Prospective Evaluation

Percutaneous Vertebral Augmentation Assisted by PEEK Implant in Painful Osteolytic Vertebral Metastasis Involving the Vertebral Wall: Experience on 40 Patients

Giovanni Carlo Anselmetti, MD[1], Antonio Manca, MD[1], Sean Tutton, MD[2], Gabriele Chiara, MD[1], Alexios Kelekis, MD[3], Francis Rocco Facchini, MD[4], Filippo Russo, MD[1], Daniele Regge, MD[1] and Filippo Montemurro, MD[1]

From: [1]Institute for Cancer Research and Treatment, Turin, Italy; [2]Medical College of Wisconsin, Milwaukee, WI; [3]Athens University School of Medicine, Athens, Greece; [4]Adventist La Grange Memorial Hospital, LaGrange, IL

Address Correspondence: Giovanni Carlo Anselmetti, MD Interventional Radiology Unit, Institute for Cancer Research and Treatment (IRCC), Strada Provinciale n° 135 Km.3,95 - 10060 Candiolo, Turin, Italy
E-mail: gc.anselmetti@fastwebnet.it

Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: None.

Manuscript received: 09-10-12
Revised manuscript received: 10-11-12
Accepted for publication: 11-27-12

Free full manuscript: www.painphysicianjournal.com

Background: Vertebral metastases are associated with significant pain, disability, and morbidity. Open surgery for fracture stabilization is often inappropriate in this cancer population due to a poor risk-benefit profile, particularly if life expectancy is short. Vertebroplasty and kyphoplasty are appealing adjunctive procedures in patients with malignancy for alleviation of intractable pain. However, these patients have a higher risk of serious complications, notably cement extravasation.

Study Design: We prospectively evaluated clinical results of polyetheretherketone (PEEK) implant (Kiva) assisted vertebroplasty performed in malignant painful osteolytic lesions at risk for cement extravasation due to vertebral wall involvement.

Setting: Department of Interventional Radiology, Institute for Cancer Research and Treatment, Candiolo, Turin, Italy

Methods: Forty patients (22 women; mean age 66.8 ± 12.4), suffering from a painful spine malignancy with vertebral wall involvement not responding to conventional therapies and without surgical indications, underwent vertebral augmentation with Kiva intravertebral implant for pain palliation. The procedure was performed with moderate sedation and local anesthesia under combined digital fluoroscopy and computed tomography guidance. After the coil-shaped PEEK implant was deployed within the vertebral lesion, bone cement was injected under continuous digital fluoroscopic control. Patients were discharged from the hospital the next procedural day. The Visual Analog Scale (VAS) for pain, Oswestry Disability Index (ODI), analgesic requirement, and use of external brace support were evaluated to determine efficacy. The primary end-point was safety and efficacy at one month after the procedure. However, all the patients were scheduled to be followed-up at month 3, 6, and every 6 months thereafter. Follow-up was prospectively evaluated in all patients after Kiva with clinical interviews. The Institution's Internal Review Board approved this study.

Results: Median pre-treatment VAS of 10 (range 6 – 10) significantly ($P < 0.001$) dropped to one (range 0 – 3), with all patients achieving a clinically relevant benefit on pain at one month. Differences in pre- and post-treatment analgesic therapy were significant ($P < 0.001$). All patients no longer use an external brace after Kiva. In 7 out of 43 (16.3%) treated vertebrae a bone cement leakage was detected.

Limitations: This is a not randomized study. Participants were limited to 40 patients.

Conclusion: The Kiva System potentially represents a novel and effective minimally invasive treatment option for patients suffering from severe pain due to osteolytic vertebral metastases.

Key words: Vertebroplasty, metastases, pain palliation, Kiva, spine

Pain Physician 2013; 16:E397-E404

Percutaneous vertebroplasty (PV) consists of the injection of polymethylmethacrylate (PMMA) into a collapsed vertebra in order to obtain pain relief and mechanical strengthening of the vertebral body. Galibert and Deramond proposed this procedure for the treatment of aggressive vertebral hemangiomas of C2 (1) and, at present, it is used extensively worldwide in osteoporotic and malignant vertebral fractures when conventional therapies are not effective or not well tolerated. Although PV has been shown in multiple prospective randomized studies to be a relatively safe and effective procedure for back-pain treatment, several authors have reported some major complications that can lead to paraplegia and death (2,3). Most of the described complications concerned pulmonary embolism, soft tissues damages, and nerve root compression related to the leakage of bone cement (4,5). With fluoroscopic observations bone cement leakage can be detected frequently in vertebroplasty as it occurs in 38% (6) to 72.5% (7,8) of patients with vertebral metastases, in 59.5% (9) and 65% (10) of patients with osteoporotic vertebral collapse or, even more, in 81% of treated patients (11) when computed tomography (CT) is carried out after PV. Even if this frequent minimal leakage is well tolerated or asymptomatic in the large majority of patients, cement extravasation is the main source of clinically relevant complications depending upon site and volume of leakage.

Vertebral metastases are associated with significant pain, disability, and morbidity. If left untreated, progression of these lesions result in painful microfractures with potential for vertebral level collapse and spinal cord compromise. Open surgery for fracture stabilization is often inappropriate in this patient population due to a poor risk-benefit profile. Given that the average life expectancy in patients with vertebral metastasis is one year (12), surgery is undesirable since the postoperative recovery consumes much of the remainder of life. Therefore, non-operative and minimally invasive techniques are the most appropriate treatment options for vertebral metastases.

Percutaneous vertebral augmentation is a minimally invasive procedure involving the injection of polymethylmethacrylate (PMMA) into a vertebral body that is either partially collapsed or at high risk for collapse due to osteolysis. Vertebral augmentation is appealing as an adjunct to radiotherapy or chemotherapy in patients with malignancy for alleviation of intractable pain despite comprehensive nonoperative management. Several studies have reported dramatic improvements in pain severity associated with osteolytic vertebral metastases following percutaneous vertebral augmentation (13-16). However, percutaneous vertebral augmentation is associated with a higher risk of complications from PMMA extravasation in cancer patients compared to osteoporotic patients due to loss of cortical integrity (8). Leakages can be reduced but may always occur even with new high viscosity PMMA (17). As such, malignancy is widely considered a relative contraindication for these procedures. We report our personal experience in vertebral augmentation of painful osteolytic vertebral metastases with vertebral wall involvement treated by a novel coil-shaped polyetheretherketone (PEEK-OPTIMA) implant designed to internally contain and thus minimize the risk of PMMA extravasation.

Methods

Population and Study Design

From February 2010 to January 2012, 40 patients (22 women; mean age 66.8 ± 12.4 years) suffering from spine malignancy (9 myeloma and 31 metastasis) were treated with percutaneous vertebral augmentation assisted by placement of 43 PEEK endovertebral devices (3 patients were treated at 2 vertebral levels) at a single institution. Patients were informed of potential treatment-related complications and each provided signed informed consent in accordance with the Declaration of Helsinki. Outcome assessments were collected prospectively and the institution's Internal Review Board approved this analysis.

Inclusion Criteria

- Age ≥ 40 years old
- Metastasis with bone marrow edema within the vertebra assessed with magnetic resonance imaging (MRI)
- Osteolytic metastasis with vertebral wall involvement assessed with CT
- Significant back pain (Visual Analogue Scale score ≥ 5)
- Tenderness to palpation over the spinous process of the fractured vertebra
- Back-pain persistence after a minimum of 4 weeks of conservative medical treatment.

Exclusion Criteria

- Systemic infection or any suspicious infective

spondylodiskitis
- Uncorrectable coagulation disorders
- Nerve root pain or neurological deficit due to the fracture or cord compression by the tumor.

In all patients MRI, spiral CT with multiplanar reconstruction (MPR) and x-ray revealed an osteolytic vertebral metastasis with involvement of vertebral body extending to the cortical vertebral wall either anteriorly and/or posteriorly (Fig. 1).

Technique

Immediately prior to the procedure, the patient was premedicated with intravenous antibiotics (vancomycin hydrochloride 1 gm and gentamycin 100 mg). The patient was placed prone on the angiographic suite table and the procedure was carried out with hybrid digital fluoroscopic and CT guidance. The entire procedure was performed under local anesthesia (3 mL of 2% lidocaine hydrocloride at the skin level and deep to include the periostium) along with continuous monitoring of vital parameters.

Using an 11-gauge needle inserted either through the costotransversal route (extrapedicular) in the thoracic spine or transpedicular approach in the lumbar spine, the upper endplate of vertebral body just lateral to the midline was targeted. A Kirschner guide-wire was inserted to allow the placement of a 6-gauge working cannula (Fig. 2 top row) just below the superior endplate directed medially.

The delivery system was inserted through the 6-gauge introducer to allow the deployment of its nitinol coil-shaped guide-wire into the central vertebral body. The Kiva implant was then delivered over the nitinol guide-wire inside the osteolytic lesion of the vertebra to form a nesting, cylindrical column; correct positioning of the device was confirmed by rotational acquisition with MPR (Fig. 2 bottom row).

Up to 4 loops of the implant were inserted into the vertebral body for a maximum coil stack of 12 mm, which re-elevates the endplate. After the coil is retracted, the radiopaque bone cement can be gradually injected using a manual screw injector through the Kiva implant and its inner channel under fluoroscopic monitoring (Fig. 3 top row). Post-procedural radiographs and CT scan with MPR were then performed to demonstrate a satisfactory bone cement distribution within the vertebral body and to detect if even minimal bone cement extravasation has occurred (Fig. 3 bottow row).

Device

The PEEK implant is part of the Kiva VCF Treatment System (Benvenue Medical, Inc., Santa Clara, CA, USA) and is offered in a kit containing an access needle, Kirschner guide-wire, dilator with working cannula, delivery system with nitinol coil guide-wire, and the implant bone cement and its manual screw injection system. The Kiva System received CE Mark approval in December 2008 and is currently under investigation for FDA approval in the United States.

Bone Cement Leakage Assessment

Bone cement extravasation was studied immediately after vertebral augmentation with MPR reconstructed from angiographic data (Allura X-per CT, Philips, The Netherlands). Two independent radiologists, blinded to clinical outcomes, performed CT evaluations.

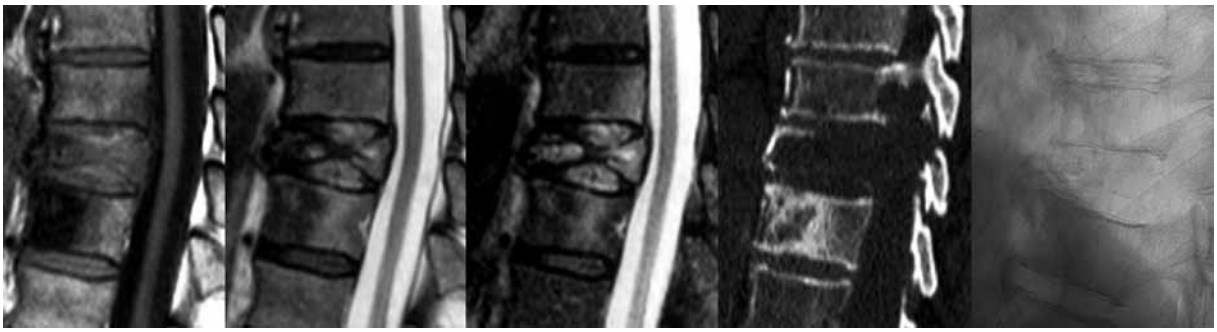

Fig. 1. *Preoperative imaging demonstrating osteolytic vertebral metastasis with complete involvement of the T10 vertebral body, extending to the cortical vertebral wall posteriorly, and partial of T9 and T11 also. T1, T2, T2-weighted Short Tau Inversion Recovery (STIR) magnetic resonance imaging, computed tomography and x-ray.*

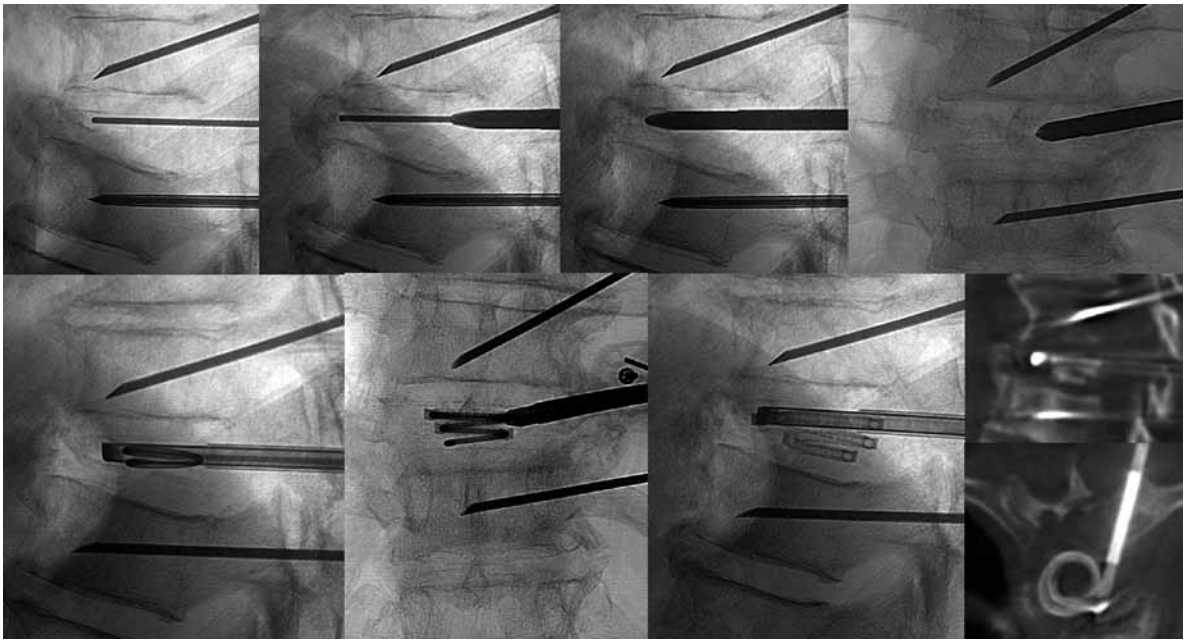

Fig. 2. *Intraoperative images demonstrating access with 11-gauge needle, introduction of the dilator, placement of working cannula in lateral and anteroposterior view (upper row) and Kiva nitinol coil, deployed PEEK implant in lateral and anteroposterior view, rotational acquisition with multiplanar reconstruction to check correct placement (lower row).*

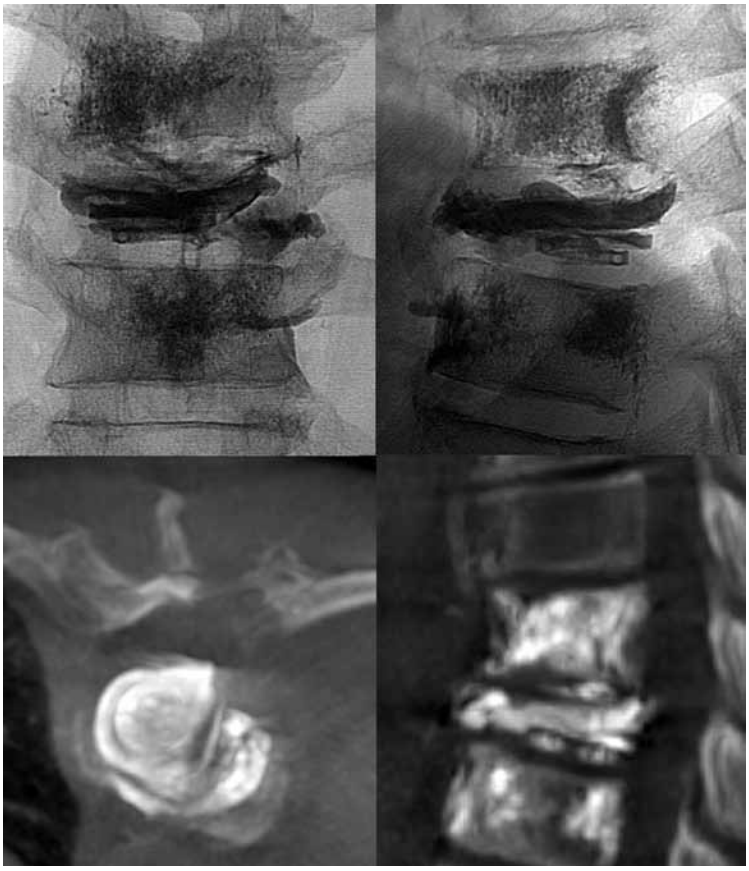

Fig. 3. *Completed procedure with cement filled Kiva implant. X-ray and reformatted postoperative computed tomography scan demonstrating satisfactory bone cement distribution within the T10 vertebral body and the absence of extravasation either anteriorly or posteriorly.*

Clinical Evaluation

Pain was evaluated at each patient visit by the 11-point pain intensity numerical rating Visual Analog Scale (VAS) where 0 represents no pain and 10 the worst experienced pain. Patients were asked to rate their worst pain experienced during the prior 3 days. Analgesic drugs prescribed at baseline and at follow-up visits were classified as none, non-steroidal anti-inflammatory drugs (NSAIDs), and oral narcotic, transdermal or intravenous narcotic.

Pain and analgesic drug use were assessed and recorded for all the patients at 3 time points: baseline (pre-procedure), 2 weeks, and 3 months post-procedure. Staff anesthesiologists performed these assessments during an office visit. Additionally, we recorded the use of external braces at baseline and 3 months after the procedure. Patients were then followed up by office visits (at 6 months and every 6 months thereafter) and any change in VAS scores was recorded. If new onset back pain was reported during routine clinical interview the patient was assessed with radiologic imaging (plain radiographs and MRI).

The Oswestry Disability Index with self-evaluation questionnaire (ODI) was compiled by the patients just before PV (baseline) as well as at the time of the last interview (endpoint). Follow-up time varied from 3 months to 12 months with a mean of 10.0 ± 3.5 months.

Statistical Methods

Because VAS and ODI scores did not follow a normal distribution, medians and their ranges were used as summary statistics and comparisons were performed by non-parametric tests. A clinically relevant improvement or worsening in pain was defined as a reduction or an increase of 2 or more VAS points, respectively, between time points. VAS scores and use of analgesic medications were compared using the Wilcoxon test. This test was also used to compare baseline ODI with the best ODI score achieved by the patient during the follow-up period. Time to treatment failure was studied by the Kaplan Meier method from the date of the procedure to the time-point at which the disease had worsened, the patient had undergone spinal surgery, a new vertebral fracture had occurred, or the patient died from disease progression. Finally, the proportions of patients on different analgesic drugs at baseline and after one month from the procedure were compared by the Marginal Homogeneity test.

Statistical analyses were performed by the SPSS Version 17 statistical package (IBM; Chicago, IL, USA) and significance was set at $P < 0.05$.

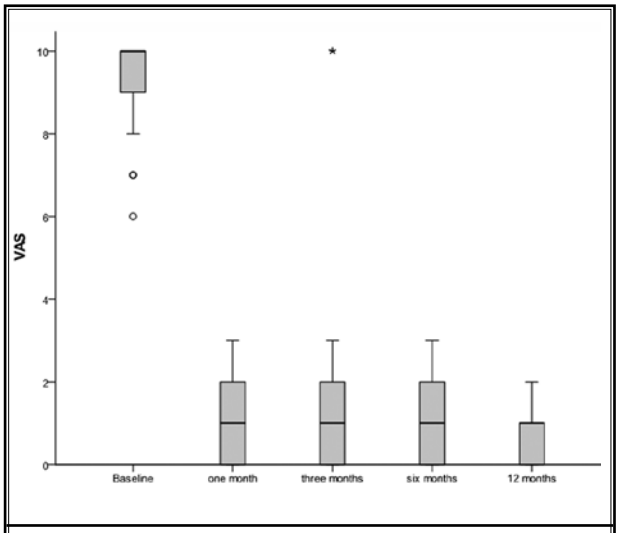

Fig. 4. *Boxplots of VAS scores at various time points. The horizontal line in the middle of each box represents the median of the scores; the length of the box represents the interquartile range; and the whiskers represent smallest and highest values that are not outliers. Outliers (values between 1.5 and 3 box lengths) and extreme values (values that are more than 3 box lengths away) are indicated by an open circle and asterisk, respectively. The difference between baseline and one month value was statistically significant by the Wilcoxon test.*

Results

All the procedures were successfully performed without clinical complications. VAS score, ODI score, and information on use of analgesics were available for all 40 patients before, one month, and three months after the procedure. Six- and 12-month determinations of VAS score, ODI score, and use of analgesics could be obtained in 36 and 22 patients respectively. Six patients died from disease progression: 3 between 3 and 6 months, and 3 between 6 and 12 months from the procedure. One patient underwent surgical treatment between one and 3 months from the procedure because of disease progression. Three patients had experienced a new vertebral fracture due to new metastases between one and 3 months after the procedure (myeloma and breast cancer metastasis). Eleven patients alive and without events did not have the 12-month assessment because of short follow-up. Figure 4 shows the median VAS values at different time points. Before the procedure, the median VAS score was 10 (range 6 – 10) and

dropped to one (range 0 – 3, $P < 0.001$) one month post-procedure (Fig. 4). All patients achieved a clinically relevant benefit on pain at one month defined as a drop in the VAS score of at least 2 points following the procedure. A total of 12 patients experienced a treatment failure (see the definition in the statistical methods). Pain significantly worsened in 4 of 40 patients between one and 3 months after the procedure (8%). Except for 2 patients undergoing vertebral surgery (both at 3 months from the procedure) and 6 patients dying from disease progression, no clinically relevant worsening of VAS scores was seen in patients with follow-up data available (Fig. 5). The proportion of patients in each category of pain medications, before and after the procedure, is summarized on Table 1. All patients on opiates, either transdermal or parenteral, could be switched to NSAIDS (15, 40%) or no treatment at all (25, 60%). The median ODI score at baseline was 82.2% (range 54.4% – 88.8%) and dropped to 4.1% during follow-up after the procedure ($P < 0.001$).

In 7 out of 43 (16.3%) treated vertebrae a bone cement leakage was detected by post-procedural CT: 2 leakages were noted in the disc, whereas 5 occurred in the paravertebral tissues or draining veins; no leakages were demonstrated inside the spinal canal.

Among the 37 patients who wore a brace before intervention, none required a brace after vertebral augmentation.

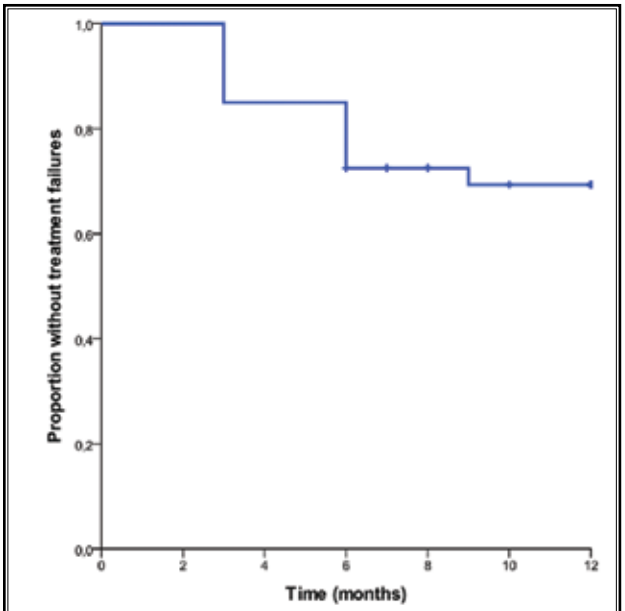

Fig. 5. *Kaplan Meier estimate of time to pain worsening. As all patients had a clinically meaningful improvement in pain (reduction of at least 2 VAS points) at one month from the procedure, time 0 corresponds to the one month assessment.*

Discussion

The treatment of painful vertebral metastases is a major therapeutic challenge. Radiation therapy is only modestly effective with marginal durability (18). Further, previously radiated vertebral levels are at elevated risk for collapse with potentially devastating neurologic consequences (19,20). This study shows that percutaneous vertebral augmentation using the novel coil-shaped PEEK Kiva implant is feasible, effective, and may reduce the risk of PMMA extravasation in the treatment of painful osteolytic vertebral metastases with diffuse cortical bone involvement. The results of this study are novel in that the Kiva implant represents a new therapeutic option for the treatment of painful vertebral metastasis where radiation therapy, traditional surgical stabilization, or balloon-based vertebral augmentation procedures may be contraindicated.

Chew et al (14) conducted a systematic review on the safety and efficacy of percutaneous vertebral augmentation for spinal metastases and myeloma. Although vertebral augmentation reduced pain severity by 47% to 87%, serious complications were reported in up to 12% of patients. The risk of cement extravasation is also notably higher in malignancies due to increased vascularity and cortical disruption (8). Resulting complications may include intercostal neuralgia, radiculopathy, myelopathy, or spinal infections (21).

Table 1. *Change in the use of analgesic medications before and one month after the procedure.*

Type of analgesic medication	Pre-Procedure Number (%)	Post- Procedure Number (%)
None	0	24 (60)
NSAIDS	1 (2)	16 (40)
Oral opiates	8 (20)	0
Transdermal or parenteral opiates	31 (78)	0

The Kiva System was designed to reduce and stabilize vertebral fractures by deploying a coiled PEEK implant, which is then augmented with cement. PMMA bone cement is injected through the lumen of the Kiva implant, which helps to contain and control the distribution of the cement. Once cured, the cement interlocks the implant to the cancellous bone. With traditional kyphoplasty and vertebroplasty procedures, PMMA is injected into cancellous bone but there is no mechanism for cement containment. Consequently, PMMA cement may leak laterally to the soft tissues, superiorly or inferiorly into the adjacent disc space, or posteriorly, where it may involve the exiting nerve root or the spinal canal (21).

A recent clinical study was conducted with the Kiva System in 26 patients (42 fractures) for treatment of vertebral compression fractures (22). Anterior cement extravasation was identified at 4.8% of levels with no reported intracanal extravasation or adverse clinical sequelae. These results compare favorably to the reported range of cement extravasation rates of 7% to 72% in previous studies (23-27).

The mechanism of pain amelioration with percutaneous vertebral augmentation is currently unknown although 2 main hypotheses prevail. Polymethyl methacrylate cement stabilizes vertebral microfractures, which eliminates painful vertebral body and periosteal micromovements (6). In addition, the thermal polymerization of PMMA following injection ablates pain receptors in trabecular bone, in vertebral periostium, and in vascular structures (28). The combination of these 2 proposed factors leads to immediate postoperative anterior column stability and pain relief (15).

Conclusion

The Kiva System potentially represents a novel and effective minimally invasive treatment option for patients suffering from severe pain due to osteolytic vertebral metastases. The novel design of the Kiva implant may reduce the risk for PMMA extravasation versus traditional vertebral augmentation procedures. Prospective studies in larger series are needed to validate the safety and effectiveness of this device in patients with vertebral metastasis. A large prospective randomized trial, the KAST trial (www.clinicaltrials.gov NCT01123512), is near completion in the United States evaluating this device in osteoporotic fractures which should provide insight and evidence for the potential benefits of this device in vertebral fracture management.

References

1. Galibert P, Deramond H, Rosat P, Le Gars D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. *Neuro-Chirurgie* 1987; 33:166-168.
2. Barragan-Campos HM, Vallee JN, Lo D, Cormier E, Jean B, Rose M, Astagneau P, Chiras J. Percutaneous vertebroplasty for spinal metastases: Complications. *Radiology* 2006; 238:354-362.
3. Laredo JD, Hamze B. Complications of percutaneous vertebroplasty and their prevention. *Skeletal Radiol* 2004; 33:493-505.
4. Choe DH, Marom EM, Ahrar K, Truong MT, Madewell JE. Pulmonary embolism of polymethyl methacrylate during percutaneous vertebroplasty and kyphoplasty. *AJR Am J Roentgenol* 2004; 183:1097-1102.
5. Yoo KY, Jeong SW, Yoon W, Lee J. Acute respiratory distress syndrome associated with pulmonary cement embolism following percutaneous vertebroplasty with polymethylmethacrylate. *Spine* 2004; 29:E294-297.
6. Weill A, Chiras J, Simon JM, Rose M, Sola-Martinez T, Enkaoua E. Spinal metastases: Indications for and results of percutaneous injection of acrylic surgical cement. *Radiology* 1996; 199:241-247.
7. Cotten A, Dewatre F, Cortet B, Assaker R, Leblond D, Duquesnoy B, Chastanet P, Clarisse J. Percutaneous vertebroplasty for osteolytic metastases and myeloma: Effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up. *Radiology* 1996; 200:525-530.
8. Mousavi P, Roth S, Finkelstein J, Cheung G, Whyne C. Volumetric quantification of cement leakage following percutaneous vertebroplasty in metastatic and osteoporotic vertebrae. *J Neurosurg* 2003; 99:56-59.
9. Gaughen JR, Jr., Jensen ME, Schweickert PA, Kaufmann TJ, Marx WF, Kallmes DF. Relevance of antecedent venography in percutaneous vertebroplasty for the treatment of osteoporotic compression fractures. *AJNR Am J Neuroradiol* 2002; 23:594-600.
10. Cortet B, Cotten A, Boutry N, Flipo RM, Duquesnoy B, Chastanet P, Delcambre B. Percutaneous vertebroplasty in the treatment of osteoporotic vertebral compression fractures: An open prospective study. *J Rheumatol* 1999; 26:2222-2228.
11. Schmidt R, Cakir B, Mattes T, Wegener M, Puhl W, Richter M. Cement leakage during vertebroplasty: An underestimated problem? *Eur Spine J* 2005; 14:466-473.
12. Aebi M. Spinal metastasis in the elderly. *Eur Spine J* 2003; 12 Suppl 2:S202-213.
13. Tancioni F, Lorenzetti MA, Navarria P, Pessina F, Draghi R, Pedrazzoli P, Scorsetti M, Alloisio M, Santoro A, Rodriguez y Baena R. Percutaneous vertebral augmentation in metastatic disease: State of the art. *J Support Oncol*

2011; 9:4-10.

14. Chew C, Craig L, Edwards R, Moss J, O'Dwyer PJ. Safety and efficacy of percutaneous vertebroplasty in malignancy: A systematic review. *Clin Radiol* 2011; 66:63-72.
15. Fourney DR, Schomer DF, Nader R, Chlan-Fourney J, Suki D, Ahrar K, Rhines LD, Gokaslan ZL. Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients. *J Neurosurg* 2003; 98:21-30.
16. Shah RV. Sacral kyphoplasty for the treatment of painful sacral insufficiency fractures and metastases. *Spine J* 2012; 12:113-120.
17. Trumm CG, Jakobs TF, Stahl R, Sandner TA, Paprottka PM, Reiser MF, Zech CJ, Hoffmann RT. CT fluoroscopy-guided vertebral augmentation with a radiofrequency-induced, high-viscosity bone cement (StabiliT):Technical results and polymethylmethacrylate leakages in 25 patients. *Skeletal Radiol* 2013; 42:113-120.
18. Roos DE, Fisher RJ. Radiotherapy for painful bone metastases: An overview of the overviews. *Clin Oncol (R Coll Radiol)* 2003; 15:342-344.
19. Rose PS, Laufer I, Boland PJ, Hanover A, Bilsky MH, Yamada J, Lis E. Risk of fracture after single fraction image-guided intensity-modulated radiation therapy to spinal metastases. *J Clin Oncol* 2009; 27:5075-5079.
20. Boehling NS, Grosshans DR, Allen PK, McAleer MF, Burton AW, Azeem S, Rhines LD, Chang EL. Vertebral compression fracture risk after stereotactic body radiotherapy for spinal metastases. *J Neurosurg Spine* 2012; 16:379-386.
21. Mirovsky Y, Anekstein Y, Shalmon E, Blankstein A, Peer A. Intradiscal cement leak following percutaneous vertebroplasty. *Spine (Phila Pa 1976)* 2006; 31:1120-1124.
22. Korovessis P, Repantis T, Miller LE, Block JE. 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. Bouza C, Lopez T, Magro A, Navalpotro L, Amate JM. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: A systematic review. *Eur Spine J* 2006; 15:1050-1067.
24. Eck JC, Nachtigall D, Humphreys SC, Hodges SD. Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: A meta-analysis of the literature. *Spine J* 2008; 8:488-497.
25. 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.
26. Wardlaw D, Cummings SR, Van Meirhaeghe J, Bastian L, Tillman JB, Ranstam J, Eastell R, Shabe P, Talmadge K, Boonen S. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): A randomised controlled trial. *Lancet* 2009; 373:1016-1024.
27. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, Venmans A, van Rooij WJ, Schoemaker MC, Juttmann JR, Lo TH, Verhaar HJ, van der Graaf Y, van Everdingen KJ, Muller AF, Elgersma OE, Halkema DR, Fransen H, Janssens X, Buskens E, Mali WP. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): An open-label randomised trial. *Lancet* 2010; 376:1085-1092.
28. Levine SA, Perin LA, Hayes D, Hayes WS. An evidence-based evaluation of percutaneous vertebroplasty. *Manag Care* 2000; 9:56-60, 63.