EVALUATION OF CLINICAL DATA REGARDING

BALLOON KYPHOPLASTY

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Evaluation of Clinical Data Regarding Balloon Kyphoplasty

1. Purpose

The purpose of this document is to evaluate available clinical data, including medical literature, to assess the safety and performance of balloon kyphoplasty for treating vertebral compression fractures.

2. Executive Summary

Vertebral body compression fractures (VCFs) are common with an estimated yearly incidence of 700,000 in the U.S.[1] Osteoporosis is the most common cause of VCF injuries. Of the VCF-related hospitalizations that occurred in 1997, approximately 3 of 4 patients are women. More than 20% of men with fractures are found to be in the 45 to 64 years of age category, whereas only 7% of women are in this age group.[2] Among young adults, VCFs occur with similar frequency among both men and women.[2] VCFs can also result from secondary osteoporosis. The third most common cause of VCFs is osteolytic damage associated with spinal malignancies. Every year, cancer is the cause of an estimated 150,000 fractures worldwide, occurring in patients that are typically below the age of 65.[3, 4]

Despite the conventional view that the pain of clinically evident VCFs subsides within 8-12 weeks with medical management alone, the clinical literature does not support this. Patients with symptomatic VCFs often fail to show improvements in pain and mobility.[5] Decrements in quality of life associated with non-surgical management can persist for years.[6] According to the U.S. Surgeon General, spine fractures have been linked with a 20% reduction in quality of life in the year following fracture and a 15% reduction after two years.[7] However, even when the acute fracture pain subsides, VCFs are associated with a constellation of adverse health effects that intensify with increasing deformity and are independent of acute fracture pain. This includes inability to perform normal daily activities, reduced pulmonary function, loss of mobility, reduction in social roles, depression, low self-esteem and low self-image. VCFs are also associated with excess mortality at a rate that is similar to the excess mortality seen with hip fractures,[8, 9] and the mortality rate increases with deformity.[10] Unfortunately, the deformity created by VCFs shifts load to the front of the spine, resulting in a downward spiral of additional VCFs and further physical and functional impairment.[11]

Healthcare utilization and costs related to osteoporotic fractures in general and vertebral fractures in particular have historically been difficult to estimate. One study prospectively designed to assess this estimated that healthcare costs for treating vertebral fractures may be higher than previously anticipated and comparable to hip fractures.[12] A significant proportion of the cost of treating a fracture may be related to comorbidities that often result in significantly higher overall healthcare expenditures.[7, 13, 14] In 1997 (prior to balloon kyphoplasty), average lengths of stay for spine fracture patients were only slightly shorter than those for hip fracture (nearly six days).[2]

Balloon kyphoplasty is the only minimally invasive treatment option available that utilizes an inflatable (balloon) bone tamp (IBT) to stabilize and at least partially correct anatomical abnormalities associated with VCFs. The procedure involves the image-guided placement of cannulae into the vertebral body through the pedicles. An IBT is

inserted through each cannula into the vertebral body. Inflation of the IBTs with radiopaque contrast medium allows the operator to carefully control the balloon volume. This compacts cancellous bone, which creates a void inside the vertebral body into which thick bone cement is delivered under fine manual control using a bone filler device (BFD). The advantage of void creation is the reduced potential for the fixation material to extend beyond the region of its intended application.[15]

The specialized IBTs used in balloon kyphoplasty and the KyphX® HV-R™ bone cement have 510(k) clearance for use by the United States Food and Drug Administration (FDA). Other tools required to perform balloon kyphoplasty are also commercially available. As of April 24, 2008, over 446,000 patients and 519,000 vertebral compression fractures have been treated worldwide, and over 13,400 physicians have been trained to perform the procedure (data on file at Medtronic Spine LLC).

Reviewed more extensively in Section 3.3, the clinical literature supporting the safety and effectiveness of balloon kyphoplasty is large and ever-growing. Data from 52 unique clinical studies show early and sustained pain relief, anatomy correction, improved mobility and function, and importantly, improved patient quality of life. Several studies show that patients' dependence on analgesics is significantly reduced following balloon kyphoplasty.[16, 17] Two important prospective concurrently controlled studies demonstrate the benefits of balloon kyphoplasty over non-surgical management.[17, 18] One of these studies shows that balloon kyphoplasty results in significantly fewer return visits to a physician owing to back pain.[19] In a recent publication, these clinical improvements were maintained at 2 and 3 years of follow-up.[20] In a prospective, multicenter, single arm study, improvements in quality of life were marked and statistically significant in all SF-36 sub-domains (except for General Health) as early as one month and at all follow-up time points out to two years.[21] Similar improvements in quality of life were found in patients with VCFs due to either osteoporosis or multiple myeloma in a single-center study.[22] Thus, it is not surprising that balloon kyphoplasty has high rates of patient satisfaction as it significantly improves the patient's ability to perform activities of daily living without pain and discomfort.

Randomized studies comparing kyphoplasty and non-surgical management are desired for more definitive assessments regarding the clinical effectiveness and safety of kyphoplasty and to understand important issues regarding comparative cost-effectiveness of these treatments. Such studies are underway; one-month results were recently published in abstract form in the proceedings of the 22nd annual meeting of the North American Spine Society.[23] In this study, 149 patients were randomized to and treated with balloon kyphoplasty. Compared to the non-surgical control, kyphoplasty significantly improved quality of life and reduced back pain and disability with no significant difference in the number of patients with serious adverse events.

The available medical literature demonstrates that balloon kyphoplasty is safe and effective. Most clinical studies demonstrate a very low rate of procedure-related adverse events with rapid clinical improvements that have been shown to be long-lasting, improving patient quality of life.

3. Overview of Vertebroplasty and Balloon Kyphoplasty

3.1. Introduction

Vertebral body compression fractures (VCFs) are a common complication of osteoporosis and metastatic or primary cancer in the spine.[3, 24] These fractures of the weakened vertebral body typically result from low-energy loading during normal daily activities.

In addition to back pain and back dysfunction,[25-27] VCFs cause substantial deficits in quality of life and contribute significantly to patient morbidity and mortality.[28-35] Standard treatment of painful VCFs has been medical management, consisting of bed rest, analgesics, and bracing. Contrary to general opinion, the clinical literature does not support the adequacy of non-operative care. For instance, several studies demonstrate failure to improve using objective quality of life measures when symptomatic VCFs are managed non-operatively. Only one study has shown an advantage of back bracing.[36] No study has demonstrated any advantages of any other non-surgical therapy. Natural history studies have found that medical management for symptomatic VCFs often fails to improve pain and mobility particularly in cases with chronic pain related to kyphotic deformity. Furthermore, long-term use of narcotic analgesics to control acute pain has various side effects, including constipation, nausea, sedation, and potential for addiction. Bed rest has been shown to cause loss of bone mineral, which may exacerbate the underlying disease state.[37] Excessive bed rest has also been shown to lead to rapid deconditioning and pulmonary compromise.[38]

Medical management alone leads to vertebral deformity, which is associated with significant long-term consequences that have been shown to be independent of acute fracture pain, including decreased pulmonary function,[39-41] early satiety,[11] gastric distress,[11] impaired gait,[11] increased future fracture risk,[42] and excess mortality.[8, 9] As a result, patients still incur long-term health risks even in cases where acute fracture pain subsides. Unfortunately even the highest standard of non-surgical management does not prevent kyphotic deformity. Medical management of painful fractures does not permit restoration of spinal alignment and may in fact compound the problem. Indeed it has been estimated that a significant proportion of the cost of treating a fracture is not related to the fracture itself or its sequelae, but rather to comorbidities resulting in significantly higher overall healthcare expenditures.[7, 13, 14]

Spinal biomechanics explain and predict the sequelae described above. As the spine collapses, shortens, and moves forward, the ribs angle downward and the gap between the ribs and the pelvis narrows until the twelfth rib rests on the iliac crest. The increase in forward-bending movement from the change in spinal alignment requires increasing the counterbalancing force using the posterior musculature and ligaments, or balance is lost. Patients attempt to counterbalance the increased forward-bending movement by flexing their hips and knees, and contracting the posterior musculature to tilt their pelvis. This brings their shoulders and head back up, but stresses the hips and knees, and tightens the hamstrings which reduces gait velocity and mobility. It also leads to paraspinal muscle fatigue, and contributes to the fatigue and chronic back pain associated with osteoporotic spinal deformity.[43]

As the spine becomes more kyphotic, the abdomen protrudes and distends, and early satiety is common, contributing to nutritional and metabolic problems. The trunk center of gravity shifts so far anterior beyond the torso, creating a force that pushes the patient forward and off balance, that the risk of falls is increased and the use of walking aids is necessary, reducing mobility. Ultimately, the position of the head and neck over the pelvis becomes fixed so that maintaining an upright posture becomes impossible. The loss of thoracic space, related to the kyphotic deformity and loss of vertebral height, restricts airways and reduces pulmonary function. Kyphosis also alters the local loading within the spine. The change in the center of gravity shifts the forces anterior and inferior, so that loads on the anterior spine are increased with each new compression fracture. These mechanical effects explain the acceleration of future fracture risk with each new compression fracture. Thus, biomechanics of the spine and the resulting compensatory mechanisms to address kyphotic posture both explain and predict most of the sequelae documented in patients with prevalent (pre-existing) VCFs.

This literature and underlying mechanical principles strongly support the goal of restoring anatomy whenever possible in the treatment of diagnosed VCFs.

3.2. Minimally invasive surgical approaches in the treatment of VCFs include balloon kyphoplasty and vertebroplasty, both of which use bone cement (typically PMMA or calcium phosphate) to stabilize the fractured vertebral body.

Developed by Deramond in France in the 1980s for stabilization of vertebral haemangioma,[44] vertebroplasty was subsequently extended for the treatment of VCFs caused by metastatic disease[45] and osteoporotic vertebral compression fractures.[46] The goals of vertebroplasty are to relieve pain through bone cement stabilization of the fracture without the need for open surgery. During percutaneous vertebroplasty, a small needle is inserted percutaneously into the vertebral body through the pedicles. PMMA-based bone cement is injected into the cancellous bone of the vertebral body. The bone cement fills the bony trabeculae to stabilize the bone. Anatomy restoration is not typically a goal of vertebroplasty though it can be achieved in selected patients with postural maneuvers.[47]

This review does not attempt to summarize all of the available data for vertebroplasty. However, as a brief overview, the published clinical literature documents the effective use of bone cement during vertebroplasty for the treatment of VCFs, along with an acceptable safety profile. For example, the literature consists of many prospective studies with follow-up > 6 months[48-55] as well as many notable retrospective studies.[56-58] One small randomized study showed that vertebroplasty improved pain, disability, and quality of life for 2 weeks in patients compared with those treated nonsurgically.[59] However, crossovers from nonsurgical care to vertebroplasty precluded longer term comparisons. In total, more than 175 clinical reports of vertebroplasty use have shown that it is safe and effective for the treatment of VCFs. The primary safety concerns during vertebroplasty are 1) symptomatic cement extravasation and 2) cement embolism. If bone cement delivered into the vertebral body leaks out, it may deposit in locations that may cause clinical symptoms. Bone cement in the neural foramina of the spine may cause radiculopathy. Bone cement leaking posteriorly from the vertebral body may cause myelopathy, including weakness and paralysis. Generally, the leakage of bone cement

during vertebroplasty is controlled by the use of fluoroscopy. Since most PMMA bone cements are radiopaque by virtue of added barium, the cement is visible during fluoroscopy. If the operator detects a leak of bone cement, he or she stops injecting, thereby limiting the occurrence of symptomatic extravasation. In vertebroplasty, cement is typically delivered using a needle, often under high intrasyringe pressures with a low-viscosity cement. These aspects of the vertebroplasty procedure may lead to cement extravasation from the treated vertebral body.[60, 61] In recent meta-analyses of the published literature, the cement extravasation rate after vertebroplasty was found to be between 20 to 41%.[60-63] The symptomatic leakage rate has been calculated at 1.6-3.0% for vertebroplasty.[63, 64] A second safety concern is cement embolism. Several articles have documented the occurrence of symptomatic cement embolism, including pulmonary embolism[65, 66] and embolism to the kidneys.[67] Since cement is radiopaque, the likelihood of embolism can be limited by use of fluoroscopy.

3.3. Balloon Kyphoplasty

Like the classic orthopaedic approach to any displaced fracture, balloon kyphoplasty is a minimally invasive technique for the reduction and internal fixation of VCFs. Consistent with the orthopaedic principles of fracture management, the goals of balloon kyphoplasty include: 1) vertebral body anatomy restoration, 2) solid internal fixation, 3) minimal tissue disruption, and 4) safe and early mobilization. First performed in 1998, balloon kyphoplasty involves the percutaneous placement of cannulae into the vertebral body through the pedicles.[68] An Inflatable Bone Tamp (IBT) is inserted through the cannula into the vertebral body. Inflation of the IBT is designed to restore vertebral body anatomy, with height restoration and angular deformity correction.[69] Similar to vertebroplasty, symptomatic bone cement leakage is of concern. IBT inflation is controlled by a pressure-measuring device; inflation of the IBT with radiopaque contrast material is visualized on intraoperative fluoroscopy. The IBT also compacts cancellous bone, which fills the fracture lines and disrupts the internal venous plexus, reducing pathways for the fixation material to go beyond the region of its intended application.[15] The IBT is removed, and the void created by the IBT is typically filled with viscous PMMA-based bone cement using a Bone Filler Device (BFD). These characteristics may allow cement delivery with a lower risk of cement extravasation outside of the vertebral body. In recent meta-analyses of the published literature, the cement extravasation rate after balloon kyphoplasty was between 7 to 9%[60-63] with a calculated symptomatic leakage rate between 0-0.3%.[63, 64]

3.3.1. Kyphoplasty Studies

This assessment stems from a computer-based literature search performed in April 2008 using the U.S. National Library of Medicine's MEDLINE® database and the search of the term *kyphoplasty* that revealed 460 published articles. Abstracts and articles were reviewed for publications containing original clinical data from > 10 patients treated with kyphoplasty where complications or clinical outcomes were reported. During the assessment, 87 reviews and meta-analyses (80 review articles, 7 meta-analyses), 17 technical reports, 33 author comments or articles that briefly mention kyphoplasty, 76 non-English reports, 35 ex vivo/biomechanical studies, 32 case reports, and 100 non-kyphoplasty articles were excluded. This left 80 publications containing original clinical data for further evaluation. Of these publications, one was a duplicative study, and four

were studies in which clinical data is reported using a device different from an IBT \ (Sky-bone expander). Five kyphoplasty clinical studies were excluded where both vertebroplasty and kyphoplasty were performed and outcomes/complications were not separated. Six more articles were excluded as there were no clinical outcomes reported. Three articles presenting kyphoplasty with open surgery, and four articles reporting traumatic fractures treated with kyphoplasty were also excluded. This left 57 original articles meeting the inclusion criteria to use in the clinical evaluation. Four studies we are aware of that were not found in the Medline search were also included: Hillmeier et al.,[70] Komp et al.,[18] Vrionis et al.,[71] and Wong et al.[68]

The 61 published articles were thoroughly investigated for cohort overlap and represent 52 unique studies involving 3,183 patients, out of which 2,865 received balloon kyphoplasty for symptomatic VCFs with data reported (2,566 for symptomatic VCFs due to osteoporosis, 285 for malignant osteolytic fractures, 3 for hemangiomas, and 11 for traumatic fractures). Of these studies there were:

- 2 prospective concurrently controlled trials (4 reports) comparing balloon kyphoplasty in 59 patients to non-operative care in 37 patients with 6, 12, 24 and 36-month follow-up (Komp et al.[18] and Grafe et al.[17, 19, 20])
- 1 prospective multi-center interventional trial of 155 balloon kyphoplasty patients with 2 year follow-up on 100 patients (Garfin et al.[21])
- 1 prospective study comparing outcomes in 47 balloon kyphoplasty patients with acute or chronic compression fractures with 18 month follow-up (Crandall et al.[72])
- 2 prospective controlled (non-concurrent) studies comparing balloon kyphoplasty in 39 patients to vertebroplasty in 33 patients with 6 and 24 month follow-up (De Negri[73] et al. and Grohs et al.[74])
- 22 additional prospective single center cohort studies of 1,000 patients with follow-up to 18 months (up to 5 years in Khanna et al.[22]) and 24 retrospective reports of 1,565 balloon kyphoplasty patients with follow-up to 2 years

Study outcomes of these original articles are summarized in tabular format in Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies. A complete kyphoplasty bibliography (as of July, 2008) can be found in Appendix 2: Bibliography of Kyphoplasty Studies. The published balloon kyphoplasty studies are noteworthy in that they uniformly show:

- **Pain Relief.** A marked, immediate, and sustained improvement in back pain (46 of 46 studies)
- **Improved Back Function.** A marked, immediate, and sustained improvement in back function (12 of 12 studies)
- **Improved Quality of Life.** A marked, immediate, and sustained improvement in QOL (6 of 6 studies)
- **Improved Radiologic Outcomes.** A marked, immediate, and sustained improvement in vertebral body height (32 of 33 studies) and kyphosis angle (27 of 27 studies)

Table 1: Previous studies of balloon kyphoplasty as of April 3rd 2008.

Outcome	Osteoporosis	Cancer only	Osteoporosis & Cancer	**Total****
Pain NRS / Pain, Descriptive	31*	6	9	**46/46**
Ambulation / Activities of Daily Living	13	4	6	**23/23**
Oswestry Disability Index or Roland Morris Disability Questionnaire	5	2	5	**12/12**
Karnofsky Score	1	0	0	**1/1**
QOL Health Survey	4	0	2	**6/6**
Vertebral Height Restoration	18	4	10	**32/33**
Angular Deformity Correction	**16**	**4**	**7**	**27/27**

* Each entry reports the number of studies in which the outcome listed was studied.
** Total column shows the number of studies in which an improved outcome was shown and the number of studies in which the outcome was examined.

Several studies are noteworthy due to the number of patients, study design and follow-up and/or clinical outcome measures. There is also an abstract of importance that describes a randomized study. These are described below.

3.3.1.1. Two nonrandomized trials comparing balloon kyphoplasty to nonsurgical care for vertebral fractures due to osteoporosis

The most important evidence to date that balloon kyphoplasty augmented with PMMA cement is safe and more effective in comparison to non-operative care comes from two independent, prospective controlled trials with concurrent cohorts, documenting statistically significant improvements in pain and function for patients who receive balloon kyphoplasty compared to patients who undergo non-operative management.[17, 18] These two prospective studies examined clinical outcomes in patients eligible for balloon kyphoplasty treatment of their symptomatic vertebral body compression fractures; some patients chose to have the procedure whereas others opted not to have the procedure. The safety profile in these studies was excellent with no cement or procedure complications.

Grafe et al. and Kasperk et al. evaluated 60 consecutive patients with osteoporosis (T-score < -2.5) with a single, chronic, persistently painful VCF.[17] Mean fracture age was > 12 months. After discussion with their physicians, patients selected either balloon kyphoplasty (40 patients) or non-surgical management (20 patients). At baseline, patients were well-matched across groups on age, sex and bone mineral density. The cohorts were similar in baseline scores for pain and function measures. At 6 weeks and 6 months post-fracture, the patients undergoing non-operative care (n=20) had no statistically significant improvement in pain or function. In contrast, the cohort treated by balloon kyphoplasty (n=40) had statistically significant improvements in pain and function at both follow-up times. There were no peri-operative adverse events related to bone cement or the kyphoplasty procedure during the study. Grafe et al. reported extended clinical follow-up of the same cohort to 1 year after kyphoplasty.[19] At 12 months post-fracture, the patients undergoing non-operative care (n=20) had no

statistically significant improvement in pain or function. In contrast, the cohort treated by balloon kyphoplasty (n=40) had statistically significant improvements in pain and function at the 12 month follow-up. However, at 12 months there was no statistical difference in function between the two groups. The authors indicate that these findings may be attributable to lack of statistical power. Grafe et al. also reports that at the 12 month follow-up, patients treated by kyphoplasty required significantly fewer back pain-related doctors' visits when compared to the control group. At one year, a mean of 12% height restoration occurred in the balloon kyphoplasty group whereas in the non-surgical group a mean of 8% of further height loss occurred. Subsequent fracture occurred half as often in the balloon kyphoplasty group compared to the non-surgical group. Clinical improvement was maintained at 24 and 36 months of follow-up as indicated by a recent publication.[20]

Komp et al. evaluated 40 patients with osteoporosis and a single, painful VCF in an orthopaedics clinic in Germany.[18] Mean fracture age was 34 days. After discussion of options with their physicians, patients selected either balloon kyphoplasty or non-surgical care (back bracing). 36 patients were followed for 6 months. At baseline, groups were matched remarkably well as to age, sex, height, weight, and concomitant illnesses. Pain and back function (Oswestry Disability Index) scores were nearly identical at baseline. In contrast, follow-up pain and back function scores were markedly and statistically significantly improved in patients undergoing kyphoplasty and nearly unchanged in patients undergoing non-surgical management. There were no perioperative adverse events related to the kyphoplasty procedure. Settling of the index fracture occurred in nearly all non-surgically treated patients and in none of the balloon kyphoplasty-treated patients. New fracture was diagnosed in 7/19 (37%) of kyphoplasty-treated patients and 11/17 (65%) of non-surgically treated patients.

3.3.1.2. Two-Year Outcomes of Balloon Kyphoplasty

Ledlie et al. reported the first publication of two-year outcomes among 77 subjects treated with kyphoplasty.[16] In this study, back pain was reduced from a preoperative mean of 8.9 (0 to 10 scale) to a post-operative mean of 2.8. Reductions in back pain persisted to two years. Similarly, ambulatory status improved remarkably, with only 45% of patients being able to walk independently at baseline and 85% being able to walk independently one week after treatment. 88% were able to walk independently at the two-year follow-up. Anterior, posterior, and midline vertebral body height measurements were all improved. For example, the midline measurement improved from a mean of 61% of predicted pre-fracture height preoperatively to 88% post-operatively. Vertebral body height was maintained throughout follow-up. Similarly, mean angular deformity (wedge index) improved from 0.61 to 0.81 degrees and the improvement persisted throughout follow-up. The perioperative safety profile was excellent, with 2 serious adverse events, none of which were attributable to the kyphoplasty procedure. One additional patient had a transient state of confusion during the procedure. Although 11% had cement extravasation, in no case was the extravasation symptomatic.

3.3.1.3. A multicenter study of balloon kyphoplasty for osteoporotic vertebral compression fractures

Medtronic Spine LLC (formerly Kyphon Inc.) sponsored a multicenter single-arm study of balloon kyphoplasty.[21] Nineteen centers enrolled 155 subjects under an IRB-approved protocol. 100 subjects (80% women, mean age 77 years) were followed for two years. Based on this study, KyphX® HV-R™ bone cement was cleared for use during kyphoplasty by the FDA.

Improvements in SF-36 scores were marked and statistically significant in all sub-domains except General Health at the first follow-up time point (one month) and all follow-up time points up to two years ($p<0.0001$ for all changes compared to baseline). Pain as measured by the Numeric Rating Scale was reduced 60% at 7 days (from a mean of 15/20 preoperatively to a mean of 6.0/20 at 7 days), and remained improved out to two years ($p<0.0001$ for all differences with baseline). The mean days in bed due to back pain was 8.8 per month before balloon kyphoplasty, which was reduced to 2.4 per month post-operative ($p<0.001$) and 1.4 days per month at two years ($p<0.001$). Marked and sustained improvements were also documented for return to activities of daily living. Fewer than 20% of patients could stand for an hour, bend down, or lift ten pounds at study entry. One month after balloon kyphoplasty, at least 50% of the patients could perform these activities of daily living, a result which was sustained or appeared to improve during the two years of follow-up. 83% of fractured vertebrae had improved vertebral body alignment, with 44% lost midline height restored. Asymptomatic cement leaks occurred in 21/214 vertebral bodies (10%).

Safety was monitored continuously throughout the two years. There were no perioperative or long-term serious adverse events related to the kyphoplasty procedure. There was one intraoperative paroxysmal supra-ventricular tachycardia (PSVT) in a patient with a history of PSVT and one myocardial infarction (MI) 28 days post-operative in a patient with pre-existing congestive heart failure (CHF). Neither was considered to be due to the procedure. There was also 1 patient who sustained 3 rib fractures while being positioned intraoperatively.

3.3.1.4. Randomized Trial Comparing Balloon Kyphoplasty to Nonsurgical Care for Osteoporosis Fractures

Though not indexed on Medline and published only in abstract form, thus not included in the literature evaluation above, one study recently published as a meeting abstract is important to mention. Wardlaw et al. report on a recent European, multi-center, randomized study of balloon kyphoplasty compared to non-surgical management.[23] One-month results from this Medtronic Spine LLC-sponsored study were recently published in abstract form in the proceedings of the 22nd annual meeting of the North American Spine Society.[23] In this study, 149 patients were randomized to and treated with Kyphon's balloon kyphoplasty introducer tools, balloon fracture reduction devices, and bone cement for fracture repair. Compared to the non-surgical control, balloon kyphoplasty statistically significantly improved quality of life and reduced back pain and disability. There was one access device-related (a patient with a soft tissue hematoma at the surgical site) and one procedure-related (a post-operative urinary tract infection) serious adverse event. Within one-month post-operative, there were no bone cement-

related adverse events in these patients and no difference in the number of patients with serious adverse events.[23]

3.3.1.5. Efficacy and Safety of Balloon Kyphoplasty in Treatment of Cancer-Related VCFs

Mounting evidence supports the efficacy and safety of balloon kyphoplasty in the treatment of VCFs in patients presenting with bone metastasis and multiple myeloma. At least 19 original studies totaling 1,201 patients have been summarized in the oncology literature, 6 of which are studies unique to oncology (that is, excluding patients with osteoporosis-related fractures). 10 of the 19 known studies are prospective in nature, with a total of 998 patients receiving treatment with balloon kyphoplasty and 285 patients presenting with cancer-related VCFs. One study did not report clinical outcomes, but this investigation included only 1 patient with cancer.

A number of noteworthy findings are described in recent studies across both metastatic and multiple myeloma patient cohorts. Pflugmacher et al.[75] demonstrated sustained pain relief and enhanced functional capacity in patients with metastatic VCFs up to 24 months following treatment with balloon kyphoplasty. 65 patients underwent balloon kyphoplasty with outcome measures (Visual Analogue Scale, VAS; Oswestry Disability Index, ODI) assessed prior to surgery and post-operatively, as well as 3, 6, 12, and 24 months following surgery. Marked improvement in both pain (VAS) and functional ability (ODI) scores was found persisting to 24 months. Radiographic outcomes of vertebral height restoration and kyphotic angle were sustained for 12 months. Minimal rates of cement extravasation and adjacent incident fracture were detected, with no serious adverse events reported by 2-year follow-up. These prospective data are consistent with two earlier prospective 1-year follow-ups demonstrating statistically significant reduction of pain scores (VAS, ODI) and positive radiographic outcomes in 31 patients with metastatic disease[76] and 20 patients with multiple myeloma.[77] Clinically asymptomatic cement leakage occurred at 12.5% and 10.4% of fracture levels, respectively.

The evidence in support of balloon kyphoplasty is particularly compelling as patients with metastatic disease may present with collapsed vertebral levels that often result in high levels of pre-operative pain severity relative to minimally compressed levels. A retrospective study of 50 patients (multiple myeloma (46%), lung (22%), breast (16%), prostate (8%), and colon, esophageal, uterine, and sarcoma (2%), respectively) treated with balloon kyphoplasty achieved complete or significant pain relief, with 20% of patients pain-free upon post-operative assessment and an additional 76% of patients reporting significant improvement. [71] Whereas all patients had failed prior conservative therapy, only 4% of patients reported no difference in pain level following treatment with balloon kyphoplasty. 69% of patients were discharged from hospitalization within 24 hours, and the majority of patients (68%) were known to be ambulatory and active at an average of 9 months follow-up.

In a small retrospective study comparing balloon kyphoplasty and vertebroplasty, 34 patients with multiple myeloma were assessed using overall VAS scores to 12 months follow-up.[78] While statistically significant improvement in pain scores was obtained in both kyphoplasty (18 patients) and vertebroplasty (16 patients) groups up to 1 year follow-up, there was also a statistically significant difference demonstrating superior

VAS score improvement in the kyphoplasty group relative to the vertebroplasty group at 6 months and 1 year, presumably due in part to enhanced biomechanical correction attained by kyphoplasty. Finally, additional studies have shown the balloon kyphoplasty procedure to be compatible in combination with spinal radiosurgery in patients with metastatic spinal tumors, yielding VAS score improvement at median 16-month follow-up.[79, 80]

3.4. Fracture Reduction Evaluation (FREE) Study

FREE is a multicenter, prospective, randomized controlled study of kyphoplasty compared to medical management alone in elderly patients with spinal fragility fractures.

3.4.1. Background

As soon as the Inflatable Bone Tamp received FDA clearance in July 1998, and with fewer than 10 people who worked at the company at the time, we prepared to conduct a multicenter, randomized, controlled clinical trial (RCT) comparing balloon kyphoplasty to medical management alone in elderly patients with spinal fragility fractures. Steven Cummings, MD, FACP advised us on the study's design. Dr. Cummings is Professor of Medicine and Epidemiology and Biostatistics, Director of the UCSF Coordinating Center, Director of the UCSF Clinical Research Program and Associate Chair of Medicine for Clinical Research, at University of California, San Francisco, and a leader in the field of osteoporosis. The study assessed pain (VAS), quality of life (SF-36) and activities of daily living (the Back Function Index from the Study of Osteoporotic Fracture), at 7 days (VAS only) and at 1, 3, 6, 12 and 24 months. Radiographic outcomes were assessed post-operatively (kyphoplasty only) and at 3, 12 and 24 months. Safety was monitored throughout the study (e.g., at each study visit including an 18-month phone contact and unscheduled visits that took place when an adverse event warranted such a visit).

We specifically sought counsel about, and concluded that, we could not include a sham surgery or vertebroplasty arm for two reasons. First, most physicians who performed kyphoplasty at that time were orthopaedic surgeons who favored general anesthesia for the procedure, and it was judged that the Declaration of Helsinki governing ethical clinical trial design would not permit this added risk for patients in the sham-surgery arm. The second reason was that no non-medical intervention was considered standard of care for these fractures. The standard of care was medical management, and it was important to compare kyphoplasty to it.

Steven Garfin, MD, Chair of the Department of Orthopaedic Surgery at University of California, San Diego, became the study's Principal Investigator, and the first patients were enrolled in 1999. After two years and opening 39 investigational sites, which were mostly academic centers, only 41 patients (out of 200 required) had agreed to be randomized. Among the 20 patients randomized to medical management alone, 14 requested a kyphoplasty or vertebroplasty within a month. The high rate of crossovers, not permitted by the protocol, precluded a randomized comparison of outcomes. This prevented the study from providing meaningful data; therefore, the study was ceased.

In 2002 we launched a single-arm version of the U.S. RCT; Dr. Garfin remained the PI of the U.S. single-arm study, with the new goal of providing a body of prospective multicenter data documenting long-term safety and effectiveness from kyphoplasty

treatment for symptomatic spinal fragility fractures treated in community-based medical practices. The one-month outcomes in 155 patients and the two-year outcomes in 100 patients were published in the journal *Spine* in 2006,[21] the results of which are discussed in more detail in Section 3.3.1.3 above.

To address the enrollment problem in a randomized study, we initiated efforts to conduct an RCT in Europe in 2002. We believed that we could be successful with our RCT in Europe because neither kyphoplasty nor vertebroplasty were widely available, and because European patients have traditionally been more willing to participate in RCTs in general. Olof Johnell, M.D., Professor of Orthopaedic Surgery at the University of Malmö, Sweden, and an internationally recognized expert in the epidemiology and impact of osteoporotic fractures, became the Principal Investigator of the Europe-based RCT. The design of this study remained similar to the design of the U.S. RCT, but with added functional (Roland-Morris Back Questionnaire) and quality of life (EQ-5D) measures. We invested in building a strong European clinical organization to match our U.S. clinical group to ensure the rigorous implementation of the study. We named the study FREE (Fracture REduction Evaluation). The first patient was enrolled in January 2003 and the last patient was enrolled in December 2005. While we also opened two U.S. centers along with the 19 European centers in the RCT, neither U.S. center was able to enroll patients.

In order to ensure that the data analysis was rigorous prior to completion of enrollment, we formed a Publication Committee consisting of the Principal Investigator, two site Principal Investigators, and an independent member expert in osteoporosis, Steven Boonen, MD, Center for Bone Diseases and Division of Geriatric Medicine, Catholic University, Leuven, Belgium. As set out in the Publication Committee charter, the physician members selected a statistician expert in clinical trial data analysis to independently verify the analysis performed by the company's consulting statisticians. The verification of data and writing of manuscripts is controlled by the Publication Committee. The Publication Committee charter also includes the option to seek additional outside advice from appropriate experts. The Committee is currently being advised by Prof. Steven Cummings of UCSF, the osteoporosis expert who assisted in the design of the original, U.S.-based RCT, and Prof. Richard Eastell, Bone Metabolism Unit at Northern General Hospital in Sheffield, UK, an osteoporosis expert with a research focus on vertebral fracture morphometry.

Shortly after enrollment of the last patient, Prof. Johnell died. Mr. Douglas Wardlaw, MBChB, FRCS, Professor of Orthopaedic Surgery at the University of Aberdeen, Scotland, UK, replaced Prof. Johnell as Publication Committee Chair.

3.4.2. Design overview

The FREE study is a multicenter, prospective randomized clinical trial comparing the effectiveness and safety of balloon kyphoplasty in osteoporosis patients compared to non-surgical supportive care. 300 adult patients with up to three acute, painful (VAS $\geq$ 4) vertebral compression fractures diagnosed within 3 months are randomly assigned to receive either balloon kyphoplasty or usual non-surgical care. Patients with fractures due to primary bone tumors, osteoblastic metastases, or fractures from trauma were excluded. Measurements include quality of life, back pain and function, days of disability assessed at baseline, and at 1, 3, 6, 12 and 24 months; subsequent fractures, vertebral body, and

kyphosis measurements will be assessed radiographically at a core lab at 3, 12 and 24 months. The primary outcome of the study is the one-month difference between groups in change from baseline scores in the physical component summary of the SF-36 questionnaire, a quality of life measure weighted on physical functioning.

3.4.3. Current Status

Enrollment and 2-year follow-up have been completed. Data analysis is underway and, as mentioned previously in Section 3.3.1.4, initial one-month analyses that include the primary endpoint were presented last year at the 22nd annual meeting of the North American Spine Society.[23] The one-year outcomes of FREE have been submitted for publication, and the two-year outcomes are being analyzed.

3.5. Cancer Patient Fracture Evaluation (CAFE) Study

CAFE is a multicenter, prospective, randomized controlled study of kyphoplasty compared to medical management alone in patients with cancer and spinal fractures.

3.5.1. Background

By 2004, Kyphon had built robust clinical departments in the U.S. and Europe, and were prepared to undertake the next RCT, comparing kyphoplasty to medical management alone in patients with cancer-related spinal fractures. The study was designed with multiple expert physicians in cancer, led by James Berenson, MD, Chief of the Bone Cancer Unit at Cedars-Sinai Hospital. Some advisors and IRBs would not accept a protocol without a cross-over component for patients randomized to medical management alone. Recognizing that the long-term safety comparison in osteoporosis patients would be available through the FREE study, we incorporated a crossover component to the study design to make it easier to enroll the study. We added the Karnofsky Scale as a functional assessment specific to cancer, but otherwise kept the study design similar to the design of FREE. Muhammad Hussein, MD, Chief of the Multiple Myeloma Unit at the Cleveland Clinic in Cleveland, became the study's Principal Investigator.

Patient enrollment began in 2005, but even though crossovers were allowed, the study enrolled very slowly. In 2006, we began to add centers in Germany, Belgium, the UK and Australia, which like the FREE study, resulted in an increased rate of enrollment. The study currently has 134 patients enrolled, with a goal of enrolling 200. Because of the nature of cancer and its complex course and treatment, we created a Data Safety Monitoring Board. The development of a Publication Committee is in process.

3.5.2. Design overview

CAFE is a multicenter, prospective clinical trial comparing the effectiveness and safety of balloon kyphoplasty in patients with cancer-related spinal fractures compared to non-surgical supportive care. Up to 200 adult patients diagnosed with a variety of cancers and 1 to 3 painful VCFs (VAS $\geq$ 4) are randomly assigned to immediate kyphoplasty or non-surgical supportive care; patients with primary bone tumors, osteoblastic tumors, or solitary plasmacytoma at the fracture site are excluded as well as patients with spinal cord compression. Measurements include back function and pain, quality of life, change in ambulation, pain medications and daily activities at baseline, and 1, 3, 6 and 12 months. Subsequent fractures, vertebral body, and kyphosis measurements will be assessed

radiographically at a core lab. This study has an optional non-surgical to kyphoplasty cross-over component at the one-month time point. The primary outcome of the study is the one-month difference between groups in change from baseline scores using the Roland-Morris Disability questionnaire, a 0- (no disability) to 24-point (maximum disability) instrument validated for assessing back-specific physical functioning, at one month.

3.5.3. Current Status

Currently 134 patients have been enrolled into the study; follow-up is ongoing but study enrollment is currently suspended and undergoing a pre-planned interim analysis of the primary endpoint.

3.6. Kyphoplasty and Vertebroplasty in the Augmentation and Restoration of Vertebral Body Compression Fractures (KAVIAR)

KAVIAR is a multicenter, randomized controlled clinical study comparing balloon kyphoplasty and vertebroplasty in acute, painful vertebral compression fractures.

3.6.1. Background

Multiple small studies were being proposed, and a few initiated, to compare kyphoplasty to vertebroplasty but the designs did not appear adequate to comprehensively address the role of the two procedures in treating fragility fractures in elderly patients. We were interested in conducting a rigorous randomized study comparing kyphoplasty and vertebroplasty. Recognizing that any study of this nature conducted by Kyphon could be viewed as biased for kyphoplasty, we took multiple steps to address this. We looked for co-Principal Investigators, one who performed kyphoplasty but not vertebroplasty, and the other who performed vertebroplasty but not kyphoplasty. The two co-PIs selected were Reginald Knight, MD, an orthopaedic surgeon performing kyphoplasty who had just left Creighton University for private practice in Washington, and Jacques Dion, MD, an interventional radiologist who brought vertebroplasty to the United States, currently Emory Professor of Neuroradiology, and Head, Division of Interventional Neuroradiology, at Emory University. Importantly, neither investigator has financial conflicts of interest with the sponsor. After developing the draft protocol with Drs. Dion and Knight, we reviewed it with a Protocol Steering Committee, also consisting of physicians expert in one of the procedures, including Isador Lieberman, MD, Cleveland Clinic (kyphoplasty), Frank Phillips, MD, Rush Medical Center (kyphoplasty), Michael Ford, MD, Women's Health Sciences Centre, Toronto (kyphoplasty), Joshua Hirsch, MD, Massachusetts General Hospital (vertebroplasty), Mary Jensen, MD, University of Virginia (vertebroplasty), and Gregg Zoarski, MD, University of Maryland, Baltimore (vertebroplasty).

Because we believe that CMS is a stakeholder in the outcomes of this study, and because CMS has tremendous expertise in clinical trials, Kyphon met with CMS on June 28, 2005 to review the company's overall clinical trial plan. A subsequent meeting took place on April 19, 2006, initiated by Mary Hailey, Kyphon's Vice President of Health Care Policy and Government Relations, and was also attended by Danny Cher M.D., Kyphon Medical Director and Cindy Domecus, Kyphon Vice President of Clinical and Regulatory Affairs.

From CMS, the meeting included several staff from the coverage and analysis group; the primary point of contact was Deirdre O'Connor. The purpose of the meeting was to spend time (CMS generally scheduled 1 hour meetings) with CMS seeking input specifically on the KAVIAR protocol, as well as reviewing the protocols and the current status of FREE and CAFE at that time. Conference calls were held to finalize the protocol with input received. Also, although IDE approval was not required for this study, since all study devices were to be used in accordance with the FDA-cleared indications for use, we chose to send the draft protocol to the Food and Drug Administration for review to obtain scientific and medical input from yet another government agency with significant clinical trial expertise. We received detailed comments from FDA, led by Barbara Buch, MD, at FDA, on April 26, 2006. After considering the input from CMS and FDA, we revised the protocol in response to some of the comments received and the final protocol was approved by the two KAVIAR co-PIs. We also provided written responses to both CMS and FDA to note which changes we planned to incorporate and justifying which changes we did not believe were warranted.

We took two additional steps to address potential bias. We powered the study to allow either kyphoplasty or vertebroplasty to be superior, rather than a one-tailed design allowing only one procedure to be superior. This doubled the number of patients required, adding significant expense. We also required that physicians who perform procedures in this study be proficient at the procedure. Thus, we set a requirement for a minimum number of procedures, and physicians performing both procedures had to meet the requirement for both. This prevented a lack of experience from potentially affecting the outcomes.

Because mainly surgeons perform kyphoplasty, and mainly radiologists perform vertebroplasty, we allowed two types of centers. The conventional centers have investigators proficient at performing both procedures. However, as this is uncommon, we also have centers with a kyphoplasty and vertebroplasty site co-PIs.

3.6.2. Design overview

The KAVIAR study is a multicenter, prospective randomized clinical trial comparing the effectiveness and safety of balloon kyphoplasty to vertebroplasty in patients with osteoporosis-related vertebral compression fractures. 1,234 adult patients with up to three acute, painful (VAS $\geq$ 4) vertebral compression fractures diagnosed within 3 months are randomly assigned to receive either balloon kyphoplasty or vertebroplasty. Patients with fractures due to primary bone tumors, osteoblastic metastases, or fractures from trauma are excluded. Measurements include quality of life, back pain and function, and days of disability assessed at baseline and 1, 3, 12 and 24 months; subsequent fractures, vertebral body and kyphosis measurements will be assessed radiographically at a core lab at 3, 12 and 24 months. Healthcare utilization will also be assessed on a monthly basis. The primary outcome of the study is the difference between groups in the proportion of patients with subsequent fractures at 12 and 24 months.

3.6.3. Current Status

The study has been ongoing since 2006. Currently approximately 250 patients have been enrolled. Before enrollment is complete, we intend to develop an independent Publication Committee.

4. Kyphoplasty Safety Analysis

As previously described, balloon kyphoplasty for treating vertebral compression fractures is a well-accepted practice. Most adverse events associated with the procedure occur within the first few weeks post-operative. A large body of prospective and retrospective literature supports the clinical safety and effectiveness of balloon kyphoplasty.

In order to investigate complaints regarding kyphoplasty, the U.S. FDA's MAUDE database was searched on May 9, 2008 (all years available: 1992-2008) for the terms "*kyphon or kyphx or kyphoplasty*". This yielded 245 Adverse Event Reports (AERs). All reports were read and evaluated. Twenty-eight AERs were excluded as they were not related to kyphoplasty; this left 217 AERs that upon close review, appear to comprise 189 unique events (Table 2).

Bone cement was implicated in 105 of 189 events. The majority of adverse events attributed to bone cement were of a cardiovascular/respiratory nature (35/105) which may be due to cement or perhaps fat embolism during the procedure. There are 46 cardiorespiratory AERs, out of which 4 were considered asymptomatic events. The analysis indicates that 30 total deaths were reported (38 deaths are reported within the 217 AERs found, but again these do not all appear to be unique events), 25 resulting from adverse cardiovascular events. For all reported deaths, 21/30 list bone cement as the device; 7 where other manufacturers' or unknown bone cements (PMMA-, calcium-based or unknown) were used, and 14 listed KyphX® HV-R™ Bone Cement.

There are a combined total of 49 unique AERs reporting paraplegia and other neurologic complications. 29/49 list bone cement as the device (26/29 are KyphX® HV-R™ Bone Cement). Extravertebral bone cement extravasation has been reported in the literature and may cause damage to the spinal cord and nerve roots. There are also five AERs where extravertebral cement extravasation occurred but did not have clinical sequelae.

There were 14 reports describing subsequent new or worsening vertebral fractures that were attributed to bone cement. Subsequent fractures of vertebral bodies may not be a result of the kyphoplasty procedure itself but the underlying osteoporosis disease state present in the majority of patients treated by kyphoplasty. For example, compared to no prevalent fractures, women with 1 prevalent fracture have a 3-fold increase in risk for another VCF, and those with 2 or more fractures have a 23-fold increase in risk.[81] Indeed, two concurrently controlled studies from Germany suggest a reduction in the rate of subsequent fractures after balloon kyphoplasty as compared to after non-surgical management.[17, 18]

There are 13 reports of infection at the treatment site, 10 of which listed bone cement as the product. Among other AERs listing bone cement as the product, one describes a hematoma and two describe soft tissue damage. Finally 7 reports of revision surgery indicate bone cement as the product; 6 of these were attributed to KyphX® HV-R™. Bone Cement.

In other reported events, inflatable bone tamps, bone filler devices, introducers, curettes or needles were indicated as the product. A pedicle fracture occurred while introducing the inflatable bone tamp. Two cases of pneumothorax (under cardiovascular in Table 2, below), related to osteointroducers, were found; both patients recovered, one after the insertion of a chest tube. Because in most cases these devices are used in conjunction with bone cement to conduct the kyphoplasty procedure, and the AERs often do not have sufficient information to determine root cause, all adverse outcomes are shown in Table 2 below. As of April 24, 2008, over 446,000 patients and 519,000 vertebral compression fractures have been treated by balloon kyphoplasty, the majority of which have been performed in the U.S. (data on file at Medtronic Spine LLC). Thus, the reported frequency of these adverse events is extremely low.

Table 2: Kyphoplasty Adverse Events Reported in the FDA MAUDE database

Adverse Event Reported	# of Events	Deaths reported	Tools listed	Bone Cement listed
Cardiovascular	46	25	11	35 (27)[1]
Paraplegia	19	0	5	14 (14)
Other neurologic problems (Paresis, radiculopathy, nerve root damage, lower extremity weakness)	30	2	16[2]	15 (12)
Bleeding or hematoma	5	1	4	1 (1)
Soft tissue damage	2	0	0	2 (1)
Infection	13	0	3	10 (10)
Allergy/toxicity	3	0	1	2 (1)
Ileus	2	0	1	1 (1)
Pedicle fracture	1	0	1	0
New or worsening fractures	14	0	0	14 (12)
Additional surgery required	8	1	1	7 (6)
Cement extravasation resulting in no clinical sequelae	5	0	2	3 (3)
Device breakage	31	0	31	0
Event, injury and patient outcome not described	10	1	9	1 (0)
Totals	189	30	85	105 (88)

[1]The number in parentheses reflects the number of AERs listing KyphX® HV-R™ Bone Cement as the product
[2]Both a tool and a cement were listed in one AER

Potential perioperative adverse events related to kyphoplasty include needle injuries resulting in local (typically neurologic) damage. Placement of kyphoplasty introducer cannulae are guided by antero-posterior and lateral fluoroscopic guidance, minimizing such injuries. Bone cement extravasation may cause neurologic syndromes or pulmonary embolism. Since bone cement is radiopaque, the likelihood of extravasation can also be limited by the use of fluoroscopy. The use of the IBT during kyphoplasty compacts the

cancellous bone, creating a void. These aspects of the procedure are thought to reduce cement extravasation rates by compacting the cancellous bone and disrupting internal venous pathways, filling fracture lines and reducing leak pathways.[15] The void allows the physician to deliver a predictable volume of highly viscous bone cement, also thought to decrease the likelihood of cement extravasation.

Several recent meta-analyses also support the safety of balloon kyphoplasty. For kyphoplasty, extravertebral cement extravasation was calculated to be 7 to 9%, most occurrences having no clinical consequences[60-63]. This leakage rate was 2-3 times less than that calculated for vertebroplasty[60, 61, 63]. Two meta-analyses calculated the serious and symptomatic complication rate of kyphoplasty to be ~2%[61, 82] compared to 3.9% for vertebroplasty.[61] The calculated symptomatic leakage rate was found to be 0-0.3% for kyphoplasty and 1.6-3.0% for vertebroplasty.[63, 74] These data are in agreement with an internal safety analysis, where the total procedure-related severe adverse event rate among the 2,865 subjects who underwent balloon kyphoplasty was 0.98% (28 pooled cases). Most studies reported the proportion of patients who experienced a procedure-related adverse event. Where reported, the frequency and type of adverse effects associated with cement leakage, and type of intervention needed to correct the problem, are tabulated (Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies) with cement-related adverse events calculated to be 7/2,865 or 0.24%. We attempted to distinguish where possible the etiology of the adverse event and whether the adverse effect was bone cement-related or not. There were also 15 (0.52%) post-operative medical complications not thought to be related to the kyphoplasty procedure (Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies). Adding all of these complications makes the total adverse event rate from this literature 43/2,865 or 1.50%. This rate is also consistent with an abstract reporting the one-month results of a randomized trial of balloon kyphoplasty; 2/149 patients (1.3%) had procedure-related serious adverse events (a hematoma and a post-operative urinary tract infection).[23] As of April 2008, there were 94 deaths reported within the 52 unique clinical studies, 4 of which were noted to have occurred in the 30-day peri-operative period, but none were considered to be device-related.[16, 71, 83]

In all cases, the published medical literature supports the safe and effective use of kyphoplasty for the proposed indications for use.

5. Summary

There is a substantial clinical literature documenting the adverse effects of VCFs, including chronic pain, reduced physical functioning, deficits in patient quality of life, reduced pulmonary function, and excess mortality. Improvements in patients with symptomatic fracture can be slow, and decrements in quality of life associated with non-surgical management can persist for years.[6] Unfortunately, VCFs left untreated can be self-perpetuating, resulting in what physicians refer to as the "downward spiral" of osteoporosis,[11] a progressive degradation of the patient's physical, social, and psychological condition, resulting in increased morbidity and mortality for those afflicted.[28-35]

Balloon kyphoplasty is the only minimally invasive treatment option available to stabilize and correct anatomical abnormalities associated with VCFs. In most instances, balloon

kyphoplasty provides almost immediate results in improving pain and disability. Because the complication rate is low, including those complications related to the use of bone cement during balloon kyphoplasty, and the clinical improvements have been shown to be long-lasting and improve patient quality of life, the benefits outweigh the associated risks.

The National Institute for Health and Clinical Excellence (NICE) has reviewed the available evidence for the safety and efficacy of balloon kyphoplasty for treating vertebral compression fractures due to osteoporosis and spinal malignancies, indicating current evidence supports its use (http://www.nice.org.uk/nicemedia/pdf/IPG166A4Updated.pdf). Additionally, the consensus statement from the International Myeloma Working Group advocates immediate vertebral augmentation for rapid pain relief over alternative analgesics, as a proactive measure to preserve structural integrity in the absence of severe pain, and as a compliance advantage enabling radiation patients to be treated in a more comfortable state.[84]

In summary, a total of 2,865 patients treated with balloon kyphoplasty have been reported in the medical literature. In addition to improvements in all clinical parameters studied, the published safety profile of balloon kyphoplasty has been excellent. Two concurrently controlled trials show that balloon kyphoplasty is superior to non-operative care for improving pain and function in patients with symptomatic vertebral compression fractures and does not increase the risk of new vertebral fracture for up to 6 months. In addition, 1 prospective interventional trial, 25 additional prospective studies, and 24 retrospective studies demonstrate rapid, marked and sustained improvements using multiple validated outcomes measures in patients with compression fractures for up to two years. The overall adverse event rate of 1.50% is low, particularly considering the elderly age of the patient with osteoporotic fractures (mean ages typically in the 70s), and the medical condition of patients battling cancer.

We believe the medical literature demonstrates improved net health outcomes in the Medicare population for patients treated with balloon kyphoplasty. The published balloon kyphoplasty studies are noteworthy in that they uniformly show:

- **Pain Relief.** A marked, immediate, and sustained improvement in back pain (46 of 46 studies)
- **Improved Back Function.** A marked, immediate, and sustained improvement in back function (12 of 12 studies)
- **Improved Quality of Life.** A marked, immediate, and sustained improvement in QOL (6 of 6 studies)
- **Improved Radiologic Outcomes.** A marked, immediate, and sustained improvement in vertebral body height (32 of 33 studies) and kyphosis angle (27 of 27 studies)

Based on the outcomes demonstrated in the medical literature, we do not support balloon kyphoplasty as a National Coverage Determination (NCD) topic.

6. Search Criteria

This assessment includes a computer-based literature search performed using the U.S. National Library of Medicine's MEDLINE® database accessed in April 2008. References were retrieved using the term *kyphoplasty*. Abstracts and articles were reviewed for publications containing original clinical data from > 10 patients treated with kyphoplasty where complications or clinical outcomes were reported. See Section 3.3.1, Kyphoplasty Studies, for further details regarding the results of the literature search.

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8. Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Grafe[19] 2005 **(all pts in Kasperk[17])**	40	40 KP 20 NS	40 OS	12 months (Extends FU from Kasperk)	VAS KP pts: 26 →44 Contrl pts: No change	KP group with improvement in daily activities (EVOS) Control: without improvement	KP: 12% VBH restoration Control: 8.2% VBH loss	**0**	**0**
Komp[18] 2004 **[Not in PubMed]**	19	19 KP 17 NS	19 OS	6 months (1-year data submitted)	VAS: KP: 5.4 → 2.0 at 6 mos Control: 5.2 → 4.8 at 6 mo	ODI KP: 84 → 24 at 6 months Control: 82 → 76 at 6 mos	> 2/3 height restoration in 11/19; > 50% in 8/19 pts	**0**	**0**
Prospective Studies									
Becker[85] 2007	60	60 (Prophylactic KP - 30 pts)	60 OS	12 months	VAS: 7 → 2 postKP & at 6 wks	SF-36 PSC: 31 & 30 → 36 & 32 at 6 wks postKP MCS: 37 & 38 →40 & 43 at 6wks postKP	NR	**0**	**0**
Berlemann[86] 2004	27	24	24 OS 1° OS – 21 Other etiology – 3	12 months	VAS: 8.4 → 3.8 postKP → 1.5 at 1yr 23/24 with pain relief at 2 months post KP	All pts could be mobilized within first 24 h postKP.	Mean local kyphosis improvement 47.7%	**0**	**0** (Postop: 1 pt with bleeding ulcer 2 days postKP

Key

HE	Hemangioma	C	Cervical	IOF	index of function	KP	Kyphoplasty	L-S	Lumbosacral	L	Lumbar	min	minimum
mod	moderate	av	average	MI	Myocardial Infarction	NR	Not Recorded	OS	Osteoporosis	PA	Pseudoarthritis	PE	Pulmonary Embolism
Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic
TR	Traumatic	VB	vertebral body	VP	Vertebroplasty	CA	Cancer	CSF	Cerebral Spinal Fluid	DVT	Deep Vein Thrombosis	hrs	hours
Ant	Anterior												

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Chung [87] 2007	52	52 (24 unilateral 28 bilateral)	52 OS	17.8 mos (12-24) & 16.6 (13-27)	VAS: 8.1 & 7.9 → 2.1 & 1.7 postKP → 1.9 & 1.8 at final FU	NR	PostKP kyphotic reduction rate: 41.3% & 67.8%	**0**	**0**
Crandall[72] 2004	86	47	43 OS 4 CA	Mean FU: 18mo Range: 6 - 24 mo	VAS 7.3→ 4.3 at 2 wks Decreased narcotic use in both groups	ODI: ≥25% postKP improvement in 60% pt All patients allowed to ambulate the postKP night	Mean VBH: 58% → 86% postKP Mean local Cobb angle: 15º → 8º postKP	**0**	**0** (Ppostop: 1pt with arrhythmia unrelated to KP)
De Negri[73] 2007	15	15 KP (18 VP)	11 OS	6 months	VAS: 8.3→ 0.7 postKP	ODI: 8.5 (77% disability) →12.1 (23% disability) postKP	NR	**0**	**0**
Deen [88] 2006	44 (15 & 29)	20	20 OS 10 - 1° OS 10 - 2° OS	12 months	VAS: 7.7 & 9.3 → 1.5 & 3.2 postKP → 2.0 & 2.9 at 1year	NR	Cobb angle improved by >5º in 3/10 pt - each group	**0**	**0**

Key

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Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic
TR	Traumatic	VB	vertebral body	VP	Vertebroplasty	CA	Cancer	CSF	Cerebral Spinal Fluid	DVT	Deep Vein Thrombosis	hrs	hours
Ant	Anterior												

Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

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Gaitanis[89] 2005	61 KP (49 OS 12 CA)	32	27 OS 5 CA	Mean: 18 months Range: 12-24 mo	VAS: 8.5 → 2.5 postKP → 1.5 at 1 month postKP	ODI: 60% → 28% at 1 month postKP Ambulation restored in all 8 nonambulatory pts	Mean AVBH 22.4 → 26.8 mm postKP Mean kyphotic deformity: 15.8º → 7.9º postKP	**0**	**1** pt with transient fever of unknown origin 1st d postKP
Garfin[21] 2006	214	155	154 OS 1 MM	Periop – 155 pts 12 mo – 119 pts 24 mo – 100 pts	VAS: 15.0/20.0 → 6.0/20.0 postKP & 2 yrs postKP	Limited activity days/28 days: 8.8 → 1.9 postkP → 1.4 at 2 yrs postKP SF-36: RP 10.6% → 48.9% 1 mo → 84.4 % 2y BP 29.3% → 75.2% 1 mo → 80.7% at 2 yrs postKP	MVB lost height restoration: 32%	**0**	**1** pt with 3 rib fractures (Postop: 1 pt with periop PSVT & 1 pt with MI at 28 days, unrelated to KP)
Gerszten[80] 2005 (KP + radiosurgery)	26	26	CA	7 - 20 months	VAS: 7.6 → 2.9 1mo postkP → 3.2 at last FU	NR	Some degree of kyphotic deformity correction in 16 pts	**0**	**0** (Postop: 1 pt without pain relief & progressive kyphosis)
Grohs[74] 2005 (Nonconcurrent comparison)	35 KP	28 KP	28 OS (1° OS - 19, 2° OS - 9)	24 months	VAS: 7.4 → 3.5 postKP → 2.0 at 2 years postKP	ODI: 61% → 38% at 4 mo → 56% at 2 yrs postKP	VBH: 80.0→85.8% postKP Kyphotic wedge: 13° → 7° postKP	**0**	**0**

Key

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Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic		
TR	Traumatic	VB	vertebral body	VP	Vertebroplasty	CA	Cancer	CSF	Cerebral Spinal Fluid	DVT	Deep Vein Thrombosis	hrs	hours		
Ant	Anterior														

Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Grohs[90] 2006	24	22	21 OS (1° OS – 15 2° OS – 6) 1 – CA	24 months	VAS: 7.5 → 2.3 postKP → 4.1 - 5.0 during FU	ODI: reduced for 4 mos	VBH: 73% → 81% post KP Kyphotic wedge: 21° → 12° postKP	**0**	**0**
Guglielmino[91] 2007	15	13	15 OVCFs	6 months	VAS: 6.2 → 3.3 postKP → 4.5 at 6 months	All QOL& QUALEFFO scores were statistically improved from baseline postKP & during FU	VBH: 53.5% → 71.2% postKP →68% at 6 months	**0**	**0**
Hillmeier[70] 2005 **[Not in PubMed]**	165	95	OS	12 months	VAS : 26.9%→ 48.7% postKP → 48.6% at 1 yr	Function improvement in 84 pts postKP PMMA pts mobilized immediately	VBH restoration of 16% postKP	**0**	**2**: 1 pt with spinal cord injury & 1 pt pt with epidural bleeding
Khanna[22] 2006	875	314 211 with FU	155 OS 56 MM	Median 10.8 mos Range: 0.3 – 54.7 mos (4 ½ yrs))	Significant pain relief	SF-36: PF 20.0 → 30.0 last FU BP 27.0 → 41.0 last FU ODI: 41.8→ 31.4 last FU	NR	**0**	**3**: 1 pt with periop MI & 2 pts with rib fractures (from Lieberman report)
Lane[92] 2004	83 46MM 37 OS	45	19 MM 26 OS	3 months	Significant pain relief comparable in MM & OS pts.	ODI: MM 49.0 → 32.6 postKP OS 47.9 → 34.0 postKP	AVBH restoration MM 37.8% in 76% levels post KP OS: 51.2% in 84%	**0**	**0**
Libicher[93] 2006	46 28 CPC 18PMMA	20 11 CPC 9 PMMA	OS	12 months	VAS: 70% improvement postKP	Mobility score (EVOS) 25% improvement postKP.	VBH restoration without significant difference between PMMA & CPC	**0**	**0**

Key

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Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic
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Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Pflugmacher[94] 2006	60	37	OS	24 mos	VAS: 8.4 → 2.6 postKP → 3.1 at 2 yrs	ODI: 73.8% → 33.2% postKP → 32.9% at 2 yrs All pts were mobilized 1 day postop.	AVBH restoration: 23.9 → 27.6 postKP → 26.0 at 2 yrs Kyphotic deformity correction: 15.7° → 6.9° postKP → 8.5°	**0**	**0**
Pfugmacher[77] 2006 (+ Radiotherapy)	48	20	20 CA (MM)	12 months	VAS: 8.2 → 2.2 postKP → 3.1 at 1 year No opiates necessary postKP	ODI: 71.5% → 27.5% at 3 mo → 31.22% at 1 yr All pts were mobilized 1 day postop.	AVBH increase of 3.8 mm Mean kyphosis correction of 6.3°	**0**	**0**
Plfugmacher[76] 2007 (+ Radiotherapy)	64	28	CA (Meta)	12 months	VAS: 8.8 → 3.1 post KP → 3.5 at 1 yr	ODI: 79% → 32% at 3 mos → 34.5% at 1 year All pts were mobilized 1 day postop	Mean AVBH increase of 1.3 mm Mean kyphotic correction of 3.3°	**0**	**0**
Phillips[95] 2003	61	29	OS	12 months	VAS: 8.6 → 2.6 postkP	18/29 pts returned to normal activity at 1 yr	Mean improvement. in sagittal alignment of 14.2°	**0**	**0** (PostKP: 1 pt with MI, 1 pt with atrial fibrillation & 1 pt with urinary infection)
Robinson [96] 2008	135	102	OS	6 months	VAS: 7.5→ 2.3 postKP → 1.4 at 6 mos	NR	NR	**0**	**3:** 1 pt with epidural abcess, 1 pt with superficial wound infection & 1 pt with hematoma (Postop: 2 pts with VB refracture)

Key

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Shindle[97]	43	25	OS	NS	NR	NR	MVBH restoration of 57% post KP	**0**	**0**
Stoffel[83] (6 pts with open KP)	118 45 OVCFs 75 burst fractures	74	74 OS	Mean: 15 months Range: 8-32 mos	VAS: 70 → 23 post KP	KPS: 51 → 71 post KP SF-36: MCS 43 → 58 postKP PCS 24 → 35 post KP	Sagittal Index: 10° → 5° postKP	**1** permanent monoparesis due to intra spinal canal cement leakage	**2** pts with transitory intraop pareses ← contusion (PostKP: 2 deaths← MI & pneumonia)
Theodorou[98] 2002	24	15	OS 1° OS - 8 pts 2° OS - 7pts	6 - 8 months	All 15 pts with significant pain relief postKP	Better respiratory function in 2 pt with COPD postKP	Mean VBH: 78.6% → 91.5% postKP Mean kyphosis: 25.5° → 15.6°	**0**	**0**
Villavicencio[99] 2005	24	20	19 OS 1 CA	NR	NR	NR	NR	**0**	**0**
Voggenreiter[69] 2005	39	30	OS	2 days	VAS: 8.7 → 2.3 postKP	NR	AVBH: 0.59 → 0.80 postKP Cobb angle: 17.0° → 10.5° postKP	**0**	**0**
Retrospective studies									
Atalay[100]7 2005	77	57	37 OS 7 CA 4 HE 10 TR	Mean: 6.5 mos	VAS: 91.08 → 11.22 postKP	All patients mobilized on the surgery day	VB compression reduction: 26.6% → 15.0% postKP Kyphotic angle: 12.2° → 5.9°		

Key

HE	Hemangioma	C	Cervical	IOF	index of function	KP	Kyphoplasty	L-S	Lumbosacral	L	Lumbar	min	minimum
mod	moderate	av	average	MI	Myocardial Infarction	NR	Not Recorded	OS	Osteoporosis	PA	Pseudoarthritis	PE	Pulmonary Embolism
Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic
TR	Traumatic	VB	vertebral body	VP	Vertebroplasty	CA	Cancer	CSF	Cerebral Spinal Fluid	DVT	Deep Vein Thrombosis	hrs	hours
Ant	Anterior												

Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Becker[101] 2006 (Open KP – 5 pts)	69	67	67 OS	6 weeks	VAS: 7.0 → 2.2 postKP → 1.6 at 6 wks postKP	SF-36: PCS 30.4 → 30.9 at 6wks & MCS 25.9 → 29.5 6 at 6 wks postKP All mobilized postKP day, but 1 paraplegic pt	NR	**0**	**0**
Boszczik[102] 2005	55	32	26 OS 5 CA 1 TR	NR	NR	NR	AVBH: 11 mm → 13 mm post KP Kyphosis correction OS 11° → 9° & CA 7° → 3° postKP	**0**	**2**: 1 pt with superficial wound infection & 1 CA pt with periop DVT
Choe[103] 2004 (Insufficient dfferentiation between KP & VP groups)	25	15	OS – 4 CA – 11	Mean: 7 months Range: 5-11 mos	NR	NR	NR	**1** MM pt with asymptomatic cement PE	**0**
Frankel[104] 2007	20	17	OS	7-10 days	14 pts with complete pain relief	NR	NR	**0**	**1** pt with rib fracture
Fribourg[105] 2005	47	38	OS 1° – 31 2° – 7	Mean: 8 mo Range:14--875 d	NR as a whole but noted as excellent pain reelief in several pts	Pts with lumbar fractures to wear corset vs thoracic fractures without brace.	NR	**0**	**0**

Key

HE	Hemangioma	C	Cervical	IOF	index of function	KP	Kyphoplasty	L-S	Lumbosacral	L	Lumbar	min	minimum
mod	moderate	av	average	MI	Myocardial Infarction	NR	Not Recorded	OS	Osteoporosis	PA	Pseudoarthritis	PE	Pulmonary Embolism
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Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

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Garfin[106] 2001	603	340	OS	Up to 18 mos	90% pain relief postKP Most pts narcotics → OTC pain medication postKP	90% functional improvement postKP	AVBH: 83% → 99% post KP AVBH in VBs with ≥15% heigh loss: 68%→84% Kyphosis correction of >50% postKP	**2: 1** pt with paresis due to cement leakage **1** transient fever & hypoxia post cement injection	**2: 1** pt with anterior cord syndrome & **1** pt with epidural hematoma
Heini[107] 2004	74	68	OS	12 mos in 24 pts	Pain decrease significant in all but 1pt post KP	NR	VBH restoration (with 25% reduction loss post KP) Mean kyphosis correction of 8°	**0**	**0**
Karam[108] 2008	66	60	OS 1° – 52 pts 2° – 8 pts	3 wks (clinical) 4 wks (imaging)	Self grading pain relief: Excellent in 42 pts & Intermediary in 13 pts	(Questonnaire on days in bed pre & postKP)	NR	**0**	**0**
Kim[109] 2007	24	24	24 OS	6 months	VAS: 8.3 →3.2 postKP	NR	Cobb angle: 18.0° → 10.1° postKP Kyphotic angle: 12.6°→ 4.6° postKP AVBH: 0.25 → 0.50 postKP	**0**	**0**
Kose[78] 2006	22 KP	18 KP	18 CA [MM]	12 months	VAS: 36.0 →12.3 at 6 wks → 8.6 at 6 mos →9.7 at 1y Analgesic use significantly decreased postKP	All pts mobilized on the same day postKP	NR	**0**	**0**

Key

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Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

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Lane[110] 2002	33	17	OS	NS	Significant pain relief (of 50%) in 15/17 pts postKP)	All patients out of bed and mobile within 24 h	NR	**0**	**0**
Ledlie[16] 2006	151	117 77 with ≥2-yr FU	113 OS 4 CA (MM)	Mean: 18.9 mos Range: 1 wk - 43.1 mos)	VAS: 8.9 →2.8 postKP →1.5 at 2 years Significant decrease in narcotic use postKP	< 2% pts able to ambulate without difficulty → 76% postKP → 81% at 2 yrs	Mean AVBH: 1.3% → 81.2% postKP → 80.9% at 2 yrs	**0**	**1** pt with periop transient confusion (Postop: 1 death due to cancer course & 1 PE 2 wks postKP)
Machinis[111] 2006	37	24	OS	72 weeks	VAS: 9.3 → 5.4 postKP → 6.1 at 72 wks	All pts able to return to daily activities within 24h	VBH: no significant height restoration	**0**	**0**
Majd[112] 2005	360	222	OS)	Mean: 21 months Range: 6-36 mos	Complete pain relief in 78% & partial in 11% pts Perstistent pain in 11% pts due to new VCFs or DDD	Ambulation encouraged ASAP	AVBH: 74% → 82% postKP Mean local kyphosis 22° → 15° postKP (in 125 pts)	**1** pt with radiculopathy due to cement leakage	1 pt with treated level abscess
Masala[113] 2004 (*In Vivo*)	16	16	12 OS 4 CA (3 MM& 1 Meta)	NS	VAS 8.2 → 2.4 postKP	NR	Kyphosis angle reduction noted radiologically & clinically Mean 85% VBH restoration noted for overlapping cohort	**0**	**0**
Moon[114] 2007	137	111	OS	Minimum 6 mos	NR	NR	NR	**1** pedicular cement leakage +decompression	**0**

Key

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Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Pradhan[115] 2006	89	65	62 OS 3 MM	Post KP	NR	NR	AVBH: 20.5 mm → 23.6 mm postKP 7.3° mean local kyphosis correction	**0**	**0**
Rhyne[116] 2004	82	52	OS	Mean: 37 weeks (9 months) Range: 4 - 99wks (1-23 months)	VAS: 9.16 → 2.91 postKP	RMDS: 9.3 → 8.1 postKP	Cobb angle: 22.5° → 19.1° postKP AVBH: 19.6 mm → 24.2 mm postKP	**0**	**0**
Ryu[117] 2007 (Unilateral KP)	37	31	31 OS	Mean: 8.6 mos Range: 6-12 mos	VAS: 8.58 →1.63 postKP →1.78 at last FU	NR	AVBH: 60.85 →81.86 postKP Kyphotic deformity: 16.1° → 8.8° postKP	**0**	**0**
Vrionis[118] 2005 **[Not in PubMed]** (Radiotherapy - 33 pts)	128	50	CA 23 MM 27 Meta	Mean: 9 months	Complete or significant pain relief in 96% pts	34 pts ambulatory & active at mean 9-mos FU	NR	**0**	**1** pt with intraop asystole with recovery (Postop: 1 death within 1 mo - the pt with asystole &comorbidites)
Wong[68] 2000 **[Not in PubMed]**	143	85	OS	Mean: 5 months Range: → 18 mo	Good pain relief in 80 pts	NR	Main VBH improvement: 99% post KP in 28 pts	**1** pt with PE, with fever & reduced PaO2	**1** patient with cord compromise due to hemorrhage

Key

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Appendix 1: Clinical Outcomes from Balloon Kyphoplasty Studies

First author Year	Levels (N)	Pts (N)	Etiology	Follow-Up	Pain Relief	Function and/or QOL	Radiologic	Bone Cement Complications	Procedure Complications‡
Zhang[119] 2007	62	38	OS	12 months	VAS: 8.2 → 2.4 postKP → 1.7 at 1 year postKP	Resumption of daily activities within hours postKP	Kypothic angle: 15° → 8° postKP AVBH: 53.10 → 82.76% postKP	**0**	**0**
TOTALS **60 reports**		**2,865 (kyphoplasty patients)**	**2,566 KP - OS** **285 KP -CA** **3KP - HA** **11 KP - TR**					**7 - 0.24%) pooled risk**	**28 PR - 0.98% pooled risk** **(15 Postop - 0.52% pooled risk)**

Key

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Pts	patients	RA	Rheumatoid Arthritis	ROM	Range of Motion	SC	Scoliosis	sig	sig	SP	Spondylosis	T	Thoracic
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Ant	Anterior												

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