Name of Policy: Percutaneous Vertebroplasty, Kyphoplasty, Mechanical Vertebral Augmentation and Sacroplasty

Policy #: 004
Category: Radiology/Surgical

Latest Review Date: July 2014
Policy Grade: B

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**
Percutaneous vertebroplasty is an interventional technique involving the fluoroscopically guided injection of polymethylmethacrylate (PMMA) through a needle inserted into a weakened vertebral body. The technique has been investigated as an option to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture or in those with osteolytic lesions of the spine, i.e., multiple myeloma or metastatic malignancies. Percutaneous vertebroplasty has also been investigated as an adjunct to surgery for aggressive vertebral body hemangiomias, and as a technique to limit blood loss related to surgery. Injection of PMMA is also being investigated for the treatment of sacral insufficiency fractures.

It has been proposed that vertebroplasty may provide an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body. However, other possible mechanisms of effect have been postulated, including thermal damage to intraosseous nerve fibers.

Percutaneous sacroplasty evolved from the treatment of insufficiency fractures in the thoracic and lumbar vertebrae with vertebroplasty. The procedure, essentially identical, entails guided injection of PMMA through a needle inserted into the fracture zone. While first described in 2000 as a treatment for symptomatic sacral metastatic lesions, it is most often described as a minimally invasive procedure employed as an alternative to conservative management for sacral insufficiency fractures (SIFs). SIFs are the consequence of stress on weakened bone and are often the cause of low back pain among the elderly population. Osteoporosis is the most common risk factor for SIF.

Balloon kyphoplasty is a variant of vertebroplasty and uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height before injection of the PMMA. Radiofrequency kyphoplasty is a modification of balloon kyphoplasty. In this procedure, ultra-high viscosity cement is injected into the fractured vertebral body, and radiofrequency is used to achieve the desired consistency of the cement. The ultrahigh viscosity cement is designed to restore height and alignment to the fractured vertebra, along with stabilizing the fracture.

It has been proposed that kyphoplasty may provide an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body. However, other possible mechanisms of effect have been postulated, one of which is thermal damage to intraosseous nerve fibers given that PMMA undergoes a heat-releasing (exothermic) reaction during its hardening process.

Like percutaneous balloon kyphoplasty, mechanical vertebral augmentation with Kiva® is an interventional technique involving the fluoroscopically guided injection of polymethylmethacrylate (PMMA) into a cavity created in the vertebral body with a balloon or mechanical device. Both these techniques have been investigated as options to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture, or in those with osteolytic lesions of the spine, i.e., multiple myeloma or metastatic malignancies.
Kiva® is a mechanical vertebral augmentation technique that uses an implant for structural support of the vertebral body and to provide a reservoir for bone cement. The implant is made from PEEK-OPTIMA®, a biocompatible polymer, and is inserted into the vertebral body over a guide wire. The implant can be customized by changing the coil stack height, with a maximum height of 12mm. PMMA is injected through the lumen of the implant, which fixes the implant to the vertebral body and contains the PMMA in a cylindrical column. The proposed advantage of the Kiva system is a reduction in cement leakage.

Another variant of kyphoplasty is vertebral body stenting, which utilizes an expandable scaffold instead of a balloon to restore vertebral height. The proposed advantages of vertebral body stenting are to reduce the risk of cement leakage by formation of a cavity for cement application and to prevent the loss of correction that is seen following removal of the balloon used for balloon kyphoplasty.

**Osteoporotic Vertebral Compression Fracture**
Osteoporotic compression fractures are a common problem, and it is estimated that up to one half of women and approximately one quarter of men will have a vertebral fracture at some point in their lives. However, only about one third of vertebral fractures actually reach clinical diagnosis, and most symptomatic fractures will heal within a few weeks or one month. However, a minority of patients will exhibit chronic pain following osteoporotic compression fracture that presents challenges for medical management. Chronic symptoms do not tend to respond to the management strategies for acute pain such as bed rest, immobilization/bracing device, and analgesic medication, sometimes including narcotic analgesics. The source of chronic pain after vertebral compression fracture may not be from the vertebra itself but may be predominantly related to strain on muscles and ligaments secondary to kyphosis. This type of pain frequently is not improved with analgesics and may be better addressed through exercise.

**Sacral Insufficiency Fractures**
Spontaneous fracture of the sacrum in patients with osteoporosis was described by Lourie in 1982 and presents as lower back and buttock pain with or without referred pain in the legs. Although common, SIFs can escape detection due to low provider suspicion and poor sensitivity on plain radiographs, slowing the application of appropriate intervention. Similar interventions are used for sacral and vertebral fractures including bed rest, bracing, and analgesics. Initial clinical improvements may occur quickly; however, the resolution of all symptoms may not occur for nine to twelve months.

**Vertebral/Sacral Body Metastasis**
Metastatic malignant disease involving the spine generally involves the vertebrae/sacrum, with pain being the most frequent complaint. While radiation and chemotherapy are frequently effective in reducing tumor burden and associated symptoms, pain relief may be delayed days to weeks, depending on tumor response. Further, these approaches rely on bone remodeling to regain strength in the vertebrae/sacrum, which may necessitate supportive bracing to minimize the risk of vertebral/sacral collapse during healing.
Vertebral Hemangiomas
Vertebral hemangiomas are relatively common lesions noted in up to 12% of the population based on autopsy series; however, only rarely do these lesions display aggressive features and produce neurologic compromise and/or pain. Treatment of aggressive vertebral hemangiomas has evolved from radiotherapy to surgical approaches using anterior spinal surgery for resection and decompression. There is the potential for large blood loss during surgical resection, and vascular embolization techniques have been used as adjuncts to treatment to reduce blood loss. Percutaneous vertebroplasty has been proposed as a way to treat and stabilize some hemangioma to limit the extent of surgical resection and as an adjunct to reduce associated blood loss from the surgery.

Policy:
Effective for dates of service on or after November 3, 2013:
Percutaneous balloon kyphoplasty and percutaneous vertebroplasty meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for the treatment of symptomatic osteoporotic vertebral fractures that have failed to respond to conservative treatment (e.g., analgesics, physical therapy, and rest) for at least six (6) weeks.

Percutaneous balloon kyphoplasty and percutaneous vertebroplasty meet Blue Cross and Blue Shield of Alabama’s medical criteria for the treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies.

Percutaneous balloon kyphoplasty and percutaneous vertebroplasty meet Blue Cross and Blue Shield of Alabama’s medical criteria for the treatment of vertebral hemangiomas with severe pain or nerve compression.

Percutaneous balloon kyphoplasty and percutaneous vertebroplasty do not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational for all other indications, including use in acute vertebral fractures due to osteoporosis or trauma.

Percutaneous sacroplasty does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage is considered investigational for all indications, including use in sacral insufficiency fractures due to osteoporosis and spinal lesions due to metastatic malignancies or multiple myeloma.

Percutaneous mechanical vertebral augmentation using any other device, including but not limited to Kiva, and vertebral body stenting does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational.

Effective for dates of service May 27, 2010 through November 2, 2013:
Percutaneous vertebroplasty and kyphoplasty meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when one of the following criteria is met:
• Sub-acute (age of fracture must be six months or less) **osteoporotic** vertebral collapse with pain for at four to six weeks that has not responded to conservative management (rest, external support, treatment with analgesics, physical therapy if indicated, and calcium) and is severe enough to cause significant immobility and impairment of activities of daily living and/or require maximal pain management; or
• Osteolytic vertebral metastasis or myeloma with severe back pain related to destruction of a vertebral body that does not involve the major part of the cortical bone and has not responded to conservative measures and/or require maximal pain management; or
• Vertebral hemangiomas with severe pain or nerve compression.

**Percutaneous vertebroplasty and kyphoplasty do not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for the **following indications:**

• Patients with healthy bone;
• Patients whose fractures or collapse of the vertebrae are due to high energy accidents or injury;
• Patients with spinal curvature, such as scoliosis or kyphosis, due to causes other than osteoporosis;
• Patients with spinal stenosis or herniated discs with nerve or spinal cord compression and loss of neurological function;
• Patients with acute (less than 1 month) vertebral fracture.

**Sacroplasty does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational.**

Use of the **arcuplasty device** with a sacroplasty **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational.**

Use of the **skyphoplasty device** with a kyphoplasty **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational.**

*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member’s contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*

**Key Points:**
The most recent literature update for this policy was performed through March, 2014.

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diagnosis, and most symptomatic fractures will heal within a few weeks or one month. However, a minority of patients will exhibit chronic pain following osteoporotic compression fracture that presents challenges for medical management. Chronic symptoms do not tend to respond to the management strategies for acute pain such as bed rest, immobilization/bracing device, and analgesic medication, sometimes including narcotic analogics. The source of chronic pain after vertebral compression fracture may not be from the vertebra itself but may be predominantly related to strain on muscles and ligaments secondary to kyphosis. This type of pain frequently is not improved with analgesics and may be better addressed through exercise.

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Vertebral hemangiomas are relatively common lesions noted in up to 12% of the population based on autopsy series; however, only rarely do these lesions display aggressive features and produce neurologic compromise and/or pain. Treatment of aggressive vertebral hemangiomas has evolved from radiation therapy to surgical approaches using anterior spinal surgery for resection and decompression. There is the potential for large blood loss during surgical resection, and vascular embolization techniques have been used as adjuncts to treatment to reduce blood loss. Percutaneous vertebroplasty or kyphoplasty has been proposed as a way to treat and stabilize some hemangioma to limit the extent of surgical resection and as an adjunct to reduce associated blood loss from the surgery.

**Percutaneous Vertebroplasty and Sacroplasty**
For treatment of osteoporosis and malignancy with percutaneous vertebroplasty or sacroplasty, the primary beneficial outcomes of interest are relief of pain and improvement in ability to function. Ex vivo cadaver studies reporting bone strength as a surrogate outcome measure have been reported but are not included in this evaluation of health outcomes. In treatment of aggressive hemangioma, the primary benefits of percutaneous vertebroplasty include relief of pain and reduction of blood loss associated with surgical treatment.

Pain and functional ability are subjective outcomes and, thus, may be susceptible to placebo effects. Furthermore, the natural history of pain and disability associated with these conditions may be variable. Therefore, controlled comparison studies would be valuable to demonstrate the clinical effectiveness of vertebroplasty and sacroplasty over and above any associated...
nonspecific or placebo effects and to demonstrate the effect of treatment compared with alternatives such as continued medical management.

In all clinical situations, adverse effects related to complications from vertebroplasty and sacroplasty are the primary harms to be considered. Principal safety concerns relate to the incidence and consequences of leakage of the injected polymethylmethacrylate (PMMA).

**Percutaneous Vertebroplasty**

The evidence on this question consists of a number of randomized clinical trials (RCTs), two of which included a sham control, and many case series. This policy was originally based on a 2000 TEC Assessment and updated with TEC Assessments in 2004, 2005, 2008, 2009, and 2010. Originally, the available data were observational. The largest of the case series reported results from a prospectively collected database with 552 patients from a large academic department. Evidence from observational studies were generally consistent in showing significant decreases in pain from an initial preoperative level of eight to nine on a visual analog scale (VAS, or similar score proportionate to the highest possible score) to two to four, typically within one day of receiving the procedure. Such pain relief appeared to be lasting in the limited studies that reported long-term outcomes. In terms of adverse outcomes, leakage of the cement outside of the vertebral body was a common event, occurring in between 19% and 72% in studies that reported its occurrence.

Beginning in 2007, data from RCTs began appearing in the literature. This policy is now focused on RCT data.

**RCTs of Vertebroplasty versus Medical Management with Sham Controls**

In 2009, two randomized trials compared vertebroplasty to a medical management using a sham placebo control (that included local anesthetic), which mimicked the vertebroplasty procedure up to the point of cement injection. Buchbinder and colleagues reported results of a four center, randomized, double-blind, sham-controlled trial that was designed to determine short-term efficacy and safety of vertebroplasty for alleviating pain and improving physical functioning in persons with painful osteoporotic vertebral fractures. A total of 78 participants with one or two painful osteoporotic vertebral fractures of duration less than one year were assigned to undergo vertebroplasty or sham procedure (i.e., injection of local anesthetic into the facet capsule and/or periosteum). Ninety-one percent of participants completed six months of follow-up. The participants, investigators (other than the radiologists performing the procedure), and outcome assessors were blind to the treatment assignment.

Recruitment took place within the practices of both general practitioners and specialists from hospital inpatient and emergency departments. In general, participants were required to have back pain of no more than 12 months and the presence of at least one but no more than two recent vertebral fractures. Participants were evaluated at baseline, then with a mailed questionnaire at one week and one, three, and six months after the procedure. The primary outcome was overall pain (over the course of the previous week) measured on a 0 to 10 VAS, with 1.5 representing the minimal clinically important difference. A sample size of 24 per group was calculated to provide 80% power with two sided $\alpha = 0.05$ to show a 2.5-point post-procedure difference assuming a three point standard deviation (SD). All analyses were performed.
according to intention-to-treat principles. Results are presented as difference from baseline. For the primary outcome of overall pain, the authors reported no significant difference in VAS pain score at three months. With reductions in pain and improvements in quality of life observed in both groups, the authors concluded vertebroplasty provided no benefit.

There was considerable variability in pain scores, which may in part be due to a lack of minimum pain score at entry. The primary outcome measure was the mean difference in VAS from baseline. For some continuous outcomes, such as pain, there is a magnitude of improvement that is clinically meaningful on an individual level; someone achieving that minimal change can be considered a responder. Under these circumstances, a fundamental limitation of continuous effect measures is failing to identify the proportion of patients experiencing a meaningful clinical response. Since a clinically meaningful important improvement has been established, the proportion of patients responding is an informative outcome that can supplement and extend the comparison of mean differences. Moreover, when considered in this manner, response or meaningful improvement (2.5 on the VAS) in overall pain at one, three, and six months tended to be more frequent with vertebroplasty—respective relative risks (RRs) of 1.2 (95% confidence interval [CI]: 0.7 to 2.0), 1.5 (95% CI: 0.9 to 2.6), and 1.3 (95% CI: 0.8 to 2.1). However, detecting an increase in clinical response rates often requires larger numbers of patients. For example, detecting an increase in response from 40% (sham) to 60% with 80% power would have required a sample exceeding 200 participants. Also, at entry, many participants had experienced pain longer than three months, suggesting that the VAS may not be as responsive as other measures for these patients. This adds to the uncertainty as to whether a mean change in VAS will capture clinically meaningful improvement.

Kallmes et al conducted a multicenter, randomized, double-blind, sham-controlled trial in which 131 participants with one to three painful osteoporotic vertebral fractures were assigned to undergo vertebroplasty or sham procedure (injection of local anesthetic into the facet capsule and/or periosteum). Participants had back pain for no more than 12 months and had a current pain rating of at least three on VAS at baseline. Participants were evaluated at baseline, then again at various time points to one year post-procedure. Ninety-seven percent completed a one month follow-up, and 95% completed three months. The primary outcomes were scores on the Roland-Morris Disability Questionnaire (RMDQ) and average back pain intensity during the preceding 24 hours at one month, with a reduction of 30% on the RMDQ and VAS pain considered a clinically meaningful difference. The study initially had 80% power to detect differences in both primary and secondary outcomes with 250 patients, with a 2-sided alpha of 0.05 on the basis of a 2.5-unit advantage for vertebroplasty over placebo on the RMDQ and 1.0 point difference on VAS. After recruitment difficulty and interim analysis on the first 90 participants, target sample size was decreased to 130 participants with 80% power for primary aims maintained. All primary analyses were performed according to intention-to-treat principles and results presented as mean score for the RMDQ and pain intensity.

For the primary endpoints at one month, there were no significant between group differences. There was a trend toward a higher clinically meaningful improvement in pain at one month (30% reduction from baseline) in the vertebroplasty group (64% vs. 48%, respectively; p=0.06). At 3 months, 43% from the control group vs. 12% in the vertebroplasty group crossed over (p<0.001). The crossovers did not affect study outcomes, as they occurred after the primary outcome.
assessment. However, significantly more participants in the control group chose to cross over than in the vertebroplasty group. By one year, 16% of patients who underwent vertebroplasty and 60% of control subjects had crossed over to the alternative procedure (p<0.001). As-treated analysis found no significant difference in RMDQ or pain scores between the two groups. ITT analysis found a modest one-point difference in pain rating, but no significant difference in RMDQ. There was a significant difference in the percentage of patients showing a 30% or greater improvement in pain (70% of patients randomized to vertebroplasty vs 45% of patients randomized to the control group).

Staples and colleagues conducted a patient-level meta-analysis of the two sham-controlled trials to determine whether vertebroplasty is more effective than sham in specific subsets of patients. This subset analysis focused on duration of pain (<6 weeks vs. >6 weeks) and severity of pain (score <8 or >8 on an 11-point numerical rating scale). Included in the analysis were 209 participants (78 from the Australian trial and 131 from the U.S. trial); 27% had pain of recent onset and 47% had severe pain at baseline. The primary outcome measures, pain scores and function on the RMDQ at one month, were not significantly different between groups. Responders’ analyses were also conducted based on a 3-unit improvement in pain scores, a 3-unit improvement on the RMDQ, and a 30% improvement in each of the pain and disability outcomes. The only difference observed between groups was a trend for a higher proportion of the vertebroplasty group to achieve at least 30% improvement in pain scores (RR: 1.32, 95% CI: 0.98 to 1.76, p=0.07), a result that may have been confounded by the greater use of opioid medications in that group. Overall, this analysis does not support the hypothesis that selected subgroups of patients, including those with pain of six weeks’ duration or less or those with severe pain, would benefit from vertebroplasty.

RCTs of Vertebroplasty versus Medical Management without Sham Controls

VERTOS II, reported by Klazen et al in 2010, was an open-label prospective randomized trial of 202 patients at six hospitals in the Netherlands and Belgium. Participants with at least one painful osteoporotic vertebral fracture with a duration of six weeks or less were assigned to undergo vertebroplasty or conservative management (i.e., bed rest, analgesia, and cast and physical support). Ninety-three participants received vertebroplasty, while 95 received conservative management; 81% of participants completed one year follow-up. The trial was designed to assess the efficacy of vertebroplasty compared to conservative management for the treatment of osteoporotic vertebral compression fractures. There was no blinding of participants, investigators, or outcome assessors to treatment assignment, due to the lack of a sham procedure.

Participants were recruited after referral from their primary care provider for spine radiography because of back pain. In general, participants were required to be at least 50 years of age or older, have compression fracture with height loss of the vertebral body of at least 15% on x-ray of the spine, the level of fracture was Th5 or lower back with pain of a duration of six weeks or less with a severity of at least five on the VAS. Participants were clinically evaluated at baseline, one day, one week, one month, three months, six months and 12 months after treatment. Primary outcome was pain relief at one month and 12 months measured on a 10-point VAS scale. A sample size of 100 per group was calculated to provide 80% power with an alpha of 0.05 to show a 25% difference in pain relief. All analyses were performed according to intention-to-treat principles. Clinically significant pain relief was defined as 30% change on the VAS (0-10 scale).
One hundred and one participants were enrolled into the treatment group and 101 into the control arm; 81% completed 12 months’ follow-up. Except for the primary outcome, difference in mean pain score from baseline at three months and 12 months, vertebroplasty resulted in greater pain relief than did medical management at one month and one year; there were significant between group differences at one month (2.6; 1.74 to 3.37, p<0.0001) and at one year (2.0; 1.13 to 2.80, p<0.0001). Survival analysis showed significant pain relief was quicker (29.7 vs. 115.6 days) and was achieved in more patients after vertebroplasty than after conservative management. There was cement leakage in 72% of patients after vertebroplasty with all patients remaining asymptomatic, and at a mean of 11.4 months’ follow-up, there was no significant difference in number of new fractures between groups, with 18 new fractures in 15 patients who had vertebroplasty compared to 30 new fractures in 21 participants undergoing medical management.

A methodologic strength of this study is the study’s focus on acute fracture, a subset of those with osteoporotic vertebral compression fractures, while other studies (Buchbinder et al 2009; Kallmes et al 2009) enrolled participants with pain out to one year. The inclusion of both chronic and acute fractures may mask the efficacy of the procedure in one subset. Klazen and colleagues also provided an a priori definition of clinically significant change in pain as one that registered a 30% difference on the 10-point VAS. These data were incorporated as events in a survival analysis as part of the analysis of the primary outcome.

A subsequent report from the VERTOS II study described the 12-month natural history of pain in patients in the conservative treatment arm. Patients in the control arm were followed until pain relief was achieved, defined as a VAS score of three or less. Results were analyzed by Kaplan-Meier survival analysis. By 12-month follow-up, 57 of 95 patients (60%) were considered to have sufficient pain relief, with most experiencing sufficient pain relief in the first three months. Comparison by logistic regression analysis with the 38 patients (40%) who still had pain (VAS >4) at 12 months did not reveal any significant differences between the groups for the clinical and imaging factors that were evaluated.

In 2011, Farrokhi and colleagues reported a randomized trial that compared vertebroplasty with optimal medical management in 82 patients. Patients had painful osteoporotic vertebral compression fractures that were refractory to analgesic therapy for at least four weeks and less than one year. The patients and the physicians involved in the treatment of the patients were not aware of the treatment that the other group was receiving. Control of pain and improvement in quality of life were measured by independent raters before treatment and at one week and 2, 6, 12, 24, and 36 months after the beginning of treatment. Radiological evaluation to measure vertebral body height and correction of deformity was performed before and after treatment and after 36 months of follow-up. At one week, the mean VAS score decreased from 8.4 to 3.3 in the vertebroplasty group and from 7.2 to 6.4 in the conservative management group, with between group differences that remained significant through six months of follow-up. Group differences on the Oswestry lower back pain score were significantly lower in the vertebroplasty group throughout the 36 months of the study. New symptomatic adjacent fractures developed in one patient (2.6%) in the vertebroplasty group and six patients (15.4%) in the conservative management group. In one patient, epidural cement leakage caused severe lower extremity pain and weakness that was treated with bilateral laminectomy and evacuation of bone cement.
Rousing et al reported on a non-blinded randomized trial in which participants were randomized to either vertebroplasty or conservative management. These participants had no conservative therapy prior to enrolling in the trial. The study enrolled 40 participants with acute fractures and 10 with subacute (two to eight weeks). While immediate pain relief was observed in the vertebroplasty group, reductions in pain from baseline to three month follow-up were similar in the two groups. The authors concluded that conservative management should be used in the acute phase. The primary limitations of this study include its small size and incomplete pain assessment at the baseline visit.

The VERTOS study was a small randomized clinical trial of 34 patients. Patients had been refractory to medical management for at least six weeks and no longer than six months. The authors noted that many patients had been referred for vertebroplasty following failed conservative treatment and did not want to be randomized to the optimized medication control group or chose to crossover to vertebroplasty after only two weeks of conservative treatment. Thus, the follow-up in the study was very short. Vertebroplasty was found to decrease analgesic use (1.9 to 1.2 vs. 1.7 to 2.6 in the optimized medication group) and resulted in a 19% improvement in the RMDQ (vs. -2% in controls) two weeks following the procedure. Excluding two patients (11%) who had adjacent vertebral compression fractures by the two week follow-up, mean VAS scores for pain decreased from 7.1 to 4.4 (vs. 7.6 to 6.4 for controls). Patients who crossed over from conservative management to vertebroplasty had improvements after the procedure.

Despite the completion of five RCTs, including two with sham control, the efficacy of vertebroplasty for painful osteoporotic compression fractures remains uncertain. The two randomized, sham-controlled trials concluded that vertebroplasty showed no significant benefit above sham for painful osteoporotic fractures. However, some uncertainty remains around the interpretation of their conclusions. While the use of a sham procedure is a major methodologic strength to control for nonspecific (placebo) effects, the sham used in the trial is not without controversy, as it might be considered an active control, given that the effect of injecting local anesthetic in the facet capsule and/or periosteum is unknown. Without a clear understanding of the short- and long-term effects of the injection on pain, questions will remain. Also, both trials were underpowered to observe and compare the proportion of participants experiencing a clinically meaningful difference in pain, which is the most clinically relevant outcome measure. Furthermore, the responder outcome measures in both trials showed trends toward an improvement in the rate of meaningful clinical response, although the differences between groups were not statistically significant.

In contrast, the four RCTs without sham control report that vertebroplasty is associated with significant improvements in pain. Three of the four trials were small, and the studies included populations with different time periods of symptoms and different prior treatments. It is possible that the effect reported in these non-sham controlled trials is due to a placebo effect, given that these studies were not blinded and the outcome of pain is a subjective, patient-reported outcome that is prone to the placebo effect. It is also possible that the differences in these trials represent a true treatment effect and that the sham control had a therapeutic effect in reducing short-term pain, thus obscuring any impact of vertebroplasty.
Other Studies
Although not randomized, there was one other comparative study specifically aimed at patients with acute fracture. Diamond et al enrolled 79 consecutive patients with acute vertebral fractures. All patients were offered vertebroplasty, and those who declined were followed as a comparison group. The two groups had balanced baseline characteristics. At 24 hours, the group undergoing vertebroplasty (n=55) had much improved pain compared to the control group (n=24). However, at six weeks and between six and twelve months, there were no differences between groups in pain scores. The control group had an identical mean pain score to the vertebroplasty group at the end of follow-up. Similar findings were shown for the Barthel index of physical functioning. At long-term follow-up, there was still slightly higher functioning in the group undergoing vertebroplasty but no difference in the percent improvement from baseline between groups. The authors interpreted these findings as demonstrating that vertebroplasty produced faster resolution of symptoms than conservative management, as was shown in the Klazen trial.

In 2011, Edidin et al reported mortality risk in Medicare patients who had vertebral compression fractures and had been treated with vertebroplasty, kyphoplasty or nonoperatively. This study was industry-funded. Using the U.S. Medicare data set, they identified 858,978 patients who had vertebral compression fractures between 2005 and 2008. The data set included 119,253 kyphoplasty patients and 63,693 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to four years). Cox regression was used to evaluate the joint effect of multiple covariates, which included gender, age, race/ethnicity, patient health status, type of diagnosed fracture, site of service, physician specialty, socioeconomic status, year of diagnosis, and census region. After adjusting for covariates, patients in the operated cohort (vertebroplasty or kyphoplasty) were found to have a higher adjusted survival rate (60.8%) than patients in the nonoperated cohort (50.0%) and were 37% less likely to die. The adjusted survival rates for vertebroplasty or kyphoplasty were 57.3% and 62.8%, respectively, a 23% lower relative risk for kyphoplasty. As noted by the authors, a causal relationship cannot be determined from this study.

Adverse Events
Yi et al assessed the occurrence of new vertebral compression fractures after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) versus conservative treatment in an RCT with 290 patients (363 affected vertebrae). Surgically treated patients were discharged the next day. Patients treated conservatively (pain medication, bed rest, body brace, physiotherapy) had a mean length of stay of 13.7 days. Return to usual activity occurred at one week for 87.6% of operatively treated patients and at two months for 59.2% of conservatively treated patients. All patients were evaluated with radiographs and magnetic resonance imaging at six months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80), 10.7% of patients had experienced 42 new symptomatic vertebral compression fractures. There was no significant difference in the incidence of new vertebral fractures between the operative (18 total; nine adjacent, nine nonadjacent) and conservative (24 total; five adjacent, 16 nonadjacent, three same level) groups, but the mean time to a new fracture was significantly shorter in the operative compared with nonoperative group (9.7 vs 22.4 months).
A systematic review of the safety and efficacy of vertebroplasty in malignancy was reported by Chew et al in 2011. Thirty relevant studies were identified, totaling 987 patients. Included in the review were a single randomized controlled trial and seven prospective studies. Most centers reported treating no more than four vertebrae per session. Pain reduction ranged between 20% and 79%. Five deaths were attributable to vertebroplasty, two from chest infections following general anesthesia, one from a cement pulmonary embolus, and two from sepsis after emergency spinal decompression. Another 19 patients suffered a serious complication related to the procedure, with 13 requiring emergency spinal decompression. Reports of complications occurred in studies with a mean cement volume of more than 4mL, suggesting a possible association between the volumes of cement injected and adverse events.

In 2012, Wang et al reported a systematic review of pulmonary cement embolism (PCE) associated with percutaneous vertebroplasty. PCE was noted in 50 cases in observational studies, with a reported incidence ranging from 2.1% in retrospective observational studies to 26% in prospective observational studies that had standard postprocedural chest. There were an additional 34 patients identified from case reports with PCE, 30 of whom were symptomatic. Five deaths due to PCE after vertebroplasty have been reported.

**Percutaneous Sacroplasty**
Sacroplasty is an evolving technique with numerous methods (short axis, long axis, balloon-assisted short axis, and iliosacral screws). No randomized trials of sacroplasty have been reported. The largest prospective report is an observational cohort study of 52 consecutive patients undergoing sacroplasty for sacral insufficiency fractures using the short-axis technique. Patients had a mean age of 75.9 years and a mean duration of symptoms of 34.5 days (range: 4-89 days) and mean VAS score of 8.1 at baseline. Improvement on the VAS scale was measured at 30 minutes and 2, 4, 12, 24, and 52 weeks postprocedure. At each interval, statistically significant improvement over baseline was observed and maintained through 52 weeks.

The largest series is a retrospective multicenter analysis of 204 patients with painful sacral insufficiency fractures and 39 patients with symptomatic sacral lesions treated with either the short-axis or long-axis technique. One hundred and sixty-nine patients had bilateral sacral insufficiency fractures and 65 patients had additional fractures of the axial skeleton. VAS improved from 9.2 before treatment to 1.9 after treatment in patients with sacral insufficiency fractures, and from 9.0 to 2.6 in patients with sacral lesions. There was one case of radicular pain due to extravasation of cement requiring surgical decompression.

Another series was a retrospective review of 57 patients treated with sacroplasty under computed tomography (CT) guidance for sacral insufficiency fractures. The short- or long-axis approach was dictated by the length and type of the fracture and patient anatomy. Follow-up data at 2.5 weeks was available for 45 patients (79%), and the outcome measures were inconsistent. For example, activity pain scores were collected from 13 patients, and rest pain scores were collected from 29 patients. Of the 45 patients with outcome data, 37 (82%) were reported to have experienced either a numerical or descriptive decrease from initial pain of at least 30%.

Additional literature reports are mostly consistent reporting immediate improvement following the procedure. Due to the small size of the evidence base, harms associated with sacroplasty have
not been adequately studied. There are complications of cement leakage with sacroplasty that are not observed with vertebroplasty. Leakage of polymethylmethacrylate (PMMA) into the presacral space, spinal canal, sacral foramen, or sacroiliac joint may result in pelvic injection of PMMA, sacral nerve root or sacral spinal canal compromise, or sacroiliac joint dysfunction. Performing sacroplasty on Zone 1 fractures only can minimize these risks.

**Balloon Kyphoplasty and Mechanical Vertebral Augmentation**

For treatment of osteoporosis and malignancy with percutaneous kyphoplasty, the primary beneficial outcomes of interest are relief of pain and improvement in ability to function. Kyphoplasty may also result in restoration of lost vertebral body height with associated reduction in kyphotic deformity. Potential health outcomes related to kyphotic deformity include pulmonary or gastrointestinal compression and associated symptoms, and vertebral compression fractures may be associated with lower health-related quality of life. Ex vivo cadaver studies reporting bone strength as a surrogate outcome measure have been reported but are not included in this evaluation of health outcomes.

Pain and functional ability are subjective outcomes and, thus, may be susceptible to placebo effects. Furthermore, the natural history of pain and disability associated with these conditions may be variable. Therefore, controlled comparison studies would be valuable to demonstrate the clinical effectiveness of kyphoplasty over and above any associated nonspecific or placebo effects and to demonstrate the effect of treatment compared to an alternative such as continued medical management.

In all clinical situations, adverse effects related to complications from kyphoplasty are the primary harms to consider. Principal safety concerns relate to the incidence and consequences of leakage of the injected polymethylmethacrylate (PMMA).

Originally the available data were observational. Evidence from observational studies were generally consistent in showing significant decreases in pain from an initial preoperative level of seven to nine on a visual analogue scale ([VAS] or similar score proportionate to the highest possible score) to two to four, typically within one day of receiving the procedure. Such pain relief appeared to be lasting in the four studies that reported long-term outcomes, although most of the studies had large losses to follow-up.

In terms of other outcomes, results generally showed improvement after kyphoplasty. For example, Coumans et al reported statistically significant improvements in several subscores of the short form-36 (SF-36), including physical function, mental health, pain, vitality, and social function. Crandall et al showed decreases in the amount of medication use over time and Ledlie et al showed that the proportion of patients fully ambulatory increased after the procedure. Two nonrandomized studies that compared kyphoplasty to conservative management for treatment of osteoporotic fractures showed that patients receiving kyphoplasty had greater improvements in pain and function.

In terms of adverse outcomes, the most common adverse outcome reported in these studies was leakage of the cement outside of the vertebral body, occurring between 6% and 38% in six studies that reported its occurrence. The early literature review also identified a publication on
treatment of pathologic compression fractures in which kyphoplasty and spinal radiosurgery were combined. The 2008 TEC Assessment found that although many case series had been published, there was a lack of rigorous comparative trials of kyphoplasty. Since case series studies are subject to many sources of bias and are generally not reliable evidence of efficacy, it was concluded that the evidence for kyphoplasty did not meet TEC criteria.

Beginning in 2009, data from randomized clinical trials (RCTs) began appearing in the literature. This policy is now focused on RCT data.

**Balloon Kyphoplasty**

**Osteoporotic Compression Fractures**

In 2009, Wardlaw et al reported on the findings of the FREE trial, an industry-sponsored multisite RCT in which 300 adult participants with one to three painful osteoporotic vertebral fractures of less than three months’ duration were assigned to undergo kyphoplasty or conservative care. Twenty-four month results of this study were reported by Boonen et al in 2011 and by Van Meirhaeghe et al in 2013. This study was designed to examine efficacy and safety of kyphoplasty for the treatment of acute vertebral compression fractures. There was no blinding in this trial. Participants were recruited from 21 sites in eight countries. Participants needed to have back pain of no more than three months’ duration and the presence of at least one but no more than three acute vertebral fractures. Participants were evaluated at baseline, then at 1, 3, 6, 12, and 24 months after the procedure. The primary outcome was the difference in change from baseline to one month in the SF-36 physical component summary (PCS) between the kyphoplasty and control groups.

A total of 138 participants who underwent kyphoplasty and 128 control patients completed one month of follow-up. Scores for the primary outcome, one-month change in SF-36 PCS score, were significantly higher for those in the kyphoplasty group. The difference between the two groups was 5.2 points (95% confidence interval [CI]: 2.9–7.4; p <0.0001). Data were available from 232 patients (77%) at 24 months. Kyphoplasty was associated with greater improvements in SF-36 PCS scores at six month follow-up (3.39 points), but not at 12 or 24 months. Greater improvement in back pain was observed over 24 months for kyphoplasty (-1.49 points) and remained statistically significant at 24 months. Participants in the kyphoplasty group also reported greater improvements in quality of life and Roland Morris disability score at short-term follow-up. At 12 months, fewer kyphoplasty patients (26.4% vs. 42.1%) had received physical therapy or walking aids, back braces, wheelchairs, miscellaneous aids, or other therapy. Fewer kyphoplasty patients used opioid medications through six months (29.8% vs. 42.9%) and fewer pain medications through 12 months (51.7% vs. 68.3%). While not a study outcome, the authors also noted that patients who received kyphoplasty had approximately 60 fewer days of restricted activity during the year than controls. Other differences between the groups were no longer apparent at 12 months; possibly due to natural healing of fractures. At 24 months, there was no significant difference between groups in the number of patients with new radiographic vertebral fractures (47.5% for kyphoplasty, 44.1% for control). Two device-related serious adverse events (a spondylitis and an anterior cement migration) were reported.

Berenson and colleagues reported the results of an international randomized multicenter clinical trial in 2011. They enrolled 134 patients with cancer who were at least 21 years of age.
Participants had at least one and not more than three painful vertebral compression fractures (VCF). (These appear to be due to osteoporosis, rather than from a metastatic lesion.) The primary outcome was change in functional status from baseline at one month as measured by the Roland Morris Disability Questionnaire (RMDQ). Treatment allocation was not blinded, and the primary outcome at one month was analyzed using all participants with data both at baseline and at one month. Participants needed to have a pain score of at least four on a 0-10 scale. Crossover to the balloon kyphoplasty arm was allowed after one month. The authors report scores in the kyphoplasty and nonsurgical groups of 17.6 and 18.2 at baseline, respectively, and 9.10 and 18.0 at one month follow-up. P-value for the between group difference in scores p=0.0001.

In 2011, Edidin et al reported mortality risk in Medicare patients who had vertebral compression fractures and had been treated with vertebroplasty, kyphoplasty, or nonoperatively. This study was industry-funded. Using the U.S. Medicare data set, they identified 858,978 patients who had vertebral compression fractures between 2005 and 2008. The data set included 119,253 kyphoplasty patients and 63,693 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to four years). Cox regression was used to evaluate the joint effect of multiple covariates, which included gender, age, race/ethnicity, patient health status, type of diagnosed fracture, site of service, physician specialty, socioeconomic status, year of diagnosis, and census region. After adjusting for covariates, patients in the operated cohort (vertebroplasty or kyphoplasty) were found to have a higher adjusted survival rate (60.8%) than patients in the nonoperated cohort (50.0%) and were 37% less likely to die. The adjusted survival rates for vertebroplasty or kyphoplasty were 57.3% and 62.8%, respectively, a 23% lower relative risk for kyphoplasty. As noted by the authors, a causal relationship cannot be determined from this study.

In summary, two moderate-sized unblinded RCTs report short-term benefits for kyphoplasty on pain and other outcomes in patients with painful osteoporotic fractures. Similar results are seen in numerous case series that report large short-term improvements in pain following kyphoplasty. There are no sham-controlled RCTs that have been completed for this technique.

The major limitation of these RCTs was the lack of a sham procedure. Nonspecific or placebo effects can be quite large for an invasive procedure such as kyphoplasty in which there is not blinding. Due to the possible sham effect observed in the recent trials of vertebroplasty, the validity of results from non-sham-controlled trials are questionable. The placebo effect may be on the order of 6 to 7mm on a 100mm scale, for invasive procedures, and even larger effects (10%) were observed in the sham-controlled vertebroplasty trials. The analyses were appropriate; however, it would have been preferable to have the number of participants reporting a clinically meaningful change as the primary outcome. In cases of chronic pain, mean differences in continuous measures may not be reflective of the percent of patients who have a meaningful clinical response.

Due to the concerns about the validity of the available RCTs, it is difficult to come to conclusions regarding the efficacy of kyphoplasty. Despite most case series showing consistent improvements in pain after the procedure, and the same conclusion being reached in the 2 RCTs, it is not possible to conclude that these improvements are a true treatment effect, or a non-specific, placebo effect.
Vertebral Body Metastasis
In the early literature reviews, three case series were reviewed evaluating a total of 52 patients. Outcome measures varied among these three studies, but all showed improvements either in VAS pain score, several aspects of physical functioning as measured by SF-36, or improvement in a disability score. There are no RCTs of kyphoplasty for vertebral body metastasis. Because the results of the comparative studies of vertebroplasty suggest possible placebo or natural history effects, case series are insufficient to make conclusions about the effect of kyphoplasty on health outcomes.

Vertebral Hemangiomas
For symptomatic vertebral body hemangioma with aggressive features, no studies reported pre- and post-procedure pain evaluations. Therefore, the findings of all studies that reported more than a single case (six studies, totaling 64 patients) were evaluated. The studies using percutaneous cementoplasty as an adjunct to surgical treatment suggest that the use of percutaneous cementoplasty to treat the vertebral body component of the vascular lesion may contribute to avoiding the substantial blood loss that has been historically described with primary surgical resection (curettage). However, the additional use of other procedures in these studies may make it difficult to attribute the lower blood loss to this procedure. These studies do not provide controlled comparisons of the morbidity of treating hemangiomas with percutaneous cementoplasty as an adjunct to surgery and the morbidity of surgical treatment without cementoplasty.

Adverse Events
Yi et al assessed the occurrence of new VCFs after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) versus conservative treatment in an RCT with 290 patients (363 affected vertebrae). Surgically treated patients were discharged the next day. Patients treated conservatively (pain medication, bedrest, a body brace, physiotherapy) had a mean length of stay of 13.7 days. Return to usual activity occurred at one week for 87.6% of operatively treated patients and at two months for 59.2% of conservatively treated patients. All patients were evaluated with radiographs and magnetic resonance imaging at six months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80), 10.7% of patients had experienced 42 new symptomatic VCFs. There was no significant difference in the incidence of new vertebral fractures between the operative (18 total, nine adjacent nine nonadjacent) and conservative (24 total, five adjacent, 16 nonadjacent, three same level) groups, but the mean time to a new fracture was significantly shorter in the operative compared with nonoperative group (9.7 vs 22.4 months).

Cement leakage, although reduced in kyphoplasty relative to vertebroplasty, remains a concern. There continue to be case reports of right ventricle perforation, cardiac tamponade, and embolism of cement into pulmonary vessels.

Mechanical Vertebral Augmentation with Kiva® versus Balloon Kyphoplasty
Kiva® System as Vertebral Augmentation Treatment (KAST) is an industry-sponsored multicenter phase 3 randomized IDE trial (NCT01123512). Vertebral augmentation with the Kiva® VCF System® was compared with balloon kyphoplasty in 300 patients with one or two
osteoporotic vertebral compression fractures. The study was completed in May 2013.
Preliminary results of this study were presented at the Society for Interventional Radiology
Annual Scientific Meeting in March 2014, reporting non-inferiority of KIVA® compared with
kyphoplasty. However, this study has not yet been published in a peer-reviewed journal.

In 2013, Korovessis reported a randomized trial comparing mechanical vertebral augmentation
with the Kiva device versus balloon kyphoplasty in 180 patients with osteoporotic vertebral body
fractures. The groups showed similar improvements in VAS for back pain, SF-36, and Oswestry
Disability Index (ODI). For example, there was a greater than 5.5 point improvement in VAS in
54% of patients in the Kiva group and 43% of patients in the balloon kyphoplasty group.
Radiological measures of vertebral height were similar in the two groups. Kiva reduced the
Gardner kyphotic angle, while residual kyphosis of more than five degrees was more frequently
observed in the balloon kyphoplasty group. Patients and outcome assessors were reported to be
unaware of the group assignment, although it is not clear if the Kiva device was apparent in the
radiographs. Cement leakage into the canal occurred in two patients treated with balloon
kyphoplasty, necessitating decompression, compared with none following the Kiva procedure.

Another 2013 study was a retrospective matched pair comparison of Kiva® versus balloon
kyphoplasty in 52 patients with VCFs. Data were collected for the Kiva® group between 2010
and 2011, and the data for the balloon kyphoplasty group were collected between 2004 and 2009.
The two groups were matched for the vertebral body treated, age, and approximate caudal
acantha. Back pain (numeric rating scale [NRS] for kyphoplasty and VAS for Kiva®) and
motility (ODI) were assessed preoperatively and at six months postoperatively. The mean
operation time was 12.7 minutes per vertebra for Kiva® and 46.5 minutes for balloon
kyphoplasty. There was no significant difference in the incidence of cement extravasion between
the Kiva® (23.1%) and kyphoplasty (30.7%) groups. At six-month follow-up, pain scores were
significantly better in the Kiva® group (10.8 NRS vs 24.6 VAS). The improvement in ODI was
similar in the two groups (43.9 for Kiva®, vs 47.4 for kyphoplasty). There were significantly
fewer adjacent and nonadjacent fractures in the Kiva® group (one and two) compared with the
kyphoplasty group (nine and five, both respectively). The mean postoperative height was 21.65
mm in the Kiva® group compared with 25.09mm in the balloon kyphoplasty group. It is not
clear whether the difference in postoperative vertebral wall height for the two procedures is
operator dependent, or whether this is a contributing factor in the occurrence of adjacent and
nonadjacent fractures.

Evidence to date includes a preliminary report of a large industry-sponsored multicenter IDE
trial, a large independent randomized trial, and a retrospective matched pair comparison. The
IDE trial has not yet been published in a peer-reviewed journal. The matched pair comparison
reported favorable outcomes for Kiva®, although this study is limited by the retrospective nature
of the study and the non-concurrent controls.

Vertebral Body Stenting versus Balloon Kyphoplasty
An RCT by Werner et al, performed independent of industry support, found no advantage of
VBS over balloon kyphoplasty. Sixty-five patients were included who had one or more fresh
osteoporotic VCFs and marked pain. A total of 100 VCFs were randomized to either vertebral
body stenting (VBS) or balloon kyphoplasty, with the condition that if there were multiple levels
in a single patient, the same procedure was used for all levels. There was no significant difference between the procedures in radiation time, or in the mean reduction of kyphosis (4.7 degrees after VBS and 4.5° after kyphoplasty). There was also no significant difference between the two intervention arms in cement leakage (20% balloon kyphoplasty and 30% VBS). Intraoperative pressure was higher and material-related complications were greater (nine of the 50 levels, including failure of the cannulas, incomplete or no opening of the stent, and balloon rupture) in the VBS group compared with one of the 50 vertebral levels (balloon rupture) in the kyphoplasty group.

Summary
Vertebroplasty has been investigated as an intervention to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture or in those with osteolytic lesions of the spine, i.e., multiple myeloma or metastatic malignancies. The results of clinical vetting in 2008 indicated uniform support for the use of vertebroplasty in painful osteoporotic fractures. After consideration of the available evidence and clinical input, it was concluded that the consistent results of numerous case series, including large prospective reports, together with the results of clinical vetting, were sufficient to determine that vertebroplasty was a reasonable treatment option in patients with vertebral fractures who fail to respond to conservative treatment (at least six weeks with analgesics, physical therapy, and rest). Given the absence of alternative treatment options and the morbidity associated with extended bed rest, vertebroplasty may be considered medically necessary in patients with vertebral fractures who fail to improve after six weeks of conservative therapy.

Subsequent literature updates performed after 2008, including two sham-controlled trials, have raised questions about the efficacy of vertebroplasty for osteoporotic fractures. These trials can be interpreted as showing that vertebroplasty is ineffective. However, alternate interpretations are possible. There are methodologic issues with these studies, including but not limited to the choice of sham procedure and the potential effect of the sham procedure having a therapeutic effect by reducing pain. Also, the appropriateness of chosen outcome measures to detect clinically meaningful differences in pain may not have been optimal, as the studies were underpowered to detect differences in clinical response rates. Because of these uncertainties in the interpretation of the literature, the policy is unchanged.

There is insufficient evidence to permit conclusions on the use of vertebroplasty for acute fractures. The VERTOS II trial is a well-done study, whose results should be replicated and verified. For acute fractures, conservative therapy consisting of rest, analgesics and physical therapy is an option, and symptoms will resolve in a large percentage of patients with conservative treatment only.

Sacroplasty is under development. Small numbers of treated patients leaves uncertainty regarding the impact of sacroplasty on health outcomes and does not permit conclusion on its use for sacral insufficiency fractures or other indications. Therefore, sacroplasty is considered investigational.

After consideration of the available evidence and uniform clinical input, it was concluded that although the scientific evidence does not permit conclusions about the impact on health
outcomes and that comparative studies with long-term outcomes are lacking; numerous case
series, including large prospective reports, consistently showed that kyphoplasty may alleviate
pain and improve function in patients with vertebral fractures who fail to respond to conservative
treatment (at least six weeks) with analgesics, physical therapy, and rest. More recent
randomized trials that compare kyphoplasty with medical management have also reported
benefit. Given the absence of alternative treatment options and the morbidity associated with
extended bed rest, kyphoplasty may be considered a reasonable treatment option in patients with
vertebral fractures who fail to improve after six weeks of conservative therapy, and therefore
may be considered medically necessary both for this patient population, as well as for patients
who have severe pain due to osteolytic lesions of the spine related to multiple myeloma or
metastatic malignancies.

There is insufficient evidence to permit conclusions on the use of kyphoplasty for an acute (<6
weeks) vertebral fracture. The scientific evidence does not permit conclusions about the impact
on net health outcome; sham-controlled comparative studies are needed. There are no additional
data to alter these conclusions.

There a single randomized trial on mechanical vertebral augmentation using the Kiva VCF
System. It is currently being studied in a pivotal FDA-regulated investigational device exemption
trial. In both trials, the Kiva system is compared to kyphoplasty.

Practice Guidelines and Position Statements
In 2012, a joint practice guideline on the performance of vertebral augmentation was published
by the American College of Radiology (ACR), the American Society of Neuroradiology (ASN),
the American Society of Spine Radiology (ASSR), the Society of Interventional Radiology
(SIR), and the Society of Neurointerventional Surgery (SNIS). This guideline addresses
vertebral augmentation in general and refers to all percutaneous techniques used to achieve
internal vertebral body stabilization, including vertebroplasty, balloon kyphoplasty,
radiofrequency ablation and coblation, mechanical void creation, and injection of bone graft
material or bone substitutes. The ACR, ASN, ASSR, SIR, and SNIS consider vertebral
augmentation to be an established and safe procedure and provide guidelines for appropriate
patient selection, qualifications and responsibilities of personnel, specifications of the procedure,
equipment quality control, and quality improvement and documentation. This guideline
addresses vertebral augmentation in general and refers to all percutaneous techniques used.

These societies (ACR, ASN, ASSR, SIR, SNIS) published a joint position statement on
percutaneous vertebral augmentation in 2014. It is the position of the societies that percutaneous
vertebral augmentation with the use of vertebroplasty or kyphoplasty is a safe, efficacious, and
durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic
fractures, when performed in a manner in accordance with public standards. The document also
states that these procedures are offered only when nonoperative medical therapy has not
provided adequate pain relief or pain is significantly altering patients’ quality of life.

In a 2014 quality improvement guideline from SIR, failure of medical therapy is defined as
follows:
1. A patient rendered nonambulatory as a result of pain from a weakened or fractured vertebral body, pain persisting at a level that prevents ambulation despite 24 hours of analgesic therapy;
2. A patient with sufficient pain from a weakened or fractured vertebral body that physical therapy is intolerable, pain persisting at that level despite 24 hours of analgesic therapy; or
3. Any patient with a weakened or fractured vertebral body, unacceptable side effects such as excessive sedation, confusion, or constipation as a result of the analgesic therapy necessary to reduce pain to a tolerable level.

In 2013, ACR updated their appropriateness criteria on the management of compression fractures. The criteria for management of these fractures state that most vertebral compression fractures are resolved within four to six weeks with the more conservative first-line treatment including the use of nonsteroidal anti-inflammatory drugs and possibly narcotic medications, and that vertebroplasty should be reserved for patients who either have failed or cannot tolerate traditional conservative treatment.

In 2010, the American Academy of Orthopaedic Surgeons (AAOS) Board of Directors approved a new clinical practice guideline on the treatment of osteoporotic spinal compression fractures, which is available online at: www.aaos.org/Research/guidelines/SCFguideline.asp. The Board approved a strong recommendation against the use of vertebroplasty or kyphoplasty for patients who “present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically “intact.” In coming out with a strong recommendation, the committee expressed their confidence that future evidence is unlikely to overturn the existing evidence. As a note, these recommendations were based on a literature review through September 2009; therefore, the Klazen et al trial was not included in the systematic review.

The United Kingdom’s National Institute for Health and Care Excellence (NICE) concluded in 2003 that the current evidence on the safety and efficacy of vertebroplasty for vertebral compression fractures appears adequate to support the use of this procedure to provide pain relief for people with severe painful osteoporosis with loss of height and/or compression fractures of the vertebral body. The guidance recommends that the procedure be limited to patients whose pain is refractory to more conservative treatment. Their 2013 technology appraisal guidance TA279 states that percutaneous vertebroplasty and percutaneous balloon kyphoplasty are recommended as treatment options for treating osteoporotic vertebral compression fractures in persons having severe, ongoing pain after a recent unhealed vertebral fracture, despite optimal pain management and whose pain has been confirmed through physical exam and imaging to be at the level of the fracture.

In 2008, NICE recommended consideration of vertebroplasty for patients with vertebral metastases and no evidence of metastatic spinal cord compression or spinal instability if they have mechanical pain resistant to conventional analgesia or vertebral body collapse. Surgery should only be performed when all appropriate specialists, including the oncologist, interventional radiologist, and spinal surgeon agree. At present, there are relatively few patients
in England receiving surgery; however, there is evidence to suggest that in a selected subset of patients, early surgery may be more effective at maintaining mobility than radiotherapy.

**Key Words:**
Percutaneous vertebroplasty, kyphoplasty, vertebroplasty, polymethylmethacrylate, PMMA, osteoporosis, vertebral body compression fracture, vertebral fracture, vertebral compression fracture, PV, VCF, optiplasty, OptiMesh, Arcuate XP device, Arcuplasty, ARCUATE™ Vertebral Augmentation System, sacroplasty skyphoplasty, SKy bone expander, mechanical vertebral augmentation, Kiva®

**Approved by Governing Bodies:**
Vertebroplasty is a surgical procedure and, as such, is not subject to U.S. Food and Drug Administration (FDA) approval. PMMA bone cement was available as a drug product before enactment of FDA’s device regulation and was at first considered what FDA terms a “transitional device.” It was transitioned to a class III device requiring premarketing applications. Several orthopedic companies have received approval of their bone cement products since 1976. In October 1999, PMMA was reclassified from class III to class II, which requires future 510(k) submissions to meet “special controls” instead of “general controls” to assure safety and effectiveness. FDA issued a guidance document on July 17, 2002 (last accessed September 2002, available at: www.fda.gov/cdrh/ode/guidance/668.pdf.) that outlines the types of special controls required and describes the recommended labeling information.

Thus, use of PMMA in vertebroplasty represented an off-label use of an FDA-regulated product before 2005. In 2005, PMMA bone cements such as Spine-Fix® Biomimetic Bone Cement and Osteopal® V were issued 510(k) marketing clearance for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures.

FDA also issued a “Public Health Web Notification: Complications related to the use of bone cement in vertebroplasty and kyphoplasty procedures,” which is available at: www.fda.gov/cdrh/safety/bonecement.html. This notification is intended to inform the public about reports on safety and to encourage hospitals and other user facilities to report adverse events related to bone cement malfunctions, either directly to manufacturers or to MedWatch, FDA’s voluntary reporting program.

The use of PMMA in sacroplasty represents an off-label use of an FDA-regulated product (bone cements such as Spine-Fix® Biomimetic Bone Cement and Osteopal® V), as the 510(k) marketing clearance was for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures. Sacroplasty was not included.

ArthroCare received FDA clearance for the Parallax® Contour® Vertebral Augmentation Device in 2010. The device creates a void in cancellous bone that can then be filled with bone cement.
Vesselplasty using Vessel-X®, (MAXXSPINE) and a similar procedure from A-Spine, are variations of vertebroplasty that are reported to reduce leakage of bone cement by containing the filler in an inflatable vessel. These devices do not have clearance for marketing by FDA.

Kyphoplasty is a surgical procedure and, as such, is not subject to U.S. Food and Drug Administration (FDA) approval. Balloon kyphoplasty requires the use of an inflatable bone tamp. One such tamp, the KyphX® inflatable bone tamp, received 510(k) marketing clearance from FDA in July 1998. Other devices with FDA 510(k) marketing clearance include AVAmex® Vertebral Balloon system (Carefusion), NeuroTherm Parallax® Balloon Inflatable Bone Tamp (NeuroTherm Inc.), Stryker iVAS® Balloon catheter, and Synthes Synflate™ Vertebral Balloon System, Synthes (USA) LLC (FDA product code NDN).

The Kiva® VCF Treatment System (Benvenue Medical) received FDA 510(k) marketing clearance in January 2014 (FDA product code NDN).

Vertebral body stenting (VBS™; Synthes, Switzerland) is available in Europe at this time.

PMMA bone cement was available as a drug product before enactment of FDA’s device regulation and was at first considered what the FDA terms a “transitional device.” It was transitioned to a class III device requiring premarketing applications. Several orthopedic companies have received approval of their bone cement products since 1976. In October 1999, PMMA was reclassified from class III to class II, which requires future 510(k) submissions to meet “special controls” instead of “general controls” to assure safety and effectiveness.

Thus, use of PMMA in kyphoplasty represented an off-label use of an FDA-regulated product before July 2004. In July 2004, KyphX® HV-RTM bone cement was given 510(k) marketing clearance by FDA for the treatment of pathologic fractures of the vertebral body due to osteoporosis, cancer, or benign lesions using a balloon kyphoplasty procedure. Subsequently, other products such as Spine-Fix® Biomimetic Bone Cement and Osteopal® V have been issued 510(k) marketing clearance for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures.

FDA also issued a “Public Health Web Notification: Complications related to the use of bone cement in vertebroplasty and kyphoplasty procedures.” This notification is intended to inform the public about reports on safety and to encourage hospitals and other user facilities to report adverse events related to bone cement malfunctions either directly to manufacturers or to MedWatch, FDA’s voluntary reporting program.

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.
Current Coding:
CPT Codes: 01936  Anesthesia for percutaneous image guided procedures on the spine and spinal cord; therapeutic (Effective 01/01/08)
          0200T  Percutaneous sacral augmentation (sacroplasty, unilateral injection(s), including the use of a balloon or mechanical device (if utilized), one or more needles (Effective 01/01/09)
          0201T  ;two or more needles (Effective 01/01/09)
          22520  Percutaneous vertebroplasty (bone biopsy included when performed), one vertebral body, unilateral or bilateral injection; thoracic
          22521  Percutaneous vertebroplasty (bone biopsy included when performed); one vertebral body, unilateral or bilateral injection, lumbar
          22522  Percutaneous vertebroplasty (bone biopsy included when performed); 1 vertebral body, unilateral or bilateral injection; each additional thoracic or lumbar vertebral body (list separately in addition to code for primary procedure)
          22523  Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device, one vertebral body, unilateral or bilateral cannulation (e.g., kyphoplasty); thoracic (Effective 01/01/06)
          22524  ;lumbar (Effective 01/01/06)
          22525  ;each additional thoracic or lumbar vertebral body (list separately in addition to code for primary procedure) (Effective 01/01/06)
          64999  Unlisted procedure, nervous system
          72291  Radiological supervision and interpretation, percutaneous vertebroplasty, vertebral augmentation, or sacral augmentation (sacroplasty), including cavity creation, per vertebral body or sacrum; under fluoroscopic guidance (Effective 01/01/10)
          72292  Radiological supervision and interpretation, percutaneous vertebroplasty, vertebral augmentation, or sacral augmentation (sacroplasty), including cavity creation, per vertebral body or sacrum; under CT guidance (Effective 01/01/10)

HCPCS codes:
          S2360  Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; cervical
          S2361  Each additional cervical vertebral body (List separately in addition to code for primary procedure)

ICD-9-CM codes:
          170.2  Malignant neoplasm of vertebrae
          198.5  Secondary malignant neoplasm of Bone and Bone Marrow
          203.00 Multiple myeloma, without mention of having achieved remission
          203.01 Multiple Myeloma in Remission
228.09  Hemangioma of Other Sites
238.6  Neoplasm of Uncertain Behavior of Plasma Cells
733.13  Pathologic Fracture of the Vertebrae

ICD-10-CM codes (effective 10/1/14):

C41.2  Malignant neoplasm of vertebral column
C79.51  Secondary malignant neoplasm of bone
C79.52  Secondary malignant neoplasm of bone marrow
C90.00  Multiple myeloma not having achieved remission
C90.01  Multiple myeloma in remission
D18.09  Hemangioma of other sites
D47.Z9  Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
M48.52XA-  Collapsed vertebra, not elsewhere classified, cervical, thoracic, and lumbar region codes
M48.57XS
M80.08XA-  Age-related osteoporosis with current pathological fracture, vertebral(e)
M80.08XS
M80.88XA-  Other osteoporosis with current pathological fracture, vertebral(e)
M80.88XS  ; sequela

Previous Coding:

76012  Radiological supervision and interpretation, percutaneous Vertebroplasty, or vertebral augmentation including cavity creation, (Effective for dates of service on or after January 1, 2006) per vertebral body; under fluoroscopic guidance (deleted effective January 1, 2007)

76013  Radiological supervision and interpretation, percutaneous vertebroplasty, per vertebral body; under CT guidance (deleted effective January 1, 2007)

S2362  Kyphoplasty, one vertebral body, unilateral or bilateral injection (deleted effective April 1, 2006)

S2363  Kyphoplasty, one vertebral body, unilateral or bilateral injection; each additional vertebral body (deleted effective April 1, 2006)

References:
17. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis or malignancy. TEC Assessments 2005; Volume 20, Tab 7.


24. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Percutaneous vertebroplasty or kyphoplasty for vertebral fractures caused by osteoporosis or malignancy. TEC Assessments 2008; Volume 23, Tab 5.


Policy History:
Medical Policy Group, November 1999
Medical Review Committee, January 2000
TEC Review, April 2000
Medical Policy Group, January 2001
Medical Review Committee, March 2001
TEC Review, May 2001
Medical Policy Group, February 2002 (2)
Medical Review Committee, March 2002
Available for Comment April 15-May 29, 2002
Medical Policy Group, June 2003 (2)
Medical Review Committee, June 2003
Medical Review Committee, July 2003
Medical Policy Administration Committee, July 2003
Available for comment July 28-September 10, 2003
Medical Policy Group, August 2003 (2)
Medical Review Committee, September 2003
Medical Policy Administration Committee, October 2003
Available for comment October 7-November 20, 2003
Medical Policy Group, October 2005 (2)
Medical Policy Administration Committee, November 2005
Available for comment November 30, 2005-January 13, 2006
Medical Policy Group, July 2006 (1)
Medical Policy Administration Committee, July 2006
Available for comment July 18-August 31, 2006
Medical Policy Group, January 2007 (2)
Medical Policy Group, June 2007 (2)
Medical Policy Group, July 2007 (2)
Medical Policy Administration Committee, July 2007
Available for comments July 16-September 3, 2007
Medical Policy Group, March 2008 (2)
Medical Policy Administration Committee, April 2008
Available for comment April 4-May 18, 2008
Medical Policy Group, May 2008 (2)
Medical Policy Administration Committee, June 2008
Available for comment June 11-July 26, 2008
Medical Policy Group, June 2009 (2)
Medical Policy Administration Committee, July 2009
Available for comment July 1-August 14, 2009
Medical Policy Panel, February 2010
Medical Policy Group, March 2010 (2)
Medical Policy Administration Committee, April 2010
Available for comment April 12-May 26, 2010
Medical Policy Panel, February 2011
Medical Policy Group, June 2011 (2): Key Points and Reference Updated
Medical Policy Panel, April 2013
Medical Policy Group, August 2013 (2): Title change to include Mechanical Vertebral Augmentation. Policy statement added that all other percutaneous mechanical vertebral augmentation devices, including but not limited to Kiva are investigational. Description, Key Points, Approved by Governing Bodies, Key Words, and Reference updated to support new policy statement and literature search.
Medical Policy Administration Committee, September 2013
Available for comment September 19 through November 2, 2013
Medical Policy Group, March 2014 (2): Corrected policy statement with addition of coverage for vertebral hemangiomas with severe pain or nerve compression.
Medical Policy Group, March 2014 (5): Added ICD-9 and ICD-10-CM diagnosis under Coding; no change to policy statement.
Medical Policy Panel, July 2014
Medical Policy Group, July 2014 (3): 2014 Updates to Key Points, Governing Bodies & References; no change in policy statements; removed policy statements for 2010 & prior years

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.