

# Percutaneous Vertebroplasty or Kyphoplasty for Vertebral Fractures Caused by Osteoporosis or Malignancy



Assessment  
Program  
Volume 25, No. 5  
September 2008

## Executive Summary

### Background

Percutaneous vertebroplasty and kyphoplasty are procedures for alleviating the pain of vertebral fractures due to osteoporosis or malignancy. Both involve the injection of bone cement into the body of the fractured vertebra. Kyphoplasty uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height before introducing mechanical fixation by injecting bone cement into the expanded cavity.

### Objective

To evaluate the evidence to determine whether vertebroplasty or kyphoplasty is an effective procedure to alleviate the symptoms from vertebral fractures caused by osteoporosis or malignancy.

### Search Strategy

Studies of vertebroplasty were identified through a computerized online search of the MEDLINE® (via PubMed) database through June 2008, using the various textwords including: “vertebroplast\*”; “cementoplast\*”; and “methylmethacrylate” combined with (“vertebral” OR “spinal”). Studies of kyphoplasty were identified through a computerized online search of the MEDLINE® (via PubMed) database through July 2008, using various textwords, including: “kyphoplast\*”; “cementoplast\*”; and “methylmethacrylate” combined with (“vertebral” OR “spinal”).

### Selection Criteria

Both studies comparing vertebroplasty or kyphoplasty to medical management (or to each other) and case series studies were sought. Case series studies needed to meet minimum sample size requirements and adequate reporting of pre- and post-procedure pain and health status.

### Main Results

Results are reported by procedure and for two indications: osteoporotic fractures and fractures due to malignancy.

**Osteoporotic Fractures, Vertebroplasty.** Two comparative studies and 6 case series studies met selection criteria. One randomized study showed improvements in disability rating and quality of life, but not visual analog scale (VAS) pain rating, over a short 2-week follow-up period. One nonrandomized study on acute fracture patients showed no difference in pain scores after 6 weeks of follow up. Case series studies showed a consistent 4- to 5-point improvement in VAS pain ratings (0–10 scale) after vertebroplasty. Long-term results showed durability of pain relief, although all studies suffered from losses to follow-up.



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**Osteoporotic Fractures, Kyphoplasty.** Two nonrandomized studies comparing kyphoplasty to medical management, one study comparing kyphoplasty to vertebroplasty, and 7 case series studies met selection criteria. The comparative studies showed greater improvement in pain scores and other outcomes compared to medical management. The study comparing kyphoplasty to vertebroplasty showed improvements in pain in both study groups, but no differences between the two procedures. The case series studies showed a consistent 4- to 5-point improvement in VAS pain ratings (0–10 scale) after kyphoplasty. The improvement appeared to be durable out past 1 year, but all studies suffered from losses to follow-up.

**Fractures Due to Malignancy, Vertebroplasty.** Three case series met inclusion criteria. All studies showed that VAS pain ratings (0–10 scale) showed 4- to 5-point reductions after the procedure.

**Fractures Due to Malignancy, Kyphoplasty.** Three case series met inclusion criteria. All studies showed improvements in pain outcomes, disability scores, or quality of life scales similar in magnitude to that for osteoporotic fractures.

#### **Author’s Comments and Conclusions**

There is a lack of rigorous comparative trials of vertebroplasty and kyphoplasty. For vertebroplasty, there is only one randomized trial with very short follow-up of 2 weeks. Two of 3 nonrandomized studies show efficacy of the procedures. Case series studies show 4- to 5-point improvements in VAS pain ratings. Nonrandomized and case series studies may not provide reliable evidence of efficacy. Both procedures appear to produce similar effects, and there are few data directly comparing the two procedures to each other. The principal adverse effect is leakage of cement out of the vertebral body, which occurs in both procedures, but appears to be more common after vertebroplasty. Complications due to this leakage are infrequent, however. Fractures in vertebrae adjacent to the treated vertebrae do occur; however, it has not been demonstrated whether this is more common after such treatment. Case series studies of patients with vertebral fractures due to malignancy generally show the same quantity of improvement of pain and health status as for osteoporotic fractures.

There is no strong comparative evidence between the two procedures. Kyphoplasty produces greater anatomic changes in kyphosis than vertebroplasty; however, these anatomic changes are not well correlated with symptomatic improvement or improvement in health status. Anatomic changes due to kyphoplasty were not reported in this Assessment.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether percutaneous vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

#### **1. The technology must have final approval from the appropriate governmental regulatory bodies.**

Vertebroplasty and kyphoplasty are surgical procedures and, as such, are not subject to U.S. Food and Drug Administration (FDA) approval.

Kyphoplasty requires the use of an inflatable bone tamp. One such tamp, the KyphX® inflatable bone tamp, received 510(k) marketing clearance from the FDA in July 1998.

Polymethyl methacrylate (PMMA) bone cement was available as a drug product prior to enactment of the 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 for purposes other than vertebroplasty or kyphoplasty 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 (accessed August 2008 at <http://www.fda.gov/cdrh/ode/guidance/668.pdf>) that outlines the types of special controls required and describes the following recommended labeling information:

**Intended Use.** PMMA bone cement is intended for use in arthroplastic procedures of the hip, knee, and other joints for the fixation of polymer or metallic prosthetic implants to living bone.

**Contraindications.** PMMA bone cement is contraindicated in the presence of active or incompletely treated infection, at the site where the bone cement is to be applied.

**Warnings.** Monitor patients carefully for any change in blood pressure during and immediately following the application of bone cement. Adverse patient reactions affecting the cardiovascular system have been associated with the use of bone cements. Hypotensive reactions have occurred between 10 and 165 seconds following application of bone cement; they have lasted from 30 seconds to 5 or more minutes. Some have progressed to cardiac arrest. Patients should be monitored carefully for any change in blood pressure during and immediately following the application of bone cement.

There have been several bone cement products cleared for marketing via 510(k) by the FDA for use in vertebroplasty or kyphoplasty (e.g., Vertaplex or Spineplex™ Radiopaque Bone Cement [Stryker], KyphX® HV-R™ Bone Cement [Kyphon, Inc.], Vertebroplastic™ Radiopaque Bone Cement [DePuy Spine, Inc.]). Continuing concern about other cement and bone-void-filling products led to an FDA Public Health Web Notification that notes the types of complications that can occur with these products, and offers advice to physicians regarding use of such products. FDA requires hospitals and facilities to report deaths and serious injuries associated with the use of such medical devices. Use of cement products not receiving FDA clearance specifically for vertebroplasty or kyphoplasty represents an off-label use.

**2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.**

There are relatively few comparative trials of vertebroplasty or kyphoplasty, but many case series have been published. Without evidence from controlled trials, it is not possible to determine the effect of vertebroplasty or kyphoplasty on health outcomes. The one published randomized trial of vertebroplasty showed efficacy of the procedure, but follow-up was only 2 weeks. Case series studies are subject to many sources of bias and generally are not reliable evidence of efficacy.

**3. The technology must improve the net health outcome; and**

**4. The technology must be as beneficial as any established alternatives.**

The evidence is insufficient to determine whether either vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy improves the net health outcome or is as beneficial as any established alternatives.

**5. The improvement must be attainable outside the investigational settings.**

Whether either vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy improves health outcomes has not been established in the investigational setting.

For the above reasons, percutaneous kyphoplasty or vertebroplasty for vertebral fractures from osteoporosis or malignancy does not meet the TEC criteria.

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**Published in cooperation with Kaiser Foundation Health Plan and Southern California Permanente Medical Group.**

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## Assessment Objective

This Assessment evaluates the available evidence to determine whether percutaneous vertebroplasty or kyphoplasty is an effective treatment for vertebral fractures caused by osteoporosis or malignancy. Vertebroplasty is a minimally invasive treatment involving percutaneous needle injection of bone cement into a diseased vertebral body. Kyphoplasty is a variation of vertebroplasty that uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close to its natural height as possible before introducing the mechanical fixation by injecting bone cement into the expanded cavity. The primary uses reported in the literature include: 1) osteoporotic vertebral compression fracture and 2) vertebral fractures caused by osteolytic destruction secondary to malignancy. Beneficial effects of interest would include relief of associated symptoms (e.g., pain) as well as improvement in ability to function (e.g., mobility and activities of daily living). Adverse effects would include complications associated with either procedure.

## Background

### Osteoporotic Vertebral Compression Fracture

Vertebral fractures are among the most common fractures in patients who have osteoporosis (Ross 1997). It is estimated that up to 50% of women and approximately 25% of men will have a vertebral fracture at some point in their lives. Multiple vertebral fractures may be expected in about half of these cases (Ross 1997). While the incidence of vertebral fracture is high, the minority of vertebral fractures (about one-third) actually reaches clinical diagnosis (Ross 1997).

Acute vertebral fracture may present with pain, although clinically silent fractures may account for one-half of all radiographically visible vertebral fractures (Ross 1997). Pain management in the acute setting is not standardized. Common management strategies include bed rest, activity modification, and local and/or systemic analgesics. Calcitonin has also been suggested to reduce pain in the acute setting. Postural bracing of the spine is another option, but this has not been reported recently in the literature (Lin and Lane 2002).

Chronic pain, usually following multiple vertebral fractures, does not tend to respond

to the management strategies described for acute pain. The source of chronic pain after vertebral compression fracture is not thought to be the vertebrae itself but is believed to relate predominantly 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 (Ross 1997).

Lyritis et al. (1989) characterized symptomatic vertebral fractures into two types of clinical trajectories. In one patient subtype, pain was intense but persisted for a relatively short mean duration of 6 weeks. In a second patient subtype, the initial pain was milder, but subsequent attacks of pain occurred over a very long period; bone deformity appeared to occur over a long period of time.

A solid understanding of the natural history of vertebral fractures would be helpful in inferring a treatment benefit from a procedure that has largely been assessed with single-arm case series studies. However, beyond the fact that some patients appear to recover from the acute episode of pain, probably coinciding to the initial fracture over a short period of weeks, it was difficult to find rigorous studies examining the course of symptoms beyond the acute period. It would be helpful to know the rate of resolution of symptoms at a point in time after the pain has become chronic.

### Vertebral Metastasis/Multiple Myeloma Lesions

Metastatic disease involving the spine generally involves the vertebral bodies with pain being the most frequent complaint (Healey 1997). Pain may be caused by any number of factors such as intraosseous tumor, vertebral fracture with associated segment instability, or extraosseous tumor producing spinal or nerve root compression. Such compression may also cause neurologic dysfunction.

Prognosis in patients with vertebral metastasis is variable and relates to a number of factors such as the patient's underlying functional status and primary tumor, as well as anatomic location of the metastasis. Restored ambulation has been associated with increased survival (Healey 1997).

Palliative treatment options include radiation therapy, chemotherapy, and/or surgical resection with fixation for stabilization. The pain associated with metastasis alone is usually

quite responsive to radiation therapy. The pain due to fractures caused by osteolytic destruction due to the metastases are often more difficult to manage. External bracing devices may be used as well; however, long-term use may be difficult for patients. Nonsurgical intervention may be preferable in patients with limited expected survival and poor functional status.

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 and the presence of fracture. Further, these approaches rely on bone remodeling to regain vertebral body strength, which may necessitate supportive bracing to minimize the risk of vertebral collapse during healing.

### **Percutaneous Approaches to Treating Vertebral Fractures**

**Percutaneous Vertebroplasty.** Percutaneous vertebroplasty is a minimally invasive treatment involving percutaneous needle injection of bone cement into a diseased vertebral body. The procedure was first reported by investigators from France in 1987 as a treatment for complicated vertebral body hemangioma (Galibert et al. 1987). Since that time, the vertebroplasty technique has been further investigated, both in the U.S. and in Europe, as a treatment option to provide mechanical support and symptomatic relief in other conditions involving osteolytic destruction of the spine. Osteoporosis, vertebral metastasis, and vertebral involvement of multiple myeloma are the most commonly reported uses of vertebroplasty in the literature. Other reported uses for vertebroplasty include treatment for symptomatic or aggressive vertebral hemangiomas, Langerhans cell histiocytosis (also known as eosinophilic granuloma), or vertebral lymphoma (Cardon et al. 1994; Martin et al. 1999).

It has been proposed that vertebroplasty provides an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body (Deramond et al. 1998). Thermal damage to intraosseous nerve fibers is another possible mechanism of effect, since the cement used in the procedure, polymethyl methacrylate (PMMA), undergoes an exothermic (heat-releasing) reaction when it hardens. One study performed vertebroplasty injections in cadaveric vertebrae and measured resultant in vitro temperature changes (Deramond 1999).

The results indicate a possible role of thermal necrosis as an explanation for the pain relief observed after vertebroplasty. However, differences between in vivo conditions and the cadaveric study conditions preclude definitive conclusions. Chemical or vascular effects have also been discussed (Cotten and Duquesnoy 1997), but at present, the mechanism of analgesia is not well understood.

### *Description of Vertebroplasty Technique*

For the purpose of this Assessment, vertebroplasty is considered to be a percutaneous procedure. The vast majority of published reports describe using a percutaneous approach. However, one published report from Switzerland (Wenger et al. 2002) describes vertebroplasty with an open surgical field in order to remove PMMA leakage immediately.

During vertebroplasty, PMMA is injected into a diseased vertebral body. PMMA is made radiopaque by the addition of barium sulfate powder and tantalum powder. The injection is performed by introducing a needle (usually 10–15 gauge, depending on the spinal level) through a transpedicular or paravertebral approach into the vertebral body. Either fluoroscopic or computed tomographic (CT) guidance is used to guide needle placement. Some investigators perform a venogram through the needle to delineate tip placement and venous outflow in an effort to avoid venous leakage of PMMA. The usefulness and necessity of preprocedural venography has been debated in the literature (Wong and Mathis 2002; Do 2002; McGraw et al. 2002; Vasconcelos et al. 2002; Gaughen et al. 2002). PMMA is then injected slowly through the needle and monitored using fluoroscopic or CT imaging. If filling of the vertebral body is insufficient on a unilateral injection, then a second injection may be made using the contralateral approach.

Vertebroplasty requires some degree of anesthesia; however, practices vary across reported series. Some investigators routinely used general anesthesia early in their experience, while more recent series use conscious sedation anesthesia techniques. The patient must lie prone for the entire procedure, which may add to the discomfort of the procedure, and some patients may require general anesthesia if they are unable to tolerate lying prone for several hours.

*Patient Screening, Evaluation and Selection*

Evaluation of the patient is necessary to establish the fractured vertebrae as the source of the pain. This includes a clinical history and physical examination to establish significant focal back pain, point tenderness, and limited mobility. Many imaging tests can identify fractured vertebrae including plain spine X-rays. Other tests commonly used include nuclear medicine bone scanning, MRI, CT, and fluoroscopy. X-rays taken in different positions may identify patients with mobile fractures. One study of kyphoplasty (Komp et al. 2004) selected only patients with mobile fractures. Some of these tests may identify fractures that cannot be visualized on plain X-ray, others can differentiate between acute and old fractures, and others might indicate other reasons for back pain. Although both acute and old fractures are treated with vertebroplasty, differentiating between them might be necessary when the patient has multiple vertebral fractures. Certain anatomic configurations of the vertebral fracture are contraindications to performing vertebroplasty, such as vertebral body collapse of more than 90%. The age of fracture and specific MRI findings have been found by some investigators to be associated with outcomes, but it is uncertain whether these factors are used to select or exclude patients from consideration. In a study of the related procedure, kyphoplasty, Kasperk et al. (2005) documented the eligibility of patients with severe pain and osteoporosis who were actually candidates for kyphoplasty. Out of 211 patients evaluated, 97 (43%) were considered eligible for the procedure.

**Complications of Vertebroplasty**

Adverse effects of vertebroplasty include localized bleeding, infection, and/or resultant pain or neurological symptoms following leakage of injected material. Injected material may also leak into the systemic venous system with the potential for pulmonary embolism. In addition, complications from patient positioning and anesthesia for the procedure may include rib fracture or systemic infection.

PMMA leakage has been reported into the venous plexus, inferior vena cava, peridural space in the spinal canal, neural foramina, intravertebral disk space, and paravertebral soft tissue. The majority of PMMA leakages are asymptomatic; however, infrequently leakages have necessitated corticosteroid therapy and/or surgical removal of extruded material. The question of whether pretreatment venography

influences the safety and effectiveness of vertebroplasty has been debated recently in the literature (Wong and Mathis 2002; Do 2002; McGraw et al. 2002; Vasconcelos et al. 2002; Gaughen et al. 2002).

Several published case reports document significant adverse events following vertebroplasty. Case reports of major neurological complications have been reported following PMMA leakage into the surrounding neurological structures (Harrington 2001; Wenger and Markwalder 2002; Ratliff et al. 2001; Wilkes et al. 1994), although some of these complications resolved after surgical removal of PMMA. Harrington (2001) reported a 66-year-old patient who developed persistent acquired thoracolumbar spinal and foraminal stenosis, with cramping thigh pain and progressive numbness and weakness of both legs after walking only a short distance. Paradoxical cerebral artery embolization of cement was reported during an open surgical vertebroplasty with multiple pulmonary emboli of PMMA that caused pulmonary hypertension and a right-to-left shunt through a patent foramen ovale (Scroop et al. 2002). Another case of PMMA pulmonary embolus was reported by Padovani et al. (1999). Transient arterial hypotension occurred following PMMA injection in a case reported by Vasconcelos et al. (2001), although no adverse sequelae occurred in that case.

An occurrence that has been noted, but is uncertain as to whether it represents a complication of vertebroplasty, is subsequent fractures occurring in adjacent vertebrae. Vertebrae treated with cement are stiffer than fractured vertebrae, and this may transmit increased force to adjacent vertebrae (Fribourg et al. 2004). The occurrence of subsequent fractures has been recorded in some of the case series included in this Assessment. Case series studies of Uppin et al. (2003) and Grados et al. (2000) reported subsequent re-fracture rates of 12 to 52% over varying periods of time. The study by Fribourg et al. estimates a rate of symptomatic recurrent fractures in an untreated population to be 5% per year, and that increases beyond that may be due to the additional stiffness caused by vertebroplasty or kyphoplasty. However, patients undergoing these procedures are at increased risk due to their underlying osteoporosis. Thus evidence is suggestive, but not definitive, that vertebroplasty increases the risk of subsequent fracture.

**Kyphoplasty.** Kyphoplasty is a variation of vertebroplasty. This procedure uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height. The vertebral body then undergoes mechanical fixation by injecting PMMA into the expanded cavity. The expansion of a cavity by the balloon tamp permits infusion of PMMA into the cavity under lower pressure than PMMA injection during vertebroplasty; however, PMMA leakage can still occur outside the vertebral cavity (Garfin et al. 2001). Kyphoplasty can be performed under general or local anesthesia with conscious sedation. The procedure requires more time than vertebroplasty.

The reduction of kyphotic deformity of the spine that kyphoplasty provides is postulated to provide additional health benefits. Kyphotic deformity can interfere with pulmonary function via loss in lung volume and may lead to early satiety and abdominal compression, though such impairments may not occur until kyphosis becomes severe (Ingram and Braunwald 2001; Ross 1997).

#### *Complications of Kyphoplasty*

Adverse effects of kyphoplasty include localized bleeding, infection, and/or resultant pain or neurological symptoms following leakage of injected material. Injected material may also leak into the systemic venous system with the potential for pulmonary embolism. In addition, complications from patient positioning and anesthesia for the procedure may include rib fracture or systemic infection.

Most case reports of complications due to cement leakage have been reported in conjunction with vertebroplasty rather than kyphoplasty. Case reports of major neurological complications have been reported following PMMA leakage into the surrounding neurological structures (Harrington 2001; Wenger and Markwalder 2002; Ratliff et al. 2001; Wilkes et al. 1994), although some of these complications resolved after surgical removal of PMMA.

Similar to vertebroplasty, concern has also been raised about possible increases in fractures in the vertebral bodies adjacent to where kyphoplasty has been recently performed (Fribourg et al. 2004).

**FDA Status.** Vertebroplasty and kyphoplasty are surgical procedures and, as such, are not

subject to U.S. Food and Drug Administration (FDA) approval.

Kyphoplasty requires the use of an inflatable bone tamp. One such tamp, the KyphX<sup>®</sup> inflatable bone tamp, received 510(k) marketing clearance from the FDA in July 1998.

Polymethyl methacrylate (PMMA) bone cement was available as a drug product prior to enactment of the 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 for purposes other than vertebroplasty or kyphoplasty since 1976. On 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 (accessed August 2008 at <http://www.fda.gov/cdrh/ode/guidance/668.pdf>), that outlines the types of special controls required and describes the following recommended labeling information:

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Cement [Stryker], KyphX<sup>®</sup> HV-R™ Bone Cement [Kyphon, Inc.], Vertebroplastic™ Radiopaque Bone Cement [DePuy Spine, Inc.]). Continuing concern about other cement and bone-void-filling products led to an FDA Public Health Web Notification that notes the types of complications that can occur with these products, and offers advice to physicians regarding use of such products. FDA requires hospitals and facilities to report deaths and serious injuries associated with the use of such medical devices (U.S. Food and Drug Administration 2004). Use of cement products not receiving FDA clearance specifically for vertebroplasty or kyphoplasty represents an off-label use.

## Methods

### Search Methods

Studies of vertebroplasty were identified through a computerized online search of the MEDLINE<sup>®</sup> (via PubMed) database through July 2008, using the various textwords including: “vertebroplast\*”; “cementoplast\*”; and “methylnmethacrylate” combined with (“vertebral” OR “spinal”). To identify more recent studies, the MEDLINE<sup>®</sup> search was supplemented by manual searches of the most recent issues of the pertinent journals and by reading the reference lists in the most recently published papers.

Studies of kyphoplasty were identified through a computerized online search of the MEDLINE<sup>®</sup> (via PubMed) database through June 2008, using various textwords, including: “kyphoplast\*”; “cementoplast\*”; and “methylnmethacrylate” combined with (“vertebral” OR “spinal”). To identify more recent studies, the MEDLINE<sup>®</sup> search was supplemented by manual searches of the most recent issues of the pertinent journals and by reading the reference lists in the most recently published papers.

### Study Selection

Studies were included in the Assessment “Review of Evidence” if the study had these characteristics:

- Full-length article published in the English language
- Population consists of patients with vertebral fractures due to osteoporosis or malignancy
- Patient population is a consecutive series of patients, or near-consecutive series (≥90%)

- Treatment uses vertebroplasty or kyphoplasty
- Reports on relevant clinical outcomes of pain, functional status, or quality of life
- Pre- and post-procedure values for outcomes are reported, as quantitative or categorical measures
- Sample size is ≥100 patients for vertebroplasty studies on osteoporosis; ≥40 for kyphoplasty studies on osteoporosis; ≥10 for malignancy; for comparative studies, no minimum sample size

Since the last TEC Assessment, there have been several additional case series studies. Case series studies with sample sizes smaller than the selection criteria, some of which were included in the prior TEC Assessment, are not included in this Assessment. Several case series included in published systematic reviews and meta-analyses did not meet selection criteria. Abstracts were not systematically included in the study selection process, and results of case series reported in abstract form only are not included in this review. One nonrandomized, comparative trial published in German was brought to our attention by a reviewer, and this study was translated and included in the Assessment. An unpublished systematic review prepared by Kyphon was also reviewed. The studies cited in the Kyphon systematic review were all case series; no comparative studies were included. The studies overlapped with those cited in this Assessment, but were slightly different, as different selection criteria were used. Overall, however, this review did not add new evidence and would not change the conclusion of this Assessment.

Adverse events were not reported in a consistent manner across studies. The efficacy outcomes reported in the case series include the outcomes in patients with adverse events. However, to give a sense of the proportions of patients with different adverse events, event rates from case series from the prior TEC Assessments on vertebroplasty and kyphoplasty (2004; Vol. 19, Nos. 12 and 13) are included in this Assessment.

### Medical Advisory Panel Review

**Current Assessment.** This Assessment was reviewed by the Blue Cross and Blue Shield Association Medical Advisory Panel (MAP) on June 10, 2008. In order to maintain the timeliness of the scientific information in

this Assessment, literature searches were performed subsequent to the Panel's review (see "Search Methods"). If the search updates identified any additional studies that met the criteria for detailed review, the results of these studies were included in the tables and text where appropriate. There were no studies that would change the conclusions of this Assessment.

**Previous Assessments.** The MAP previously reviewed the topics of kyphoplasty and vertebroplasty in October 2004 (Vol. 19, Nos. 12 and 13) and in December 2000 (Vol. 15, No. 21). For previous Assessments, it was felt that because of limitations in the quality of the available evidence, neither kyphoplasty nor vertebroplasty met TEC criteria. The available evidence was judged as insufficient to permit conclusions of the effect of percutaneous vertebroplasty or kyphoplasty on health outcomes.

## Formulation of the Assessment

### Patient Indications

**Osteoporosis.** Patients who have painful vertebral body compression fracture(s) associated with osteoporosis. This indication does not include patients with evidence of spinal cord compression or compromise. Clinical history and appropriate use of imaging tests, which may include MRI, should be used to exclude other causes of back pain and to locate the vertebral bone that is causing the pain. The fracture must be anatomically suited for the procedure.

**Malignancy.** Patients who have painful vertebral fractures associated with osteolytic destruction from malignant disease (e.g., bone metastasis). This indication does not include patients with evidence of spinal cord compression or compromise.

### Technologies to Be Compared

**Osteoporosis.** For these patients, the usual comparator is continued medical management. The initial treatment for osteoporotic vertebral body compression fractures includes conservative measures such as bed rest, use of an immobilization/bracing device, and analgesic medication, sometimes including narcotic analgesics. Second-line treatment alternatives in this setting are not well established and may include exercise, continued conservative treatment, or other methods of pain relief.

**Malignancy.** These patients seek palliation from pain. Because these patients have limited remaining life span and may have poor health due to the underlying malignant disease, treatment choices are complex. Osteolytic vertebral body destruction may result in pain and/or instability with the potential for neurological compromise from tumor growth and vertebral collapse. Patients may simply be medically managed. Destructive lesions due to malignancy may be treated with local radiation therapy to shrink the tumor and relieve pain. The effectiveness of radiation therapy in reducing pain may be delayed several days to weeks and some tumors may not be radiation sensitive. In addition, prior radiation therapy in that same spinal location may contraindicate further radiation therapy due to dose limitations. For patients with local spinal instability from extensive destruction, surgical stabilization may be an option; however, patients with extensive malignancy may not be considered suitable candidates for aggressive surgical intervention.

### Health Outcomes

**Osteoporosis.** The primary health outcomes of interest include pain and ability to function particularly with regard to activities of daily living. Beneficial effects of treatment would include reduction in pain and increased ability to function, which is primarily achieved through decreased pain and increased mobility. Although kyphosis is improved among some patients undergoing kyphoplasty, this is an intermediate outcome unless actual health outcomes result from this improvement. Thus, data on anatomic changes are not included in this Assessment.

Potential harmful effects include complications associated with the procedure or the associated anesthesia.

**Malignancy.** The primary health outcomes of interest include pain and ability to function. However, quick onset of response is important for this indication, and durability of relief may be less important given the patients' limited remaining life span.

### Specific Assessment Question

1. What are the effects of vertebroplasty or kyphoplasty on health outcomes for vertebral fractures due to osteoporosis?

## 2. What are the effects of vertebroplasty or kyphoplasty on health outcomes for vertebral fractures due to malignancy?

For each procedure, comparative studies will first be reviewed. Unpublished comparative studies will also be described because of the small number of comparative studies. Then, case series studies will be reviewed.

### Review of Evidence

The available published evidence describing the outcomes of vertebroplasty and kyphoplasty consists mostly of uncontrolled studies including case series. Only one published, randomized trial was found comparing vertebroplasty to medical management. There were 3 non-randomized studies comparing either vertebroplasty or kyphoplasty to continued conservative management. Also, one nonrandomized study comparing kyphoplasty to vertebroplasty that reported clinical, rather than just anatomic, outcomes was found.

The case series are mostly retrospective, and it is sometimes difficult to determine the criteria for patient selection for the procedure. In the uncontrolled studies, reported outcomes most commonly included measures of pain, degree of analgesic use, and procedure-related adverse events. Few studies report functional status or activities of daily living. Some studies on kyphoplasty also report changes in the degree of thoracic curvature or vertebral height; however, this is an intermediate outcome that has not yet been correlated to symptomatic improvements such as improved pulmonary or gastrointestinal function. Many studies are limited with regard to reporting detail of outcome measures and results with significant amounts of missing follow-up data in many studies. Most studies are retrospective in nature, and the length of follow-up is relatively short in many studies.

#### Vertebroplasty: Vertebral Fractures Due to Osteoporosis

**Comparative Studies of Vertebroplasty for Osteoporotic Fractures.** There were two studies found that compared vertebroplasty to medical management (description of studies in Table 1, outcomes in Table 2). Voormolen et al. (2007) conducted a small randomized clinical trial of 34 patients. Patients had been refractory to medical management for at least 6 weeks

and no longer than 6 months. The follow-up in the study is very short because patients were allowed to have vertebroplasty after 2 weeks. In terms of the outcome of pain judged by the VAS scale, differences between vertebroplasty and medical management were statistically significant after one day, but not after 2 weeks. However, other outcomes such as an ordinal analgesic use scale, a quality of life questionnaire, and the Roland-Morris Disability questionnaire showed significance at 2 weeks after the procedure. Two patients in the vertebroplasty group had new fractures adjacent to the vertebroplasty site within 2 weeks of having the vertebroplasty procedure. Patients who crossed over from conservative management to vertebroplasty had improvements after the procedure.

Diamond et al. (2003) 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 6 weeks and between 6 and 12 months, there were no differences between groups in pain score. 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 interpret these findings as demonstrating that vertebroplasty produced faster resolution of symptoms than conservative management.

The findings of these two comparative studies are suggestive of a short-term improvement in pain after vertebroplasty. The randomized, controlled trial of Voormolen et al. (2007) does not show statistical significance for the VAS pain scale at 2 weeks; however, the study was very small. The study by Diamond et al. (2003) is notable from most other studies of vertebroplasty in that patients were enrolled within 6 weeks of fracture. Thus, the study group probably included a greater number of patients than other studies who would improve with conservative management, making it more difficult to show an effect of vertebroplasty.

**Table 1.** Comparative studies of Vertebroplasty for Osteoporotic Vertebral Fractures: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Sx Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
Diamond et al. 2003	Prospective case series with comparison group	79	71	<p>Consecutive pts presenting to emergency room (n=37) or admitted to hospital (n=42) with acute vertebral fracture, and:</p> <ul style="list-style-type: none"> <li>– Pain for 1–6 weeks unrelieved by analgesics</li> <li>– Osteoporosis by densitometry</li> <li>– No malignancy, osteomyelitis, or coagulopathy</li> </ul> <p>All patients offered VP (n=79), 55 accepted, 24 declined and used as comparison group</p>	≤6 weeks	6.8 mos. (mean)	<p>Outcomes assessed at 24 hours, 6 weeks, and 6–12 mos. post-procedure</p> <ul style="list-style-type: none"> <li>– VAS pain score, 0–5 scale for each of 5 activities (0–25 total)</li> <li>– Functional status (Barthel index)</li> <li>– Complications</li> </ul>
Voormolen et al. 2007	Randomized clinical trial	34		<p>Osteoporotic fractures, refractory to medical Rx for 6 weeks–6 months randomized to vertebroplasty or optimal medical management</p>	6 wks– 6 mo.	2 weeks	<p>Outcomes assessed at 1 day and 2 weeks</p> <ul style="list-style-type: none"> <li>– VAS pain score, 0–10 scale</li> <li>– Analgesic use, 0–3 scale</li> <li>– RMD questionnaire</li> <li>– Quality of life questionnaire</li> </ul>

Abbreviations: See Appendix Table

**Table 2.** Comparative Studies of Vertebroplasty for Osteoporotic Vertebral Fractures: Outcomes

Study/yr	n	F/U	Outcome Measure		Pre-treatment	Post-treatment <sup>1</sup>			p-value	Comments
						1 day	6 wks.	6–12 mos.		
Diamond et al. 2003	55	6.8 mos. (mean)	Pain (0–25 VAS):	VP	19 ± 4	9 ± 5*	5 ± 4	4 ± 4	*p<0.0001	n unstated for long-term follow-up
				Ctrl	20 ± 5	19 ± 6	7 ± 5	4 ± 6		
			Barthel index:	VP	14 ± 4	18 ± 3*	19 ± 2	19 ± 1		
				Ctrl	13 ± 5	13 ± 5	17 ± 4	18 ± 3		
Voormolen et al. 2007	34	2 wk	Pain (0–10 VAS)	VP	7.1	4.7	4.9	NS	p-values inferred from CI, between group difference between pre-treatment and 2 wks	
				Ctrl	7.6	7.1	6.4			
			Analgesic use (0–3)	VP	1.9	1.1	1.2	<0.05		
				Ctrl	1.7	2.5	2.6			
			Quality of life	VP	60		53	<0.05		
				Ctrl	67		67			
			RMD questionnaire	VP	15.7		13	<0.05		
				Ctrl	17.8		18			

Abbreviations: See Appendix Table

### Unpublished Comparative Studies of Vertebroplasty for Osteoporotic Fractures.

In a study presented at the American Society of Neuroradiology Meeting in 2002, Kallmes et al. reported the findings of a small pilot study in 5 patients with subacute fractures (i.e., less than 2 months in duration). This sham-controlled, randomized trial permitted blinded crossover after 14 days if a patient failed to respond to initial treatment. Three patients were initially assigned to receive the sham procedure and 2 were assigned to receive vertebroplasty; however, one sham patient suffered a new compression fracture 48 hours after the sham treatment and was excluded from the analysis. Thus, results are available in 4 subjects.

Both subjects initially treated with the sham procedure had minimal relief after treatment and crossed over to vertebroplasty, but results after vertebroplasty were similar with minimal pain relief observed. Both subjects who initially underwent vertebroplasty had minimal relief in symptoms and crossed over to receive the sham procedure. One of these patients reported complete pain relief after the sham procedure. All 5 patients were asked to guess which procedure they had received in order to assess how well the blinding had worked and all guessed that they had received the sham procedure on the first treatment session. This study provides some anecdotal support for the concern that nonspecific placebo effects may occur in some patients after vertebroplasty.

Do et al. (2002) randomized 51 patients with acute painful vertebral body compression fractures to receive either vertebroplasty (n=17) or continued medical therapy (n=14). Results on pain (0–10 scale), activity (6-point scale), and analgesic use (0–5 scale) were measured after 6 weeks. Medical therapy patients were permitted to cross over to vertebroplasty after completing follow-up. Reported results were:

All patients offered [percutaneous vertebroplasty] had significant improvement in measured outcomes regardless of whether they were offered [percutaneous vertebroplasty] first or after a trial of medical therapy. For the group that were [sic] offered [percutaneous vertebroplasty] first, the mean pre and post outcome scores are: 9.4 and 3.3 (VAS), 3.8 and 1.9 (activity), 3.6 and 1.7 (analgesic), [p<0.05]. There were [sic] no improvement in outcomes of patients offered medical therapy. However, when this group was offered

[percutaneous vertebroplasty], their outcome scores improved significantly pre and post [percutaneous vertebroplasty]: 8.7 and 2.1 (VAS), 3.3 and 1.6 (activity), 3 and 1.1 (analgesic), [p<0.05].

This study compares outcomes between vertebroplasty and continued medical management and finds significant improvements in pain, activity, and analgesic use after vertebroplasty.

### Case Series Studies of Vertebroplasty for Osteoporotic Fractures.

Six published case series studies were found that met selection criteria. Characteristics of the studies are shown in Table 3. Some studies included some patients with vertebral fractures due to malignancy, but these patients' outcomes were not reported separately. All studies enrolled patients with severe pain, but they varied with respect to the duration of the pain prior to the procedure. Most studies used some form of VAS to report pain outcomes.

The results are generally consistent in that all show statistically significant decreases in pain from an initial starting value between 7–9 on the VAS to about 2–4 after the procedure (Table 4). Such pain relief appears to be lasting in the 3 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 vertebroplasty. Layton et al. (2007) and Trout et al. (2005) showed a reduction in the Roland-Morris Disability questionnaire, up to 2 years after vertebroplasty. Do et al. (2005) showed that most of subscales of the SF-36 improved after vertebroplasty.

Adverse outcome event rates from studies abstracted from the prior TEC Assessment (2004) are shown in Table 5. Leakage of the cement outside the vertebral body is a common occurrence, occurring between 19% and 72% in 8 studies that reported its occurrence. The study by Zoarski et al. (2002) only counted “undesirable” cement extravasation as a complication, which, apparently, did not occur. Of the leaks that occur, a small proportion causes symptoms. The one patient that developed a symptomatic leak in the study by Chen et al. (2004) required surgical decompression; no other studies reported that surgery was necessary. One patient in the study by Cyteval et al.

**Table 3.** Case Series of Vertebroplasty for Osteoporotic Vertebral Fractures: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Symptom Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
McGraw et al. 2002	Prospective case series	100	156	Consecutive pts with painful vertebral fracture (92/100 due to osteoporosis), and: – Refractory to medical therapy	NR	Periop period <sup>1</sup>	Outcomes assessed 12–24 hrs postop – VAS pain score, 0–10 scale – Complications
Kobayashi et al. 2005	Retrospective case series	175	250	Pts with symptomatic acute osteoporotic vertebral fractures confirmed by imaging, and: – Unsatisfactory conservative treatment >1 wk	19 days (mean)	1 day	Outcomes assessed after procedure – 1 day VAS pain score, 0–10 scale – Time interval mobilization among those immobilized at baseline due to pain
Alvarez et al. 2005	Retrospective case series	278	423	Pts with symptomatic osteoporotic vertebral fractures	NR	3 weeks	Outcomes assessed after procedure – discharge VAS pain score, 0–10 scale – 3-wk VAS pain score, 1–10 scale – 3-wk categories of post-procedure VAS score
Layton et al. 2007	Retrospective case series	552	1,000	All patients in one institution receiving PVP, 84% for osteoporosis, 11% for neoplasm, 5% for hemangioma or trauma	3.6 mos. (mean)	2 years	Outcomes at 1 wk, 1, 6, 12, 24 mo – VAS pain score, 0–10 scale – RMD Disability questionnaire
Do et al. 2005	Prospective case series	167	207	Osteoporotic compression fractures, refractive to medical therapy, within 4 months of fracture	2 wks to 4 mos.	6 mos.	Outcomes assessed at 1 mo, 6 mo – VAS pain score, 0–10 scale – Analgesic use, 0–5 scale – Mobility scale, 0–5 scale – SF-36 scale
Trout et al. 2005	Prospective case series	113	164	Consecutive series of PVP patients, typical indications	NR	Up to 1 year	Outcomes assessed once at various time points out to one year – VAS pain score at rest, 0–10 scale – VAS pain score activity, 0–10 scale – Roland Disability Questionnaire, 0–23

<sup>1</sup> Patients followed up only through the immediate pre- and postoperative periods

<sup>2</sup> Validated rating system for musculoskeletal conditions, including modules for pain and disability, satisfaction, physical function, mental function

**Table 4.** Case Series Studies of Vertebroplasty for Osteoporotic Vertebral Fractures: Outcomes

Study/yr	n	F/U	Outcome Measure	Pretreatment	Post-treatment <sup>1</sup>			p value <sup>1</sup>	Comments
McGraw et al. 2002	100	Periop period	Pain (0–10 VAS)	8.9 ± 1.1	2.0 ± 2.0			<0.0001	93% of patients reported improvement in back pain
Kobayashi et al. 2005	175	1 day	Pain (1–10 VAS) % pain-free, VAS=0 % VAS improved	7.22 ± 1.89	<b>1 day</b> 2.07 ± 1.19 22.4% postop VAS = 0 74% postop VAS improved ≥1 unit			<0.0001	Interval to mobilization 1.9 mean days. 94/115 mobile by 24 hours
Alvarez et al. 2005	278	3 weeks	Pain (1–10 VAS) Postop VAS scores % ≤3 VAS “complete” % 4–6 VAS “moderate” % ≥7 VAS “no relief”	8.9	<b>3 weeks</b>	<b>last f/u</b> (range 3 weeks–96 mos.) 2.7		NR	2 or fewer fractures, ASA status 1, MRI signal changes, <70% vertebral height loss, associated with higher probability of better outcome
Layton et al. 2007	552	1 week to 24 months	Rest pain (1–10 VAS) Activity pain (1–10 VAS) RMD Disability (0–23)	4.5 8.4 18.4	<b>1 week</b>	<b>6 mos.</b>	<b>2 yrs.</b>	<0.0001 all values from baseline	response rate declines from 89% to 62% out to 24 mos.
Do et al. 2005	167	1 month up to 3 years	Pain score (0–10 VAS) Analgesics (0–5 VAS) Mobility (0–5 VAS) SF-36 Score	8.71 2.93 2.66 various	<b>1 mos.</b>	<b>6 mos.–3 yrs.</b>		<0.001 from baseline	55% response rate for 1 mo SF-36 47.3% response rate for 6 months to 3years SF-36
Trout et al. 2005	113	Up to 1 year	Pain at rest (0–10 VAS) Pain w/ activity (0–10 ) Roland DQ (0–23)	4.1 8.5 18.2	<b>1 week</b>	<b>1 mos.</b>	<b>6 mos.</b>	<b>1 yr.</b>	All statistically significant from baseline Follow-up ranges from 86% at 1 week to 78% at 1 year (but n=15 at 1 year), most pts not yet out to 1 year

Abbreviations: See Appendix Table

**Table 5.** Complication Rates of Vertebroplasty for Osteoporotic Fractures

Study	n		Adverse Events <sup>1</sup>							Comments
	Pts	VB	Leak	Leak-Sx	PE	MI	CHF	Rib Fx	Bleed	
<b>Case Series Studies</b>										
Grados et al. 2000	25	34	28%							1 pt. with asymptomatic cement embolism, 52% with new vertebral fractures on follow-up
McGraw et al. 2002	100	156	—	—	—	—	—	1%	—	1 pt. with transient radiculopathy
Kaufmann et al. 2001	75	122	—	—	—	—	—	—	—	
Chen et al. 2004	70	87	38%	1.4%	1.4%	—	—	—	—	Pt. with leak requiring surgery
Winking et al. 2004	38	45	26%	2%	—	—	—	—	—	Sciatic symptoms resolved
Zoarski et al. 2002	30	54	*	—	3%	—	—	—	—	1 epidural leak, asymptomatic
Cyteval et al. 1999	20	23	40%	5%	—	—	—	—	—	Persistent crural pain after proc
Chen et al. 2002	50	86	19%	0%						
Kobayashi et al. 2005	175	250	76%	0%					0.5%	32/205 new fractures at 15.3 months follow-up
Alvarez et al. 2005	278	423	72%	4.3%				2%		12 patients with radicular symptoms resolved in 1 week 1 pt with leak required surgical decompression
McKiernan et al. 2004	46	66	15%	0%						6.5% new fractures within 6 mos.
<b>Comparative Study</b>										
Diamond et al. 2003	55	71	—	—	—	—	—	2%	2%	

<sup>1</sup> Adverse event rates based on %pts with complication

\* More stringent definition of leakage defined in this study, none reported

**Key**

Leak: all cement leaks, with or without any clinical symptoms; Bleed: postoperative, clinically significant bleeding;

Leak-Sx: cement leaks causing clinical symptoms; PE: pulmonary embolus; CHF: congestive heart failure;

MI: myocardial infarction; Rib Fx: rib fracture

Other Abbreviations: See Appendix Table

(1999) developed persistent crural pain due to cement leakage. Across all studies, 2 patients had pulmonary emboli. Bleeding and rib fractures are other complications that were uncommonly reported.

In sum, the case series show improvement in pain scores and other functional scores when compared to baseline. Evidence regarding the durability of benefit is weakened by the losses to follow-up reported in most studies, but is consistent with effectiveness at least to 2 years. The major limitation of this body of evidence is that there is no control group; thus, placebo effects and natural history may account for some of the apparent benefits of treatment. Retrospective studies raise concerns about unknown selection biases which may affect the results.

### **Kyphoplasty: Vertebral Fractures Due to Osteoporosis**

**Comparative Studies of Kyphoplasty for Osteoporotic Fractures.** There were 2 non-randomized comparison studies of kyphoplasty versus conservative management for treatment of osteoporotic fractures and one nonrandomized comparison between kyphoplasty and vertebroplasty (Tables 6 and 7). Kasperk et al. (2005) enrolled 60 patients with vertebral fractures present for greater than 12 months. All patients were evaluated as being suitable for having kyphoplasty. Patients were then offered kyphoplasty; those who refused became the control group. The patients had no statistically significant differences in characteristics at baseline. In the principal clinical outcomes, the kyphoplasty group had greater improvements in VAS pain score and European Vertebral Osteoporosis Study (EVOS) functional score than the control group. There were slight reductions in the use of opiate medication in both groups (formal statistical analysis not reported) and fewer back-pain-related physician visits in the kyphoplasty group. In other secondary analyses, they found no correlation between the degree of kyphosis correction and pain or functional outcomes, and no difference in treatment effect across subgroups.

The other comparative study by Komp et al. (2004) compared 19 patients receiving kyphoplasty to 17 patients receiving conservative therapy. This study was published in a German-language journal in a brief format (3 pages). Patients presented, on average, 34 days after

the injury thought to have caused the fracture, and all patients had “functionally unstable fractures” as revealed by images of the vertebral body at flexion and extension. The results were reported without formal statistical testing, but show an improvement in the kyphoplasty group in the VAS pain scale from 91 to 25 at 6 months (uncertain group measure, probably mean or median). The control group showed less improvement from 91 to 83 at 6 months. The pain score as evaluated by North American Spine Society (NASS) score showed similar results, as did functional status as assessed by the Oswestry disability scale.

In sum, these 2 small nonrandomized studies are suggestive of a benefit of kyphoplasty when compared to conservative management. Nonrandomized studies, however, may be biased due to unmeasured risk differences between treated and untreated groups. These 2 studies enrolled different types of patients with respect to age of fracture; the study by Kasperk et al. (2005) enrolling patients with greater than 1-year-old fractures, and Komp et al. (2004) enrolling patients with acute fractures who met specific radiologic criteria for instability. The brief format of the Komp study does not allow an assessment of the similarity of the kyphoplasty and control groups. Contrary to a nonrandomized study of vertebroplasty by Diamond et al. (2003), the control groups in this study did not improve appreciably over a period of weeks to months.

Finally, Grohs et al. (2005) published a non-randomized study comparing vertebroplasty to kyphoplasty. Patients were treated after a median of 8 weeks of symptoms. In this study, VAS pain scores improved in both kyphoplasty and vertebroplasty groups compared to baseline. However, Oswestry disability scores decreased only in the kyphoplasty group at follow-up times of 4 months and 1 year, but not at 2 years. The vertebroplasty group had no improvement in Oswestry disability scores at any time point. There were no statistical analyses performed comparing the outcomes of vertebroplasty to kyphoplasty, but the authors conclude that kyphoplasty is superior to vertebroplasty based on a greater magnitude of pain reduction. Given that there is no formal analysis comparing vertebroplasty to kyphoplasty, this study provides limited information regarding the comparative outcomes between the 2 procedures. Lack of improvement in Oswestry

**Table 6.** Comparative Studies of Kyphoplasty for Osteoporotic Vertebral Fractures\*: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Symptom Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
Kasperk et al. 2005	Prospective case series with comparison group	60		Consecutive patients evaluated with painful vertebral fractures, pain and fractures present for >12 months, who met evaluation criteria as being suitable for kyphoplasty	>12 mos.	6 mos.	Outcomes assessed at 3 mos., 6 mos. – VAS pain score, 50–0 scale – EVOS functional score, 0–60 scale
Komp et al. 2004	Prospective case series with comparison group	36		40 patients evaluated with vertebral fractures, all with positive bone scans, functionally unstable, 28 with “active” vertebral fractures	34 days (mean)	6 mos.	Outcomes assessed at 6 wk, 6 mos. – VAS pain score, 50–0 scale – NASS pain – NASS neurology – Oswestry disability score
Grohs et al. 2005	Prospective case series with comparison group	51		51 patients with osteoporotic vertebral fractures, treated with either kyphoplasty or vertebroplasty	8 weeks	2 years	Outcomes assessed out to 2 years – VAS pain score, 0–10 scale – Oswestry disability score

\*Some studies include a few patients with malignant disease that are not reported separately

Abbreviations: See Appendix Table

**Table 7.** Comparative studies of Kyphoplasty for Osteoporotic Vertebral Fractures: Outcomes

Study/yr	n	F/U	Outcome Measure		Pretreatment	Post-treatment	p value <sup>1</sup>	Comments	
Kasperk et al. 2005	40	6 mos.	Pain (50–0 VAS):	KP	26.2	<b>3 mos.</b> 42.4	<b>6 mos.</b> 44.2	3 mos.: 0.012 6 mos.: 0.007 3 mos.: 0.205 6 mos.: 0.031 (all between- group)	Vertebral height and kyphosis angle analyzed but not abstracted. Change in pain medication use not formally analyzed.
	20			Ctrl	33.6	33.9	35.6		
	EVOS (60–0):		KP	43.8	52.7	54.4			
			Ctrl	39.8	45.1	43.8			
Komp et al. 2004	19	6 mos.	Pain (0–100):	KP	91	<b>6 weeks</b> 20	<b>6 mos.</b> 25	NR	Uncertain whether outcome measures represent mean or median
	17			Ctrl	91	88	83		
	NASS pain:		KP	5.4	1.9	2.0			
			Ctrl	5.2	4.9	4.8			
	NASS neuro:		KP	1.1	1.1	1.1			
			Ctrl	1	1.1	1.1			
	Oswestry: (100–0)		KP	84	22	24			
			Ctrl	82	78	76			
Grohs et al. 2005	28	2 years	Pain (0-10)	KP	7.4	<b>1 yr.</b> 2.7	<b>2 yrs.</b> 2	All pre-post <0.05 <0.05 NS at 2 yrs NS at 2 yrs	No between-group p-values provided
	23			VP	7.8	5.8	5.6		
	Oswestry		KP	61	42	56			
			VP	49	46	52			

<sup>1</sup> p-values for pre- post- (within-group) comparisons unless otherwise specified

Abbreviations: See Appendix Table

disability score at 2 years for either procedure is difficult to interpret given the lack of a non-treated control group.

**Case Series Studies of Kyphoplasty for Osteoporotic Fractures.** Seven published case series studies were found that met selection criteria. Characteristics of the studies are shown in Table 8. Some studies included some patients with vertebral fractures due to malignancy, but these patients' outcomes were not reported separately. All studies enrolled patients with severe pain, but they varied with respect to the duration of the pain prior to the procedure. Most studies used some form of VAS to report pain outcomes.

The results are generally consistent in that all show statistically significant decreases in pain from an initial starting value between 7–9 on the VAS to about 2–4 after the procedure (Table 9). Such pain relief appears to be lasting in the 3 studies that reported long-term outcomes beyond 1 year, although most of the studies had large losses to follow-up.

In terms of other outcomes, results generally showed improvement after kyphoplasty. Garfin et al. (2006) showed a higher proportion of patients reporting able to lift a 10-pound object at all follow-up times. Coumans et al. (2003) reported statistically significant improvements in several subscores of the SF-36, including physical function, mental health, pain, vitality, and social function. Ledlie et al. (2006) showed that the proportion of patients fully ambulatory increased after the procedure, but the study had progressive losses to follow-up over time. Crandall et al. (2004) showed decreases in the amount of medication use over time.

Rates of adverse outcomes from studies abstracted from the prior TEC Assessment (2004) are shown in Table 10. Leakage of the cement outside the vertebral body is a common occurrence, occurring between 6% and 38% in 6 studies that reported its occurrence. Among all the series, there was only 1 patient who had symptoms due to the leak. Other adverse effects such as pulmonary embolus, myocardial infarction, and congestive heart failure infrequently occurred.

In sum, the case series show a consistent improvement in pain scores and other functional scores when compared to baseline. Evidence regarding the durability of benefit

is weakened by the losses to follow-up reported in most studies, but is consistent with effectiveness at least to 2 years. The major limitation of this body of evidence is that there is no control group; thus, placebo effects and natural history may account for some of the apparent benefits of treatment. Retrospective studies raise concerns about unknown selection biases that may affect the results.

### **Conclusions Regarding Vertebroplasty and Kyphoplasty for Osteoporotic Fractures**

Due to the lack of comparative trials of sufficient size and rigor, it is difficult to come to conclusions regarding the efficacy of vertebroplasty and kyphoplasty. Despite most case series showing consistent improvements in pain after the procedure, it is difficult to separate out placebo and natural history effects from actual efficacy.

### **Vertebroplasty: Vertebral Fractures Due to Malignancy**

There are no comparative studies of vertebroplasty for the indication of fracture due to malignancy. Thus, only case series studies are reported here.

**Case Series Studies of Vertebroplasty for Fractures due to Malignancy.** Three studies evaluating a total of 70 patients were found that met criteria for minimum sample size and quality of outcome reporting. Descriptive characteristics of the studies evaluating vertebroplasty for patients with malignant vertebral lesions are shown in Table 11. All patients had severe pain unresponsive to conservative management. All studies evaluated pain relief using VAS both before and after the procedure. However, evaluating the duration of benefit in these patients is problematic because of their very short remaining life span and due to other treatments being performed such as radiation that may alleviate pain. In all of the studies, there were substantial losses to follow-up due to death as early as 1 month after the procedure.

The change in pain scores was consistent across the 3 studies, showing that mean VAS pain scores went from 7–10 at baseline to 0–3 after the procedure, all changes from baseline statistically significant across all studies (Table 12). Regarding other outcomes, Alvarez et al. (2003) showed that the proportion of fully ambulatory patients improved from 38% to 76%, but the study by Fourney et al. (2003) showed no statistically significant improvement

**Table 8.** Case Series of Kyphoplasty for Osteoporotic Vertebral Fractures\*: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Sx Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
Garfin et al. 2006	Prospective case series	155	214	Multicenter 19-center study of patients with osteoporotic vertebral fractures	median 54 days	2 year <sup>s</sup>	Outcomes assessed postoperatively, 1 week, 1 mo., 3 mos., 6 mos., 1 yr – VAS pain score, 0–20 scale – 8 back activities, 0–3 scale – 4-week recall of back disability – SF-36 scores
Robinson et al. 2008	Prospective case series	102	130	Kyphoplasty patients with positive MRI for nonhealing fracture, kyphotic deformity >15 degrees, 12 weeks refractory to medical management	not stated	6 mos.	Outcomes assessed postoperatively, 1 day, 6 mos. – VAS pain score, 0–10 scale
Ledlie et al. 2006	Retrospective case series	117	151	Consecutive pts with lumbar vertebral fractures due to osteoporosis or other osteolytic processes and: – Failed medical management – No pregnancy, coagulopathy, burst fractures	2.6 mos.	1 week to 2 years (range)	Outcomes assessed postoperatively, 1 week, 1 mo., 3 mos., 6 mos., 1 yr, 2 yrs – VAS pain score, 0–10 scale – Ambulatory status – Complications
Coumans et al. 2003	Prospective case series	78	188	Consecutive pts with vertebral compression fractures (n=15 with multiple myeloma) – No evidence of “long-standing” fracture on MRI	7 mos.	≥1 year	Outcomes assessed at last f/u, all pts followed for at least 1 yr – VAS pain score, 0–10 scale – Functional status (SF-36) – Oswestry disability index (ODI) – Complications
Crandall et al. 2004	Prospective case series	47	86	Pts. with osteoporotic vertebral fractures, divided into acute (<10 wks old) and chronic (>4 mos. old)	<10 weeks >4 mos.	18 mos. (mean)	Outcomes assessed at 2 weeks and 6 weeks – VAS pain score, 0–10 scale – Pain medication usage
Rhyne et al. 2004	Retrospective case series	49	82	Pts. with osteoporotic vertebral fractures, unresponsive to conservative management	31 weeks (mean)	9 mos.	Outcomes assessed postoperatively only – VAS pain score, 0–10 scale – Roland-Morris disability scale
Khanna et al. 2006	Prospective case series	211		155 with osteoporosis, 56 with multiple myeloma	7.5 mos.	Mean 55 weeks	Outcomes assessed short term (3–12 wks) and at various long time points – SF-36 scales – ODI

\*Some studies include a few patients with malignant disease that are not reported separately  
Abbreviations: See Appendix Table

**Table 9.** Case Series of Kyphoplasty for Osteoporotic Vertebral Fractures: Outcomes

Study/yr	n	F/U	Outcome Measure	Pre-treatment	Post-treatment					p-value <sup>1</sup>	Comments
					1 wk	3 mo	1 yr	2 yr			
Garfin et al. 2006	155	2 years	Pain (0–20 VAS)	15	6.0	~5.5	~5.5	~5.5 (estimate)		<.0001	55 patients (35.4%) lost to follow-up at 2 yrs
			Lifting 10-lb object (%)	19	55	60	60	65 (estimate)		<0.001	
			Days in bed prior month		significantly improved at all times						
			Limited activity prior mo.		significantly improved at all times						
			SF-36 scales		most scales significantly improved						
Khanna et al. 2006	211		ODI	Results reported as change from baseline	<b>Short-term 3–12 wks</b>		<b>Long-term &gt;24 wks</b>			<0.001	n=126 for short term n=65 for long term Only those with some follow-up included
			Various SF-36 scales		-10.5	-13.5		<0.05 or better			
				8/10 scales improved		9/10 scales improved					
Robinson et al. 2008	102	6 months	Pain (0–10 VAS)	7.5	<b>1 day 6 mo</b>				NR	% follow-up not reported	
					2.3	1.4					
Ledlie et al. 2006	117	1 week to 2 years (range)	Pain (0-10 VAS)	8.9	<b>1 wk</b>	<b>1 mo</b>	<b>3-6 mos</b>	<b>1 yr</b>	<b>2 yr</b>	<0.0001	77 patients followed out to 2 years, lost to follow-up not reported
			% pts fully ambulatory	45	2.8	2.4	1.6	1.5	1.5	NR	
Crandall et al. 2004	47	18 mos. (mean)	Pain (0–10 VAS)		<b>2 wks</b>		<b>6 wks</b>				“90% pain relief” Number of patients at later f/u not reported
			Acute	7.3	4.3	4.3		0.001			
			Chronic	7.3	4.0	4.0		0.001			
			Medication use, Combined groups	5.4		<b>last f/u</b>	3.6	0.001			
Rhyne et al. 2004	49	9 mos.	Pain (0–10 VAS)	9.16	<b>Post-op</b>					<0.05	
			Disability Score	19.3	2.91						<0.05

**Table 9.** Case Series of Kyphoplasty for Osteoporotic Vertebral Fractures: Outcomes (cont'd)

Study/yr	n	F/U	Outcome Measure	Pretreatment	Post-treatment	p value <sup>1</sup>	Comments	
Coumans et al. 2003	78	≥1 year			<b>Post-op</b>		n=40 at last f/u	
					<b>Last f/u (≥1 yr, mean 18 mos.)</b>			
			Pain (0–10 VAS)	7	3.2	3.4	<0.0001	
			Disability (ODI, 0–100)	48	33	35	<0.001	
			SF-36: Phys Fxn	22		38	<0.005	
			Mental Hlth	51		64	<0.001	
			Gen Hlth	58		48	NS	
			Pain	20		42	<0.001	
			Vitality	27		36	<0.05	
			Social Fxn	36		58	<0.001	
			Role Phys	3		29	<0.005	
			Role Emot	50		74	<0.05	
					47.4			
			Mental Hlth	59.2		71.1	0.02	
			Gen Hlth	55.0		61.0	NS	
			Pain	11.6		58.7	0.0001	
			Vitality	24.8		47.9	0.001	
			Social Fxn	28.6		69.0	0.0004	
			Role Phys	1.2		29.8	NS	
			Role Emot	68.0		62.0	NS	
					3.8	1.7	1.5	

<sup>1</sup> p-values for pre- post- (within-group) comparisons unless otherwise specified

Abbreviations: See Appendix Table

**Table 10.** Adverse Events of Kyphoplasty for Osteoporotic Fractures

Study	n		Adverse Events <sup>1</sup>							Comments
	Pts	VB	Leak	Leak-Sx	PE	MI	CHF	Rib Fx	Bleed	
Ledlie et al. 2003	96	133	13%	1%	1%	—	—	—	—	1 pt with respiratory failure
Coumans et al. 2003	78	188	6.4%	0%	—	1.3%	—	—	—	
Lieberman et al. 2001	30	70	20%	0%	—	—	—	—	—	
Phillips et al. 2003	29	61	9.8%	0%	—	3%	3%	—	—	1 pt with urinary retention
Berlemann et al. 2004	24	27	38%	0%	—	—	—	—	—	
Crandall et al. 2004	47	86	NR	0%						2 balloons ruptured
Rhyne et al. 2004	49	82	9.8%							
Gaitanis et al. 2005	32	61	9.8%	0%						2 balloons ruptured, 2 new fractures within 6 weeks

<sup>1</sup> Adverse event rates based on % pts with complication

**Key**  
 Leak all cement leaks, with or without any clinical symptoms  
 Bleed postoperative, clinically significant bleeding  
 Leak-Sx cement leaks causing clinical symptoms  
 PE pulmonary embolus  
 CHF congestive heart failure  
 MI myocardial infarction  
 Rib Fx rib fracture

Other Abbreviations: See Appendix Table

**Table 11.** Case Series Studies of Vertebroplasty for Vertebral Fractures Due to Malignancy: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Sx Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
Alvarez et al. 2003	Retrospective case series	21	27	Consecutive pts with vertebral fractures due to metastatic disease seen at one institution, and: – Intractable pain unresponsive to conservative treatment – No evidence of myeloma	NR	3 mos.	Outcomes assessed post-procedure and at 3 mos.: – VAS pain score, 0–10 scale – Complications
Fourney et al. 2003	Retrospective case series	34	NR	Vertebroplasty subset of patients who underwent vertebroplasty or kyphoplasty seen at one institution, and: – Intractable pain unresponsive to conservative treatment – No significant kyphosis – Cannot tolerate anesthesia or long procedure	3.2 mos. (mean)	4.5 mos. (mean)	Outcomes assessed post-procedure out to 1 year if alive or available – VAS pain score, 0–10 scale – Complications
Chow et al. 2004	Retrospective case series	15	19	Patients with malignancy and spinal metastases or compression fractures, and: – Intractable pain unresponsive to conservative treatment – No infection – No neural compression	NR	3 mos.	Outcomes assessed at 2–12 weeks – VAS pain score, 0–10 scale – Edmonton symptom assessment scale (ESAS) – Townsend functional assessment scale (TFAS)

Abbreviations: See Appendix Table

**Table 12.** Case Series Studies of Vertebroplasty for Vertebral Fractures Due to Malignancy: Outcomes

Study/yr	n	F/U	Outcome Measure	Pretreatment	Post-treatment	p-value <sup>1</sup>	Comments
Alvarez et al. 2003	21	3 mos.	Pain (0–10 VAS)	9.2	<b>Post-op</b> 3.2	<0.001	4 pts died in hospital due to cancer
			% pts fully ambulatory	38	76		
Fourney et al. 2003	34	1 year	Pain (0–10 VAS)	8	<b>Post-op</b> 2	<0.05	23% complete pain relief 63% improved
			Ambulatory status (Frankel grades)	NR	NR—“not statistically significant”		
Chow et al. 2004	15	3 mos.	Pain (0–10 VAS)		<b>2–12 wks</b>		3 patients died within 8 weeks
			With movement	10	1	<0.00001	
			At rest	7	0	<0.00001	
			TFAS	NR	NR		
			ESAS	NR	“statistically significant improvement, nausea and depression”		
Analgesic use	NR	“not statistically significant”					

<sup>1</sup> p-values for pre- post- (within-group) comparisons unless otherwise specified

in ambulatory status. The study by Chow et al. (2004) reported that changes in analgesic usage were not statistically significant, and changes in nausea and depression in the Edmonton Symptom Assessment Scale were statistically significant, but specific quantitative results are not reported.

The adverse effects reported in these studies revealed a rate of leakage of cement ranging from 9% to “most,” with a small proportion of the patients with cement leakage having symptoms due to the leak.

#### **Kyphoplasty: Vertebral Fractures Due to Malignancy**

There are no comparative studies of kyphoplasty for the indication of fracture due to malignancy. Thus, only case series studies are reported here.

**Case Series Studies of Kyphoplasty for Fractures due to Malignancy.** Three studies were found reporting a total of 52 patients for this indication (Tables 13 and 14). Two of the studies (Dudeney et al. 2002; Lane et al. 2004) included only patients with multiple myeloma. Each of the studies reports a different set of outcomes. Dudeney et al. (2002) reports improvements in several SF-36 subscales, including physical function, pain, vitality, and social function. Fourney et al. (2003) reported improvements in pain score from a mean of 8 preoperatively to 2 postoperatively. Lane et al. (2004) reported improvement in the Oswestry Disability Index score from 48.94 to 32.6 at 3 months. Qualitatively, these improvements appear to be similar to the degree of pain relief that occurs in patients with osteoporotic vertebral fractures who undergo kyphoplasty.

In terms of adverse events, leakage of cement occurred in 11%, 0%, and 26%, in the 3 studies. None of the leaks caused symptoms. Fourney et al. (2003) reported that over time, 14% of patients had recurrent fractures at other sites. Without a control group, it is not possible to attribute these fractures to the kyphoplasty procedure.

The major limitation of this body of evidence is that there is no control group; thus placebo effects and natural history may account for some or all of the apparent benefits of treatment.

#### **Conclusions Regarding Vertebroplasty and Kyphoplasty for Fractures Due to Malignancy**

The amount of evidence for this particular indication is much less than that for osteoporotic fractures. The magnitude of pain relief appears to be equivalent to that for osteoporotic fractures, but the only evidence for this indication is based on case series.

### **Discussion**

There is a lack of rigorous comparative trials of vertebroplasty and kyphoplasty. For vertebroplasty, there is only one randomized trial with very short follow-up of 2 weeks. Two of 3 nonrandomized studies show efficacy of the procedures. Case series studies show 4- to 5-point improvements in VAS pain ratings. Nonrandomized and case series studies may not provide reliable evidence of efficacy. Both procedures appear to produce similar effects, and there are few data directly comparing the two procedures to each other. The principal adverse effect is leakage of cement out of the vertebral body, which occurs in both procedures, but appears to be more common after vertebroplasty. Complications due to this leakage are infrequent, however. Fractures in vertebrae adjacent to the treated vertebrae do occur; however, it has not been demonstrated whether this is more common after such treatment. Case series studies of patients with vertebral fractures due to malignancy generally show the same quantity of improvement of pain and health status as for osteoporotic fractures.

There is no strong comparative evidence between the two procedures. Kyphoplasty produces greater anatomic changes in kyphosis than vertebroplasty; however, these anatomic changes are not well correlated with symptomatic improvement or improvement in health status. Anatomic changes due to kyphoplasty were not reported in this Assessment.

#### **Current Clinical Trials of Vertebroplasty and Kyphoplasty**

There are currently several clinical trials of these procedures currently in progress. VERTOS-II is a randomized trial based in the Netherlands comparing vertebroplasty to conservative management. The trial is finished recruiting patients, and 1 year of follow-up will be completed in May 2009.

**Table 13.** Case Series Studies of Kyphoplasty for Vertebral Fractures Due to Malignancy: Study Characteristics

Study/yr	Study Design	n		Eligibility Criteria/Population	Sx Duration	F/U	Outcomes/Outcome Assessment
		Pts	VB				
Dudeny et al. 2002 (overlaps Lieberman et al. 2001)	Prospective case series	18	55	Consecutive pts undergoing kyphoplasty at one institution with compression fractures due to multiple myeloma.	11 mos.	7.4 mos. (mean)	Outcomes assessed preoperatively and at last f/u – Functional status (SF-36)
Fourney et al. 2003	Retrospective case series	15	NR	Kyphoplasty subset of patients who underwent vertebroplasty or kyphoplasty at one center with malignancy, and: – Intractable pain unresponsive to conservative treatment – Kyphosis >20 degrees – Can tolerate anesthesia or long procedure	3.2 mos. (mean)	4.5 mos. (mean)	Outcomes assessed post-procedure out to 1 yr if alive or available – VAS pain score, 0–10 scale – Complications
Lane et al. 2004	Prospective case series	19	46	Patients with pain and deformity due to multiple myeloma	>3 mos.	3 mos.	Outcomes assessed at 3 mos. – Oswestry Disability Index Score – Complications

Abbreviations: See Appendix Table

**Table 14.** Case Series Studies of Kyphoplasty for Vertebral Fractures Due to Malignancy: Outcomes

Study/yr	n	F/U	Outcome Measure	Pre-treatment	Post-treatment	p-value <sup>1</sup>	Comments
Dudenev et al. 2002 (overlaps with Lieberman et al. 2001)	18	7.4 mos. (mean)	SF-36: Phys Fxn	21.3	50.6	0.001	
			Mental Hlth	NR	NR	NS	
			Gen Hlth	NR	NR	NS	
			Pain	23.2	55.4	0.0008	
			Vitality	31.3	47.5	0.01	
			Social Fxn	40.6	64.8	0.01	
			Role Phys	NR	NR	NS	
			Role Emot	NR	NR	NS	
Fourney et al. 2003	15	4.5 mos. (mean)	Pain (0–10 VAS)	8	<b>Post-op</b> 3	<0.05	7% complete pain relief 73% improved
			Ambulatory status (Frankel grades)	NR	NR—“not statistically significant”		73% follow up available at 1 mo.
Lane et al. 2004	19	3 mos.	Oswestry Disability Index Score	48.94	<b>3 mos.</b> 32.6	<0.001	

<sup>1</sup> p-values for pre- post- (within-group) comparisons unless otherwise specified

Abbreviations: See Appendix Table

The INVEST trial is a randomized, sham-controlled trial of vertebroplasty versus medical management that is nearing the end of enrollment as of July 2008. One month post-procedure outcomes may be available in December 2008.

An unpublished randomized, clinical trial of kyphoplasty versus nonsurgical management was presented at the first International Society for Minimal Intervention in Spinal Surgery (ISMIS) Congress (Istanbul, Turkey; April 2007) on “Minimal Invasive Spine Surgery and Interventional Treatments.” A brief abstract is available online (Muller et al. 2008).

### Summary of Application of the Technology Evaluation Criteria

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether percutaneous vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

#### 1. The technology must have final approval from the appropriate governmental regulatory bodies.

Vertebroplasty and kyphoplasty are surgical procedures and, as such, are not subject to U.S. Food and Drug Administration (FDA) approval.

Kyphoplasty requires the use of an inflatable bone tamp. One such tamp, the KyphX<sup>®</sup> inflatable bone tamp, received 510(k) marketing clearance from the FDA in July 1998.

Polymethyl methacrylate (PMMA) bone cement was available as a drug product prior to enactment of the 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 for purposes other than vertebroplasty or kyphoplasty 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 (accessed August

2008 at <http://www.fda.gov/cdrh/ode/guidance/668.pdf>), that outlines the types of special controls required and describes the following recommended labeling information:

**Intended Use.** PMMA bone cement is intended for use in arthroplastic procedures of the hip, knee, and other joints for the fixation of polymer or metallic prosthetic implants to living bone.

**Contraindications.** PMMA bone cement is contraindicated in the presence of active or incompletely treated infection, at the site where the bone cement is to be applied.

**Warnings.** Monitor patients carefully for any change in blood pressure during and immediately following the application of bone cement. Adverse patient reactions affecting the cardiovascular system have been associated with the use of bone cements. Hypotensive reactions have occurred between 10 and 165 seconds following application of bone cement; they have lasted from 30 seconds to 5 or more minutes. Some have progressed to cardiac arrest. Patients should be monitored carefully for any change in blood pressure during and immediately following the application of bone cement.

There have been several bone cement products cleared for marketing via 510(k) by the FDA for use in vertebroplasty or kyphoplasty (e.g., Vertaplex or Spineplex<sup>™</sup> Radiopaque Bone Cement [Stryker], KyphX<sup>®</sup> HV-R<sup>™</sup> Bone Cement [Kyphon, Inc.], Vertebroplastic<sup>™</sup> Radiopaque Bone Cement [DePuy Spine, Inc.]). Continuing concern about other cement and bone void filling products led to an FDA Public Health Web Notification that notes the types of complications that can occur with these products, and offers advice to physicians regarding use of such products. FDA requires hospitals and facilities to report deaths and serious injuries associated with the use of such medical devices. Use of cement products not receiving FDA clearance specifically for vertebroplasty or kyphoplasty represents an off-label use.

#### 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

There are relatively few comparative trials of vertebroplasty or kyphoplasty, but many case

series have been published. Without evidence from controlled trials, it is not possible to determine the effect of vertebroplasty or kyphoplasty on health outcomes. The one published randomized trial of vertebroplasty showed efficacy of the procedure, but follow-up was only 2 weeks. Case series studies are subject to many sources of bias and generally are not reliable evidence of efficacy.

- 3. The technology must improve the net health outcome; and**
- 4. The technology must be as beneficial as any established alternatives.**

The evidence is insufficient to determine whether either vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy improves the net health outcome or is as beneficial as any established alternatives.

- 5. The improvement must be attainable outside the investigational settings.**

Whether either vertebroplasty or kyphoplasty for vertebral fractures from osteoporosis or malignancy improves health outcomes has not been established in the investigational setting.

For the above reasons, percutaneous kyphoplasty or vertebroplasty for vertebral fractures from osteoporosis or malignancy does not meet the TEC criteria.

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# Appendix

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Table of Abbreviations

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CHF	congestive heart failure
Ctrl	control
EVOS	European Vertebral Osteoporosis Study score
f/u	follow-up
fx	fracture
fxn	function
hlth	health
KP	kyphoplasty
MI	myocardial infarction
MMA	polymethyl methacrylate
mo(s)	month(s)
MRI	magnetic resonance imaging
NASS	North American Spine Society
neuro	neurologic
NR	not reported
NS	not significant
ODI	Oswestry disability index scale/score
PE	pulmonary embolus
phys	physical
pt(s)	patients
PVP	percutaneous vertebroplasty
sx	symptoms
VAS	visual analog scale
VB	vertebral bodies
wk(s)	week(s)
yr(s)	year(s)

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