement filler and pusher. The position of the cannula was continuously controlled in both planes. Then, an expander is inserted bilaterally and inflated. After creation of the desired void, PMMA (Osteopal V, Spinal column stabilization; Heraeus Medical GmbH, Hanau, Germany) that is a high-viscosity bone cement is slowly injected after removal of the Expander. In the case of severe cortex destruction, the "egg shell" technique was used to reduce PMMA leakage.[25]

The Balex (Taeyeon Medical Co, Ltd) expander balloons should ideally be centered between the endplates in the anterior two-thirds of the vertebral body. Inflation of BK balloons was stopped when 1 of the endpoints of inflation was reached: the pressure raised over 300 ψ, the balloon contacted the cortical wall of the vertebra or the maximal inflation volume of the balloon was reached. The mean balloon inflation volume was 4.1 mL (range, 1.3–5.5 mL). All patients in both groups were treated with the same preoperative assessment and postoperative protocol and were mobilized 1 day postoperatively.

Operative Details

The BK procedure took on average 12 (8–16) minutes for each vertebra, whereas it was 7 (5–10) minutes in the Kiva group.

Radiographical control including anteroposterior and lateral standing roentgenograms of the whole spine were made on the first postoperative day. Analgesia was adapted to the severity of the back pain. When advised by oncologists, oncological treatment (radiation therapy and/or chemotherapy) was started 2 to 4 weeks postintervention.

Statistical Analysis

Block randomization with random block size was used (nQuery; Statsol, Cork, Ireland) for the purpose of this prospective randomized study[31]. The paired and unpaired *t* tests were used to compare changes of the same group or between different groups respectively with parametric values. The χ^2 test was used for nonparametric comparisons. Pearson correlation coefficient (*r*) was used for correlations between different parameters. As the lowest level of significance for the paired and unpaired *t* tests and the χ^2 test was considered, *P* value was less than 0.05. Pearson correlation coefficient $r > 0.45$ was considered as significant at the *P* value level less than 0.001. VAS improvement of more than 5 points on the 0 to 10 scale and ODI score more than 25 points on the 0 to 100 scale were considered as a significant improvement.

Tomita Prognostic Score and Functional Results

All patients showed a preoperative Tomita prognostic score between 6 and 7. Patient-related outcomes in BK- and Kiva-treated patients exhibited a marked improvement of back pain in all 47 patients of both groups: VAS improved from an average ± standard deviation of 8.3 ± 3.2 and 8.1 ± 4 preoperatively to 3.2 ± 2 and 3.0 ± 2.5 postoperatively in Kiva and BK, respectively (both groups $P < 0.001$). ODI improved postoperatively from 81 ± 7 and 79 ± 8 to 38 ± 8 and 37 ± 9 in Kiva and BK, respectively postoperatively (both groups $P < 0.001$).

Radiographical Results

Fifty percent of the vertebral augmentations with either Kiva or BK technique involved the levels L2 to L5 (Figure 2). Twenty-one patients (51%) of the Kiva group and 20 patients (47%) of BK group received single-level augmentation, whereas the remaining patients received 2 to 5 level augmentations (Figure 3).

For technical reasons, there was no case with Kiva augmentation above T11, whereas no case with BK augmentation below L5 vertebra. Kiva was implanted in sacrum because of severe osteolysis (Tomita 3). Inter- and intrarater agreement for preoperative and postoperative roentgenographic data was high (κ, 0.98–1.00).

Preoperative baseline values of anterior vertebral body height ratio, middle vertebral body height ratio, and posterior vertebral body height ratio and wedge vertebral angle did not differ between the 2 groups (Table 1).

Anterior vertebral body height ratio and posterior vertebral body height ratio values increased, although insignificantly postoperatively equally in both groups (Table 1). However, MVBHr increased statistically marginally ($P = 0.07$) in the

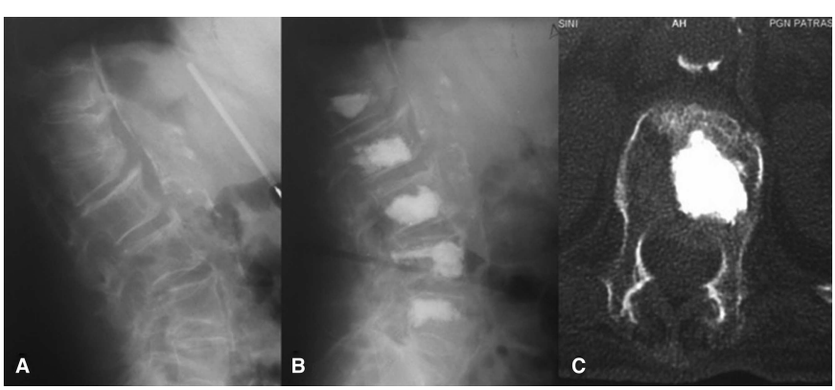

Figure 6. A, Lateral standing roentgenogram of 81-year-old female with osteolyses L1–L5 vertebrae (Tomita 3). **B**, Lateral standing roentgenogram after balloon kyphoplasty. **C**, Postoperative axial CT disclosing sufficient PMMA containment. PMMA indicates polymethylmethacrylate; CT, computed tomography.

Kiva group. No significant change was seen in kyphosis Gardner angle pre- to postoperatively in both groups (Table 1).

Complications

Neither general nor surgical complications (death, neurological, embolic, or cardiovascular complications) were observed in any patient in both groups in the early perioperative period. PMMA cement leakage was radiologically (plain roentgenograms, CT scans) recorded in 4/43 (9.3%) augmented with BK vertebral bodies; in 1 vertebra PMMA leaked anteriorly (Figure 7); in 1 case to the adjacent disc; and in the remaining 2 cases posteriorly to the spinal canal without associated neurological impairment (Figure 7).

All 4 leakages occurred in vertebral body with osteolyses Tomita grades 3.

Although low viscosity cement was used in the Kiva group no leakage occurred in the vertebrae augmented with Kiva implant.

DISCUSSION

Spinal metastasis occurs in 5% to 30% of patients with cancer and metastatic epidural spinal cord compression affects about 20% of these patients.[31–37]

Metastasis to the spine, can result in various complications, including vertebral body fracture, wedge deformation, instability, and neurological complications. These complications are commonly associated with severe pain, neurological impairment and may deteriorate the general health of these sick patients and increase disability, morbidity and mortality.[31–37]

In the past, major surgery included corpectomy through a transthoracic approach was propagated to decompress and stabilize the spine in symptomatic metastatic disease with or without neurological compromise. However, in patients with cancer, with increased comorbidities a major surgery cannot be performed with a significant risk.

With the advent of modern MIS techniques, various percutaneous methods have been introduced to treat painful osteolytic vertebral body osteolytic metastases. Most of these techniques are mainly palliative, and aim to reduce intractable axial spinal pain and simultaneously to improve the quality of life of patients with cancer. These techniques include percutaneous vertebral body augmentation by means of VP, BK, and Kiva and in some instances MIS may be combined with radiofrequency.

The null hypotheses of this comparative study were as follows: (1) both Kiva and BK can equally restore sagittal vertebral body heights and kyphotic segmental deformity; (2) cement leakage rate is similar both in BK and Kiva; and (3) postoperative short-term functional outcomes are similar in both BK and Kiva groups.

In this study, we compared 2 different percutaneous vertebral body augmentation techniques used for spinal osteolytic metastasis in 2 matched populations. The obtained results from each group and for each parameter were compared with each other regarding vertebral body restoration with the use of established radiological parameters, vertebral body

TABLE 1. Comparative Radiological Data Pre- to 1-Month Postintervention in 47 Patients With 84 Vertebral Body Metastatic Osteolyses

Group	AVBHr			PVBHr			Changes (%)	MVBHr			Changes (°)	SKA			Changes (°)
	Preop	Postop	*P*	Preop	Postop	*P*		Preop	Postop	*P*		Preop	Postop	*P*	
Kiva	0.95 ± 0.09	0.98 ± 0.05	**0.28**	16 ± 9.15	3.3 ± 7.6	**0.35**	3.7 ± 11	0.94 ± 0.13	0.99 ± 0.06	**0.16**	5.1 ± 14.5	13.7 ± 11.2	14.7 ± 10.6	**0.78**	+1 ± 6
BK	0.89 ± 0.19	0.96 ± 0.07	**0.30**	0.94 ± 0.10	0.94 ± 0.12	**0.32**	3.9 ± 7.6	0.87 ± 0.22	0.93 ± 0.11	**0.24**	7.2 ± 19	12.1 ± 9	10 ± 6.8	**0.38**	−2 ± 4
Intergroup *P*	**0.22**	**0.27**		**0.38**	**0.23**		**0.7**	**0.23**	**0.07**		**0.74**	**0.65**	**0.13**		**0.13**

All values are shown as average ± standard deviation.
BK indicates balloon kyphoplasty; AVBHr, anterior vertebra body height ratio; PVBHr, posterior vertebra body height ratio; MVBHr, middle vertebral body height ratio; SKA, segmental kyphosis angle; preop, preoperative; postop, postoperative. Bold value represents statistically significant.

Figure 7. A, Lateral MRI of 72-year-old male with osteolyses at T12, L2, L4, and L5 vertebrae without epidural expansion. **B**, Lateral CT scan after balloon kyphoplasty disclosing anterior leakage at T12 vertebrae. **C**, Postoperative axial CT disclosing intracanal leakage at L2 without neurological impairment. CT indicates computed tomography; MRI, magnetic resonance imaging.

osteolysis geography,[12] and short-term functional outcome measures (VAS, ODI), and rate plus direction of bone cement leakage.

The advantages of our study are that it reports on solely vertebral osteolytic metastases, which all were operated by the same surgeon in the same institution in contrast to the previous ones that reported on BK and VP for treating vertebral fractures of different etiology (hemangiomas, osteoporosis, multiple myeloma, and metastasis).[22,27,38–40]

The findings retrieved from this study indicate that, in selected patients with cancer with painful vertebral body metastatic osteolysis, without neurological impairment, percutaneous Kiva and BK are well tolerated, and are not associated with general complications.

All patients in both groups reported similar significant improvement of functional outcome (pain score $>$ 5 VAS units; ODI $>$ 25 units) in the early postoperative period and this outcome is within that previously reported in similar studies.[23,24,27,40]

Both BK and Kiva offered postoperatively almost similar sagittal radiological vertebral body restoration, and the observed PMMA leakage rate in BK was within that previously reported.[24,40–42] Although, historically BK increases vertebral body height postintervention,[24,40,41,43,44] this increase has been expressed differently (percentage, millimeters) in each study, this making comparison difficult.[25–27,40,43] In our study, vertebral body dimensions measurements were highly reliable because we used absolute values, that are not influenced by magnification on roentgenograms. Pooled analysis of previously published data[25–27,40,43] showed increases in both anterior and midline vertebral body height after BK. Insignificant postoperative increases in anterior, and posterior vertebral body heights were shown in either group (BK, Kiva), but some statistically marginal increase ($P < 0.07$) of the middle vertebral body height in the Kiva group. We cannot assume that this increase may have any clinical relevance, but the latter is due to the unique function of PEEK implant to construct together with PMMA a column that elevates and supports the middle third of the vertebral body that is usually eroded by the osteolytic metastasis.

BK improves sagittal vertebral body wedge deformity in spinal metastasis, but follow-up analysis disclosed loss of the initial restoration, with the absolute value of the wedge angle ultimately approaching the preoperative levels.[23–29,43,45,46] These radiographical outcomes after BK were seen by others to return to preoperative levels at 12 months and beyond.[2,46] No significant restoration of kyphotic segmental vertebral deformity was shown in our series, because the preoperative vertebral body wedge deformity was little averaging from 12% to 13% for BK and Kiva, respectively.

A common complication that may occur during percutaneous BK and VP procedures is bone cement leakage. Cement leakage may be potentially disastrous in osteolytic vertebral body metastasis when PMMA leaks to the spinal canal, particularly if there is a cavity inside a vertebral body.[41,42] Previous reports showed 0% to 21.8% symptomatic and asymptomatic leakage rate in patients who underwent percutaneous vertebral augmentation for metastatic osteolyses.[23,24,40–42,47,48] The leakage rate in the BK group of our study was 9.3%, within that previously reported. Kiva was not associated with any leakage even in the presence of significant extent of osteolysis (Tomita grades 2, 3).

A sensitivity analysis showed that prospective studies demonstrated a higher rate of leakage (11.2%) than retrospective studies (0.51%).[4] No relationship was found with other factors such as specific etiology (multiple myeloma *vs*. metastasis) or estimated age of the fracture.[4]

The well-established factors that contribute to PMMA leakage are: viscosity and amount of injected PMMA cement.[39,49] It is documented that PMMA leakage is usually caused by excessive bone cement injection.[50] In an experimental study, Bohner *et al*[51] defined a model that could predict what factors affect the risk of cement extravasation and how to minimize cement extravasation. The model predicted that the extravasation risk was decreased when the cement viscosity, the bone pore size, the bone permeability and the bone porosity were increased, and when the diameter of the extravasation path and the viscosity of the marrow were decreased. In the case of Kiva the cement used was of low viscosity facilitating its flow through the fine needle used to inject PMMA into the PEEK implant. Although low viscosity bone cement was used, leakage did not occur in this series and this depicts the safety of using Kiva even in severe vertebral body osteolysis.

Although poorly reported across the studies, a small number of patients treated with BK, VP, and Kiva experienced medical complications, but no deaths were reported in the first month postintervention.[22,24,52]

It is generally thought that VP and BK are contraindicated in patients with 75% or more loss of vertebral body height, 20% or more spinal canal compromise due to

epidural disease, posterior vertebral body cortex violation, more than 3 levels requiring treatment, radiculopathy, and/or uncorrected coagulopathy.[41,42,44,47,48] In persons with these contraindications, VP or BK will likely result in a higher rate of complications than is seen in patients without these contraindications (39% *vs*. 11%, respectively).[44] No patient in any group in our study had these above-mentioned contraindications for BK and Kiva.

Although small studies[22,53–60] have shown that VP and BK are rapid, safe, durable, and effective palliative treatments for metastatic vertebral fractures, the literature lacks analyses of a large cohort of patients.

There are 3 potential limitations in this study: the short follow-up for the patients of both groups; the lack of preoperative power analysis and the use of Kiva solely in sacral metastasis. However, neither of these 3 limitations jeopardized the significance of the results derived from this study: this comparative study was so designed to investigate the early results of both vertebral augmentation techniques in vertebral body restoration, their safety regarding bone cement leakage and early functional outcomes. Because life expectancy of these very sick, end-stage patients with cancer was too short, long-term results cannot be obtained. Because of the absence of a prior power analysis, the results derived from this study were interpreted carefully by the authors. However, the differences in the obtained results (VAS, ODI) between the groups were very small. Copay *et al*[61] found minimally clinically important difference values of 12.8 points for ODI, 1.2 points for VAS back pain. The differences that we observed in this clinical study (2 points for ODI and 0.2 for VAS) were much smaller. Thus, preoperative powering of our study on aforementioned minimally clinically important differences would not have led to statistical significance in the presence of the small clinical differences that we observed. Regarding the third limitation, Kiva according to manufacturer's prescriptions should not be implanted above the T11 because of the width of the pedicles and vertebral body size, but it was successfully used in the sacrum in great osteolysis (Tomita 3) where BK could not safeguard PMMA containment.

CONCLUSION

On the contrary, the strengths of this study were the prospectively acquired data, the matched anthropometric parameters similar to the inclusion criteria. Thus, this study possibly does not include acquired bias and finally supports our assumption that the results retrieved from this study are valuable and therefore sound conclusions can be safely drawn. We recommend both percutaneous BK and Kiva techniques to stabilize vertebrae immediately affected by metastases and thus to improve short-term quality of life in patients with cancer with osteolytic metastasis Tomita grades 1 to 3 of different origin without neurological involvement.

➢ Key Points

- ❑ This is a prospective, comparative randomized parallel-group study.
- ❑ In symptomatic osteolytic metastatic spinal disease both percutaneous Kiva and BK with PMMA showed a tendency for restoration of anterior and posterior vertebral body height and kyphotic Gardner angle, but only Kiva restored MVBHr.
- ❑ Kiva was not complicated by PMMA leakage, whereas BK showed 10% leakage rate.
- ❑ Back pain (VAS), and ODI scores improved equally significantly in the patients of both groups 1-month postoperatively.
- ❑ Both Kiva and BK can safely augment painful thoracic and lumbar vertebral osteolytic metastases grades 1 to 3 Tomita and prognostic Tomita score 6-8, whereas Kiva additionally reinforced sacral metastasis too.

Acknowledgment

The authors thank Peter Fennema, medical statistician, AMR Advanced Medical Research GmbH, Männedorf, Switzerland, for his assistance in statistical analysis.

References

1. Lad SP, Patil CG, Lad EM, et al. Trends in pathological vertebral fractures in the United States: 1993 to 2004. *J Neurosurg Spine* 2007;7:305–10.
2. Lunt M, O'Neill TW, Felsenberg D, et al. European prospective osteoporosis study group characteristics of a prevalent vertebral deformity predict subsequent vertebral fracture: results from the European prospective osteoporosis study (EPOS). *Bone* 2003;33:505–13.
3. Borgström F, Zethraeus N, Johnell O. Costs and quality of life associated with osteoporosis-related fractures in Sweden. *Osteoporos Int* 2006;17:637–50.
4. Bouza C, Lopez T, Palma M. Hospitalised osteoporotic vertebral fractures in Spain: analysis of the national hospital discharge registry. *Osteoporos Int* 2007;18:649–57.
5. Cockerill W, Lunt M, Silman AJ, et al. Health-related quality of life and radiographic vertebral fracture. *Osteoporos Int* 2004;15:113–19.
6. Papaioannou A, Kennedy CC, Ioannidis G, et al. Determinants of health-related quality of life in women with vertebral fractures. *Osteoporos Int* 2006;17:355–63.
7. Puffer S, Torgerson DJ, Sykes D, et al. Health care costs of women with symptomatic vertebral fractures. *Bone* 2004;35:383–6.
8. Gilbert RW, Kim JH, Posner JB. Epidural spinal cord compression from metastatic tumor: diagnosis and treatment. *Ann Neurol* 1978;3:40–51.
9. Grados F, Depriester C, Cayrolle G, et al. Long-term observations of vertebral osteoporotic fractures treated by percutaneous vertebroplasty. *Rheumatology (Oxford)* 2000;39:1410–14.
10. Perez-Higueras A, Alvarez L, Rossi RE, et al. Percutaneous vertebroplasty: long-term clinical and radiological outcome. *Neuroradiology* 2002;44:950–54.
11. Boriani S, Weinstein JN, Biagini R. Primary bone tumors of the spine: terminology and surgical staging. *Spine* 1997;22:1036–44.
12. Tomita K, Kawahara N, Kobayashi T, et al. Surgical strategy for spinal metastases. *Spine (Phila Pa 1976)* 2001;26:298–306.
13. Klimo P, Jr, Thompson CJ, Kestle JR, et al.. A meta-analysis of surgery *versus* conventional radiotherapy for the treatment of metastatic spinal epidural disease. *Neuro Oncol* 2005;7:64–76.
14. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet* 2005;366:643–48.

15. Yao KC, Boriani S, Gokaslan ZL, et al. *En bloc* spondylectomy for spinal metastases: a review of techniques. *Neurosurg Focus* 2003;15:E6.
16. Lieberman IH, Dudeney S, Reinhardt MK, et al. Initial outcome and efficacy of kyphoplasty in the treatment of painful osteoporotic vertebral compression fractures. *Spine* 2001;26:1631–38.
17. Phillips FM, Ho E, Campbell-Hupp M, et al. Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. *Spine* 2003;28: 2260–65.
18. Bouza C, Lopez T, Magro A, et al. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: a systematic review. *Eur Spine J* 2006;15:1050–67.
19. Gill JB, Kuper M, Chin PC, et al. Comparing pain reduction following kyphoplasty and vertebroplasty for osteoporotic vertebral compression fractures. *Pain Physician* 2007;10:583–90.
20. Hulme PA, Krebs J, Ferguson SJ, et al. Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. *Spine* 2006;31:1983–2001.
21. Taylor RS, Fritzell P, Taylor RJ. Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis. *Eur Spine J* 2007;16:1085–1100.
22. Korovessis P, Repantis T, Miller LE, et al. Initial clinical experience with a novel vertebral augmentation system for treatment of symptomatic vertebral compression fractures: a case series of 26 consecutive patients. *BMC Musculoskelet Disord* 2011;12:206.
23. Dudeney S, Lieberman IH, Reinhardt MK, et al. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. *J Clin Oncol* 2002;20:2382–87.
24. Fourney DR, Schomer DF, Nader R. Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients. *J Neurosurg* 2003;98:21E2–30E2.
25. Gaitanis IN, Hadjipavlou AG, Katonis PG, et al. Balloon kyphoplasty for the treatment of pathological vertebral compressive fractures. *Eur Spine J* 2005;14:250–60.
26. Grohs JG, Krepler P. Minimal-invasive stabilisierung osteoporotischer wirbelkorpereinbruche. *Radiologe* 2004;44:254–59.
27. Masala S, Lunardi P, Fiori R, et al. Vertebroplasty and kyphoplasty in the treatment of malignant vertebral fractures. *J Chemother* 2004;16:30–33.
28. Masala S, Fiori R, Massari F, et al. Kyphoplasty: indications, contraindications and technique. *La Radiol Med* 2005;110:97–105.
29. Weisskopf M, Herlein S, Birnbaum K. Kyphoplasty—a new minimal invasive treatment for repositioning and stabilising vertebral bodies. *Zeit Orthop Inre Grenz* 2003;141:406–11.
30. Fairbank J, Pynsent P. The Oswestry Disability Index. *Spine* 25:2940–53.
31. Aaron AD. The management of cancer metastasis to bone. *JAMA* 1994;272:1206–09.
32. Siegal T. Surgical decompression of anterior and posterior malignant epidural tumors compressing the spinal cord: a prospective study. *Neurosurgery* 1985;17:424–32.
33. Sundaresan N, Digiacinto GV, Hughes JE. Surgical treatment of spinal metastases. *Clin Neurosurg* 1986;33:503–22.
34. Wong DA, Fornasier VL, MacNab I. Spinal metastases: the obvious, the occult, and the impostors.*Spine (Phila Pa 1976)* 1990;15:1–4.
35. Riley LH, III, Frassica DA, Kostuik JP, et al. Metastatic disease to the spine: diagnosis and treatment. *Instr Course Lect* 2000;49: 471–7.
36. Jacobs WB, Perrin RG: Evaluation and treatment of spinal metastases: an overview. *Neurosurg Focus* 2001;11:e10.
37. Perrin RG, Laxton AW. Metastatic spine disease: epidemiology, pathophysiology, and evaluation of patients. *Neurosurg Clin N Am* 2004;15:365–73.
38. Cortet B, Cotten A, Boutry N, et al. Percutaneous vertebroplasty in patients with osteolytic metastases or multiple myelomas. *Rev Rhum Engl Ed* 1997;64:177–83.
39. Cotten A, Dewatre F, Cortet B, et al. Percutaneous vertebroplasty for osteolytic metastases and myeloma: effects of the percentage of lesion filling and the leakage of methylmethacrylate at clinical follow-up. *Radiology* 1996;200:525–30.
40. Pflugmacher ZR, Taylor ZA, Agarwal ZI, et al. Balloon kyphoplasty in the treatment of metastatic disease of the spine: a 2-year prospective evaluation. *Eur Spine J* 2008;17:1042–8.
41. Kose KC, Cebesoy O, Akan B, et al. Functional results of vertebral augmentation techniques in pathological vertebral fractures of myelomatous patients. *J Natl Med Assoc* 2006, 98: 1654–58.
42. Pflugmacher R, Kandziora F, Schroeder RJ, et al. Percutaneous balloon kyphoplasty in the treatment of pathological vertebral body fracture and deformity in multiple myeloma: a one-year follow-up. *Acta Radiol* 2006;47:369–76.
43. Pflugmacher R, Schulz A, Schroeder RJ, et al. A prospective two-year follow-up of thoracic and lumbar osteolytic vertebral fractures caused by multiple myeloma treated with balloon kyphoplasty. *Z Orthop Ihre Grenzgeb* 2007;145:39–47.
44. Lane JM, Hong R, Koob J, et al. Kyphoplasty enhances function and structural alignment in multiple myeloma. *Clin Orthop Relat Res* 2004;426:49–53.
45. Persaud R, Bland JM, Altman DG. Correlation, regression, and repeated data. *BMJ* 2000;308:1510.
46. Pflugmacher R, Beth P, Schroeder RJ, et al. Balloon kyphoplasty for the treatment of pathological fractures in the thoracic and lumbar spine caused by metastasis: one-year follow-up. *Acta Radiol* 2007;48:89–95.
47. Calmels V, Vallée JN, Rose M, et al. Osteoblastic and mixed spinal metastases: evaluation of the analgesic efficacy of percutaneous vertebroplasty. *AJNR Am J Neuroradiol* 2007;28:570–74.
48. Cheung G, Chow E, Holden L, et al. Percutaneous vertebroplasty in patients with intractable pain from osteoporotic or metastatic fractures: a prospective study using quality-of-life assessment. *Can Assoc Radiol J* 2006;57:13–21.
49. Cotten A, Boutry N, Cortet B, et al. Percutaneous vertebroplasty: state of the art. *Radiographics* 1998;18:311–20.
50. Martin JB, Jean B, Sugiu K, et al. Vertebroplasty: clinical experience and follow-up results. *Bone* 1999;25:11S–15S.
51. Bohner M, Gasser B, Baroud G, et al. Theoretical and experimental model to describe the injection of a polymethylmethacrylate cement into a porous structure. *Biomaterials* 2003;24:2721–30.
52. Vrionis FD, Hamm A, Stanton N, et al. Kyphoplasty for tumor-associated spinal fractures. *Tech Reg Anestha Pain Manag* 2005;9:35–9.
53. Byung G Lim, Jea Yeun Lee, Mi Kyoung Lee, et al. Kyphoplasty for the treatment of vertebral compression fractures in a cancer patient with neurological deficits and anterior vertebral wall destruction. *Pain Physician* 2011;14:539–44.
54. Gray LA, Jarvik JG, Heagerty PJ, et al. Investigational vertebroplasty efficacy and safety trial (INVEST): a randomized controlled trial of percutaneous vertebroplasty. *BMC Musculoskelet Disord* 2007;8:126.
55. Layton KF, Thielen KR, Koch CA, et al. Vertebroplasty, first 1000 levels of a single center: evaluation of the outcomes and complications. *AJNR Am J Neuroradiol* 2007;28:683e9.
56. Bartels RH, van der Linden YM, van der Graaf WT. Spinal extradural metastasis: review of current treatment options. *CA Cancer J Clin* 2008;58:245e59.
57. Hirsch AE, Medich DC, Rosenstein BS, et al. Radioisotopes and vertebral augmentation: dosimetric analysis of a novel approach for the treatment of malignant compression fractures. *Radiother Oncol* 2008;87:119e26.
58. Pilitsis JG, Rengachary SS. The role of vertebroplasty in metastatic spinal disease. *Neurosurg Focus* 2001;11:e9.
59. Jha RM, Yoo AJ, Hirsch AE, et al. Predictors of successful palliation of compression fractures with vertebral augmentation: single-center experience of 525 cases. *J Vasc Interv Radiol* 2009;20:760e8.
60. Lavelle W, Carl A, Lavelle ED, et al. Vertebroplasty and kyphoplasty. *Anesthesiol Clin* 2007;25:913–28.
61. Copay AG, Glassman SD, Subach BR, et al. Minimum clinically important difference in lumbar spine surgery patients: a choice of methods using the Oswestry Disability Index, Medical Outcomes Study questionnaire Short Form 36, and pain scales. *Spine J* 2008;8:968–74.