NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of balloon kyphoplasty for vertebral compression fractures

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2005

Procedure name

Balloon kyphoplasty

Specialty societies

British Orthopaedic Association
British Society of Skeletal Radiology
British Association of Spinal Surgeons
Royal College of Radiology

Description

Indications

Vertebral compression fractures (VCFs) are one of the most common types of osteoporotic fractures. Osteoporotic fractures are common in the elderly and in particular post-menopausal women but can also be associated with other factors such as chronic steroid usage. Other causes of vertebral compression fractures include malignancy in the vertebrae or more rarely haemangioma.

Pain is the most common symptom in patients with vertebral compression fractures. Vertebral compression fractures however can lead to progressive spinal deformity and changes in the spine, namely abnormal curvature (kyphosis). This can lead to increased risk of further fracture at adjacent levels or progressive malalignment, deformity, and pain. Patients with kyphosis often have a reduced appetite due to bloating and/or bowel obstruction. They also have an increased risk of falls.

Current treatment and alternatives

Conventional treatment for vertebral compression fractures is focused on the alleviation of symptoms with analgesic medications and spinal support. The majority of patients with osteoporotic vertebral fractures become symptom free through these measures and surgery is rarely indicated.
Surgery may be considered in patients who are refractory to medical therapy and where there is continued vertebral collapse and severe pain.
Recently there has been increased interest in minimally invasive procedures for the treatment of vertebral compression fractures including kyphoplasty and vertebroplasty. Balloon kyphoplasty is variation of vertebroplasty.

What the procedure involves

Balloon kyphoplasty is performed under local or general anaesthesia assisted by fluoroscopy. One or more levels of the spine can be treated at one session.

A small incision is first made in the patients back to gain access to the fractured vertebra. A channel is then created by a hand drill through which a balloon-like device (inflatable bone tamp) can be inserted into the fractured vertebra. The inflatable tamp is then positioned in the vertebral body and filled with a radiopaque contrast medium for visualisation. The balloon is slowly inflated until normal height of the vertebral body is restored or the balloon reaches its maximum volume. The balloon is then deflated and removed. This creates a cavity that is then filled with cement (typically polymethylmethacrylate PMMA) at a low pressure. The cement hardens thereby increasing the strength of the vertebra.

Efficacy

Pain after balloon kyphoplasty was reported to be decreased from preoperative levels in the majority of patients at a maximum follow-up of 24 months. Three non randomised studies were reviewed: two comparing balloon kyphoplasty to conventional medical care (physical and analgesic therapy) and one to vertebroplasty. All three studies found that patients that had undergone balloon kyphoplasty had improved pain scores.

In the two non-randomised controlled trials that had follow-up of 12 months or more, physical function following balloon kyphoplasty, as measured by the European Vertebral Osteoporosis Study Group questionnaire (EVOI) or Oswestry Disability Index (ODI) was shown to be significantly improved from baseline at 12 months. However in one of these studies this difference was similar to the improvement in those receiving medical care (54.5 ± 3.04 versus 44.3±5.07) and in the second study physical function (ODI) at two years was not found to be significantly different from preoperative values in either the balloon kyphoplasty (61% vs 56%) or vertebroplasty group (61% vs 52%).

Vertebral height and kyphosis where measured was reported to be corrected in patients following balloon kyphoplasty. In a study of 222 patients (360 procedures), a greater than 20% restoration of lost vertebral height was achieved in 63% and 69% of fractures at the anterior and midline. The kyphosis angle also decreased from 22^{o} to 15^{o}.In a study comparing kyphoplasty with conventional medical care midline vertebral body height was significantly increased in the kyphoplasty group compared with that at baseline and at 12 months was significantly greater than in the controls (66.7% vs 55.8%).

The Specialist Advisors expressed uncertainties around whether the improvements following kyphoplasty (pain and height restoration) are maintained in the long term. Advisors also questioned whether height restoration actually improved pain relief.

Safety

The most commonly reported complications following balloon kyphoplasty were cement leaks or new fractures. Thirty-eight cement leaks (11%) were found in a study of 222 patients (360 fractures), with one resulting in an episode of radiculopathy. In another study of 102 patients (192 procedures) cement leaks were reported from eight vertebral bodies (7.1%), all of which were asymptomatic. There were seven clinically asymptomatic cements leaks (9%) in a non-randomised study that included 40 patients (72 procedures) who had undergone balloon kyphoplasty. In the non-randomised controlled trial that compared balloon kyphoplasty with vertebroplasty; the incidence of cement leaks was 23% (8/35) in the balloon group, with one observed leakage to the disc space. In the vertebroplasty group the rate was 28% (8/29); with leaks to the epidural or vertebral bodies observed in two and four cases respectively. Not all studies reported on cement leakages.

In one study of 115 osteoporotic patients (225 procedures) that specifically addressed the issue of post-kyphoplasty fracture it was found that 26 patients (23%) developed a post procedure fracture. It was further reported that the incidence of fracture in primary osteoporosis patients was 11.2% and 48.6% in the group with secondary osteoporosis. The incidence of new fractures was reported in two of the non-randomised controlled studies. In the study comparing balloon kyphoplasty to standard medical care seven new fractures were observed in seven balloon kyphoplasty patients (7/40 17.5%) compared to 11 fractures in 10 patients in the control group (11/20 55%). In the other non-randomised study six adjacent fractures were observed in the balloon group at four months compared to one adjacent facture in those undergoing vertebroplasty.

Other adverse events during or after balloon kyphoplasty reported in the studies included balloon rupture (2 cases), motor deficits due to a faulty puncture (1 case) and epidural bleeding (1 case). There is some evidence to suggest that where other complications did occur that these were often related to a learning curve.

It was reported in a review of complications following balloon kyphoplasty reported to the Food and Drug Administration Medical Device web site that there were 33 major complications in patients (denominator estimated between 40,000 – 60,000 procedures) following balloon kyphoplasty. This included one death, five cases of canal intrusion with permanent paralysis, radiculopathy, paresthesias or loss of motor function and 13 cases of canal intrusion/cord compression.

The Specialist Advisors listed cements leakages as the most common complications following balloon kyphoplasty. They also listed infection, allergy and spinal cord or nerve root injury due to needle placement as potential complications.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to balloon kyphoplasty. Searches were conducted via the following databases, covering the period from their commencement June 2005 MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies included. Efficacy: Emphasis was placed on identifying good quality studies i.e controlled trials, prospective studies with long-term follow-up. Safety: Emphasis was placed on identifying large studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with vertebral compression fractures
Intervention/test	Balloon kyphoplasty.
Outcome	Key efficacy outcomes: Pain, vertebral body height, kyphosis correction, quality of life, reduction in spinal deformity Key safety outcomes: Intraoperative and postoperative complications
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on: three non randomised controlled trials, five case-series studies, a review of complications reported to the FDA and an unpublished registry report.

Existing systematic reviews/health technology assessments on balloon kyphoplasty

Three reviews were identified on balloon kyphoplasty; one was an unpublished systematic review commissioned by the manufacturer and two were published health technology assessments. The details of the reviews are listed below and Appendix B includes a summary of the findings of the published assessments. These reviews have been not included in the main data extraction table as a substantial amount of literature has been published on balloon kyphoplasty in the last 12 months, including two non randomised comparative studies.

Title of report: Percutaneous kyphoplasty for Vertebral Fractures Caused by Osteoporosis and Malignancy [1]

Commissioning body: BlueCross Blue Shield Association

Literature search date: November 2004 Publication date: December 2004

Number and type of studies included: Ten studies were included in the review. All studies are uncontrolled; either case reports or case series.

Title of report: Balloon kyphoplasty: health technology literature review [2]

Commissioning body: Ontario Health Technology Advisory Committee

Literature search date: September 2004 Publication date: December 2004

Number and type of studies included: Twelve studies were included in the review. Eleven of the studies were case series, and the remaining paper was a comparative study published in German that had been translated into English.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional Procedures

Interventional procedures guidance documents have been previously issued for both balloon kyphoplasty (IPG020) and vertebroplasty (IPG0012).

The Interventional Procedures Advisory Committee will also be considering the procedure percutaneous cementoplasty in the near future.

Technology Appraisals

None

Clinical Guidelines

There is a clinical guideline in development on osteoporosis. This guideline focuses on the assessment of fracture risk and pharmacological and non pharmacological (e.g. vitamin D) for reducing fracture risk. Surgical interventions are not considered.

Public Health

None

Table 2 Summary of key efficacy and safety findings on balloon kyphoplasty

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

<table>
<tr><th>Study Details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Grafe (2005) [3] Kasperk et al (2005) [4] Germany

Non randomised controlled trial

May 2002- September 2002.

60 patients

40 patients underwent kyphoplasty (73 procedures)
- Mean age was 68.7 years
- 30 patients had more than 3 fractures

20 patients received conservative management
- Mean age was 70.1 years
- 14 patients had more than 3 fractures

Mean duration of symptoms: greater than 12 months for all patients.

Maximum follow-up: 12 months

Selection criteria: Patients with primary osteoporosis with one or more painful osteoporotic vertebral factures requiring chronic pain medication were eligible. Vertebral fractures had to be present for > 12 months

Conflict of interest/Funding source: Several companies, including Kyphon.</td>
<td>Outcomes measured (mostly at 6 months): midline vertebral height, kyphosis angle and new vertebral fractures, pain (VAS), daily activity (EVOS), medication and health service usage

<table>
<tr><td>Outcome</td><td>Kyphoplasty</td><td>Control</td></tr>
<tr><td>Pain (VAS)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>26.2</td><td>33.6</td></tr>
<tr><td>6 months</td><td>44.2</td><td>35.6</td></tr>
<tr><td>12 months</td><td>44.4</td><td>34.0</td></tr>
<tr><td>Improved scores at 12 months</td><td>31/40 (77.5%)</td><td>11/20 (55%)</td></tr>
</table>

At 6 and 12 months VAS scores were significantly improved in the kyphoplasty groups compared with the controls (however the number of patients was not significant).

<table>
<tr><td>Daily activity/Physical function (EVOS)</td><td>Kyphoplasty</td><td>Control</td></tr>
<tr><td>Pre-procedure</td><td>43.8</td><td>39.8</td></tr>
<tr><td>6 months</td><td>54.5</td><td>43.8</td></tr>
<tr><td>12 months</td><td>54.5</td><td>44.3</td></tr>
<tr><td>Improved scores at 12 months</td><td>30/40 (75%)</td><td>11/20 (55%)</td></tr>
</table>

At 6 months there was a statically significant difference between the two groups in regards to EVOS scores, however this was not sustained at 12 months (the number of patients also did not reach significance).</td>
<td>Complications:
Cement leaks:
In 84 treated vertebral bodies, 12 (9.0%) cement leakages were observed.
- 5 ventral leaks
- 7 lateral leaks

Authors note that there were no complications of neurological, embolic or cardiovascular symptoms.

New Fractures (12 months)

In the kyphoplasty group there were 7 fractures in 7 patients (17.5%).

In the control group 11 fractures in 10 patients (50%).

There was a significant difference between the groups at 12 months.

Authors make a comment on the learning curve in establishing kyphoplasty at their centre [4].

Two adverse events occurred among the first nine cases
- a case of permanent paresis to one leg
- and an epidural haematoma in the spinal canal after 24 hours
After these events 35 procedures were performed event free.</td>
<td>Authors note that the patients were consecutive. – they also record reason for ineligibility.

Some inconsistency of reporting between the earlier and later study in respect to complications.

Group assignment was decided by the patient. All patients were offered surgery and informed of risk and benefits.

Authors note that there was no evidence of statistically significant differences between the groups at baseline.

Earlier study reports on 6 month outcomes [4]

All participants received medical treatment and physiotherapy.

Radiomorphometirc measurements were performed by two independent examiners

Results are included in the study abstract but mostly in graph form in the body of the paper.

Pain (VAS) – higher the value the less pain patients experienced.</td>
</tr>
</table>

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key efficacy findings	Key safety findings	Comments
Grafe (2005) [3] Kasperk et al (2005) [4] Cont…			

Midline vertebral height		
Pre-procedure	59.2%	60.9%
6 months	66.8%	58.2%
12 months	66.7%	55.8%

At 6 months and 12 months the midline vertebral body height was significant greater in the kyphoplasty group than in the controls.

Health service usage (12 months)	Mean number of visits to doctor 5.3/patient	Mean number of visits to doctor 11.6/patient

Medication usage – 6 months (% reduction in number of patients)	12.5% reduction	5% reduction

Kyphosis angle: vertebrae treated by kyphoplasty exhibited a relatively constant kyphosis angle during follow-up, whereas there was a significant increase of the kyphosis angle in the controls after 6 months.

Authors note that there was no significant correlation between the degree of height restoration and the observed improvement of pain or mobility.

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

<table>
<tr><th>Study Details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Grohs et al 2005 [5]

Germany

Non randomised controlled trial

2001 - 2002

51 patients

28 patients underwent kyphoplasty (35 fractures)
- Mean age was 70 years
- median age of fractures was 8 weeks
- 19 patients with primary and 9 patients with secondary steroid-induced osteoporosis.

23 patients underwent vertebroplasty (29 fractures)
- Mean age was 71 years
- median age of fractures was 9 weeks
- 12 patients with primary and 8 patients with secondary steroid-induced osteoporosis.

Mean follow-up: 2 years

Selection criteria: osteoporotic compressions fractures of the lumbar or thoracic spine, severe local pain, majority deformity of the vertebral bodies or increasing deformity in x-ray control with radiological signs of osteopenia and fracture activity on imaging.
Exclusion criteria: spondylitis, neurologic compression fractures.

Conflict of interest/Funding source: Not reported</td>
<td>Outcomes measured: pain, disability (ODI) , kyphotic wedge and vertebral height

<table>
<tr><td>Outcome
Pain (VAS)</td><td>Kyphoplasty</td><td>Vertebroplasty</td></tr>
<tr><td>Pre-procedure</td><td>7.4*</td><td>7.8*</td></tr>
<tr><td>1 year</td><td>2.7 (1.6-3.8)</td><td>5.7 (3.8-6.6)</td></tr>
<tr><td>2 years</td><td>2.0 (0.5-5.3)</td><td>5.6 (0.6-6.3)</td></tr>
<tr><td>ODI</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>61%</td><td>61%*</td></tr>
<tr><td>1 year</td><td>42%</td><td>46%</td></tr>
<tr><td>2 years</td><td>56%</td><td>52%</td></tr>
<tr><td>Kyphotic wedge</td><td>Decreased 6 degrees</td><td>No change (not aim of procedure)</td></tr>
<tr><td>Vertebral height</td><td>Increased by 5.8%</td><td>No change (not aim of procedure)</td></tr>
</table>
</td>
<td>Complications:
Kyphoplasty
Cement leaks
In 8 vertebral bodies (8/35), a cement leakage to the disc space was observed. No cement leakage to the epidural space or segmental vessels.

New Fractures
Within 4 months, in six adjacent levels another fracture occurred.

Vertebroplasty
Cement leaks
In two vertebral bodies cement leakage was found in the epidural space and segmental vessels respectively. In 4 vertebral bodies, a cement leakage to the disc space was observed. Total 8/29

New Fractures:
Within 4 months, in one adjacent level another fracture occurred.</td>
<td>Unclear how patients were assigned to groups. Baseline characteristics were compared – no differences were found.

Reporting of results are inconsistent. Different results are given in the tables/graphs (those figures indicated by*).

Authors state that an independent assessor performed the entire review of the follow-up visits.

Subgroup analysis was conducted in the kyphoplasty group.</td>
</tr>
</table>

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

<table>
<tr><th>Study Details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Komp et al (2004) [6]

Germany

Non randomised controlled trial

2000 - 2003

40 patients (36 available for follow-up)

19 patients underwent kyphoplasty - Mean age was 74.3 years

17 patients treated conservatively - Mean age was 72.4 years

Maximum follow-up: 6 months

Mean duration of symptoms: 34 days

Selection criteria: osteoporotic compressions fractures of the lumbar or thoracic spine, severe local pain, majority deformity of the vertebral bodies or increasing deformity in x-ray control with radiological signs of osteopenia and fracture activity on imaging.
Exclusion criteria: spondylitis, neurologic compression fractures.

Conflict of interest/Funding source: Not reported</td>
<td>Outcomes measured (6 months): pain (VAS and, NASS), neurology (NASS) disability (ODI) ,

<table>
<tr><td>Outcome</td><td>Kyphoplasty</td><td>Control</td></tr>
<tr><td>Pain (VAS)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>91 (80-100)</td><td>91 (75-100)</td></tr>
<tr><td>6 weeks</td><td>20 (0-35)</td><td>88 (65-100)</td></tr>
<tr><td>6 months</td><td>25 (0-30)</td><td>83 (35-100)</td></tr>
<tr><td>Pain (NASS)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>5.4</td><td>5.2</td></tr>
<tr><td>6 weeks</td><td>1.9</td><td>4.9</td></tr>
<tr><td>6 months</td><td>2.0</td><td>4.8</td></tr>
<tr><td>NASS (neurology)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>1.1</td><td>1</td></tr>
<tr><td>6 weeks</td><td>1.1</td><td>1.1</td></tr>
<tr><td>6 months</td><td>1.1</td><td>1.1</td></tr>
<tr><td>Disability (ODI)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>84</td><td>82</td></tr>
<tr><td>6 weeks</td><td>22</td><td>78</td></tr>
<tr><td>6 months</td><td>24</td><td>76</td></tr>
<tr><td>Self-reported satisfaction</td><td>13 patients very satisfied, 6 patients satisfied</td><td>2 patiens moderately satisfied, 15 patiens dissatisfied.</td></tr>
</table>

Vertebral height (after kyphoplasty)
In 11 cases the fractured vertebral body was straightened to at least 2/3 of the height of the adjacent vertebral body. In the remaining cases a straightening of at least 50% was achieved.</td>
<td>Complications:
Kyphoplasty group:
Authors report that there no complications during the operation.

In two cases a perforation of the fractured end plate appeared radiologically during the operation but was without consequence.

Seven patients had slumping of the cranially adjacent vertebral bodies (unclear whether these are considered new fractures).

Control group:
At final follow-up, 11 patients were found to have new fractures.</td>
<td>Translation provided (original paper published in German).

Allocation to groups was through discussion with the patient i.e. 19 patients refused surgery and requested to continue conservative treatment.

Authors note that there that were no striking differences between the group with respect to sex, height, age, weight and concomitant illnesses.

Treatment in the control group: physical and analgesic therapy

4 patients were excluded from the analysis (two in each group).

In the kyphoplasty group one patient died from unrelated causes, one moved way.

In the control group two patients were hospitalised.

Outcomes are poorly reported.</td>
</tr>
</table>

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key efficacy findings	Key safety findings	Comments
Hillmeier et al (2004) [7] German (2 hospitals) Prospective case series 102 patients (192 vertebral bodies) Mean age: 71 years (56-88 years) Mean duration of symptoms: In 82 patients the fractures were old, and in 20 patients with proven osteoporosis the cause of the vertebral body fracture was a trauma which had occurred within the previous 4 weeks. Mean number of levels/patient 1.9 Follow up: 102 patients (100%) 1 week 96 patients (94%) 1 month 94 patients (92%) 3 months 94 patients (92%) 6 months 42 patients (41%) 12 months Selection criteria: Patients with osteoporotic vertebral body fractures with a follow-up period of at least 6 months. Patients were excluded who had malignancies, vertebral body metastases, traumatic vertebral body fractures and chronic disc lesions. Conflict of interest/Funding source: Not reported	**Outcomes assessed:** pain (VAS, EVOS), angle of kyphosis, vertebral height, Pain was significantly improved in 73% of the patients and moderately so in 16%. Both the reduction in pain and improvement in function being maintained over the entire period of observation to date (12 months). In 11% of the patients there was no improvement. Vertebral body height increase: 17% average height increase for all vertebral bodies (n=192) 15% height increase for old fractures (n=172) 31% height increase for recent fractures (n=20)	**Complications**: 8 vertebral bodies had cement leakage but with no clinical symptoms. 5 cases of fractures in the immediately adjacent vertebral bodies at 12 months. 1 patient had epidural bleeding after kyphoplasty 1 patient suffered motor deficits in one leg due to a faulty puncture technique. Authors note that the two serious complications occurred during the period in which the first 15 patients were treated.	Translation provided (Original paper published in German). Graphs have not been reproduced in translated version. In 40 patients Calcibon cement was used (instead of PMMA) Unclear when outcomes have been assessed. Proposed initial method of assessing vertebral height proved to be unsuitable. Recruitment of patients not described clearly.

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key efficacy findings	Key safety findings	Comments
Coumans et al (2003) [8 9] USA May 1999 – December 2000 78 consecutive patients (188 procedures) - 63 patients had osteoporosis - 15 had multiple myeloma Mean age: 71 years (44-89 years) Mean duration of symptoms: 7 months Mean number of levels/patient 2.4 Follow up: 18 months (max) Selection criteria: Patients were excluded if the fracture was long standing. Had to have at least 12 months follow-up. Conflict of interest/Funding source: Not reported	**Outcomes measured:** Quality of life (SF-36), pain (VAS), Oswestry Disability Index Quality of life SF-36 – no raw figures given in the body of the report. There appeared to be significant improvements post-surgery in seven measures of the SF36 - persisting throughout the follow-up period (read from graph as no numbers given in text). However there was decline in the measure of general health at last follow-up examination. Pain The VAS scores improved from a preoperative level of 7 to 3.4 at last follow-up. Disability The ODI scores improved from a preoperative level of 48 to an initial postoperative level of 33 and were at 35 by the last follow-up.	**Complications** (30 days): 5 cases of asymptomatic PMMA extravasation - 1 case inside spinal canal -3 cases paraspinal - 1 case intradiscal 1 patient had a postoperative myocardial infarction	Earlier study from same centres included in the IP Overview completed 2003 [9]. Thirteen patients died prior to the 1-year follow-up as a result of tumour progression or unrelated illness. Data collection was complete in 40 (62%) of the remaining patients (denominator is unclear in the reporting on the paper). One of the authors is a consultant to the manufacturer. Limited information presented in the results section. Authors also not that the incidence of cement leakage may be underestimated because it is based on analysis of radiographs rather than CT scans.

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

<table>
<tr><th>Study Details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Crandall et al (2004) [10]
USA
Prospective case series

47 patients (86 fractures, 55 procedures)
- 23 acute patients
- 24 chronic patients

March 2000 – December 2001[i]

Mean age: 74 years (47-91 years)

Mean duration of symptoms:
Acute group: 1.3 months
Chronic group: 11 months

Number of levels/patient :
30 were single level
25 were multilevel surgeries

Mean follow-up: 18 months (6 -24 months)

Selection criteria: History of primary or secondary osteoporosis. Had to have imaging evidence of incomplete fracture healing

Conflict of interest/funding source: Not reported.</td>
<td>Outcomes assessed: pain (VAS), Back pain (ODI), medication usage, vertebral height restoration, kyphosis correction.

<table>
<tr><td>Outcome</td><td>Acute</td><td>Chronic</td></tr>
<tr><td>Pain (VAS)</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>7.3</td><td>7.3</td></tr>
<tr><td>2 weeks</td><td>4.3</td><td>4.3</td></tr>
<tr><td>Vertebral height % of normal height</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>58%</td><td>56%</td></tr>
<tr><td>Post-procedure</td><td>86%</td><td>79%</td></tr>
</table>
However 10% of less correction of height lost occurred in 20% of chronic fractures and 8% of acute fractures.

<table>
<tr><td>Kyphosis</td><td></td><td></td></tr>
<tr><td>Pre-procedure</td><td>15^0</td><td>15^0</td></tr>
<tr><td>Post-procedure</td><td>8^0</td><td>10^0</td></tr>
<tr><td>Pain medication</td><td colspan="2">All patients</td></tr>
<tr><td>Pre-procedure</td><td colspan="2">5.4</td></tr>
<tr><td>At least follow-up (1-12 months)</td><td colspan="2">3.6</td></tr>
<tr><td>ODI</td><td colspan="2">Scores improved for almost all of the patients , with 60% of patients having at 25% improvement in their score</td></tr>
</table>
</td>
<td>Complications:

1 patient had cardiac arrhythmia (unrelated to the kyphoplasty procedure)

No other complications occurred. Authors note that in early experience there were two cases of balloon rupture (2 patients) but neither patient experienced any complications.</td>
<td>Acute fractures were 10-16 weeks old
Chronic fractures were 4 or more months old.
Subacute fractures (between 10 weeks and 4 months) were omitted.

Pain medication usage was qualitatively analysed by summating scores created when the medication data were transformed to an ordinal scale (1=no medication; 2= over the counter; 3 anti-inflammatory and muscle relaxants; 3=mild narcotics; 4=strong narcotics).

Outcomes not well reported.

Unclear when some outcomes are assessed – and while mean follow-up is 18 months, some outcomes ie pain the authors have only reported outcomes at 2 and 6 weeks.

Absolute data not given for every outcome.</td>
</tr>
</table>

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

<table>
<tr><th>Study Details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Majd et al (2005) [11]
USA
Retrospective case series

December 2000 – July 2003

222 patients (360 vertebral compression fractures, 254 procedures)

Mean age: 76 years (28-98 years)

Mean duration of symptoms: 5.7 months (range 2 days to 2 years, median 2.2 months)
Average fracture age at time of treatment: 5.7 months

Number of levels/ treated: 140 patients had on e level treated, 58 patients had two levels treated, and 1 patiens had five levels treated.

Mean follow up: 21 months (6-36 months)

Selection criteria: Patients with osteoporotic vertebral body fractures which had not responded to conventional treatment. Only nonhealed, painful fractures with positive MRI or bone scan results were considered.

Conflict of interest/Funding source: Not reported</td>
<td>Outcomes measured: pain (nonvalidated measure), vertebral height, kyphosis

Pain (completed data only available in 174 patients)
78% of patients indicated complete pain relief
11% of patients experienced at least partial pain relief.
11% of patients had persistence pain due to new fractures or underlying degenerative disc disease (all received additional balloon kyphoplasty procedures which resolved pain).

<table>
<tr><td></td><td colspan="4">% Predicted height</td></tr>
<tr><td></td><td colspan="2">Anterior</td><td colspan="2">Midline</td></tr>
<tr><td></td><td>Preop</td><td>Post-op</td><td>Preop</td><td>Post-op</td></tr>
<tr><td>All fractures</td><td>74</td><td>82</td><td>75</td><td>85</td></tr>
<tr><td>Thoracic</td><td>69</td><td>77</td><td>72</td><td>82</td></tr>
<tr><td>Lumbar</td><td>80</td><td>87</td><td>79</td><td>88</td></tr>
<tr><td>Thora-columbar</td><td>74</td><td>80</td><td>75</td><td>84</td></tr>
</table>

<table>
<tr><td></td><td colspan="2">% Collapse restored</td></tr>
<tr><td></td><td>Anterior</td><td>Midline</td></tr>
<tr><td>All fractures</td><td>30</td><td>50</td></tr>
<tr><td>Thoracic</td><td>7</td><td>24</td></tr>
<tr><td>Lumbar</td><td>56</td><td>76</td></tr>
<tr><td>Thora-columbar</td><td>27</td><td>54</td></tr>
</table>

Overall a greater than 20% restoration of lost vertebral height was achieved in 63% and 69% of fractures at the anterior and midline.

Kyphosis thoracic spine (n=125)
Preoperative 22^0 (range $1\text{-}59^0$)
Postoperative 15^0 (range $1\text{-}52^{0)}$</td>
<td>Complications:
38 cases of cement extravasation (n=360) with one case of radiculopathy (see below)

10 medical and 3 surgical complications were noted (0.3% per fracture).

Authors note that the most of the medical complications were related to pre-existing cardiac, pulmonary or liver disease.

Surgical complications (n=3):
-1 patient required surgical debridement, irrigations and closure of a wound 3 weeks after the procedure. The patient had spinal stenosis due to degeneration in the disc.

-1 patient had L1 radiculopathy caused by leakage of cement in the foramen. This patient recovered with selective nerve block and rehabilitation.

- 1 patient had an infection at the level of kyphoplasty 2 months after the procedure

New fractures:
12% of patients required 1-2 additional procedure to treat 36 additional fractures. Two thirds of these fractures were adjacent to a previously treated level.</td>
<td>Pain was categorised as completely gone, less pain, same level or more pain.

A researcher not involved in the procedure measured vertebral height.

Authors noted that the results from some surgeries could not be evaluated because of missing preoperative or postoperative responses from patients who were usually seen as hospital consults.

Outcome data was not available on all patients.</td>
</tr>
</table>

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key efficacy findings	Key safety findings	Comments
Garfin (2003) [12] Registry report Last patient enrolled June 2001 155 patients (214 vertebral compression fractures) Mean age: unclear Mean duration of symptoms: 18.4 weeks Age of fractures: 2 weeks to 7 years Follow up: 149 patients had 7 day 134 patients had 1 month 131 patients had 3 months 108 had 12 month 100 had 24 month follow-up Conflict of interest/Funding source: Registry maintained by manufacturer	**Outcomes reported:** (other outcomes were measured but not reported on here) Pain, median number of days per month patients remained in bed, quality of life (SF-36), back function, individual satisfaction Author notes that patients had a 60% reduction in mean 'average back pain' by 7 days, and a 55% reduction in the mean 'worst possible' back pain by 7 days (this reduction was maintained during follow-up) Patients experienced an improvement in quality of life outcomes. Patients experienced improvements in back function i.e. bending, lifting weights and standing for an hour. Patients reported a high level of satisfaction from 7 days after the procedure to end of follow-up. 80% of patients had a mid-vertebral height restoration of a t least 10%. The mean mid-vertebral height restoration for the group was (32.2%)	Peri-operative complications: 1 patient suffered 3 rib fractures Post-operative: 1 patient had a short episode of paroxysmal supraventricular tachycardia Extravasation of fixation material outside of the vertebral body was observed in 10% of treated fractures. In all cases the extravasation were asymptomatic. A total of 23 of the 100 patients (with 24 moth follow-up) had a new fractures (11.5% per year)	Unpublished (submitted for publication). Essentially a post-marketing registry that is a narrative rather than scientific publication. 55 patients were lost to follow-up (reasons given for 46). Author states that there were no significant differences in baseline characteristics to those that were included in the study. No information given on the centres that undertook the experience or the surgeons. Represents experience until 2001 – part of a study that Kyphon can conducted as part of FDA clearance. The study stopped recruiting in 2001 when the FDA informed Kyphon that further assessment was needed. Baseline characteristics – what was measured what efficacy measures. Key effectiveness results are presented in this report (i.e. not all data) Subjective measured. Issues around whether radiographs submitted to the manufacture were adequate to assess height restoration.

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key safety findings	Study Details
Harrop et al (2004) [13] Retrospective case series October 1999 – November 2001 115 patients (225 procedures) - 80 patients with primary osteoporosis - 35 patients with secondary osteoporosis as a result of steroid medication usage. Mean age was 74 years (45-89 years). Mean follow up: 11 months (3-33 months). Selection criteria: Patients with insufficient follow-up (less than 3 months), or malignancy related compression fractures were excluded.	**Outcomes assessed:** subsequent fracture After initial treatment 26 patients developed a post-kyphoplasty VCF. - 19 fractures were adjacent - 9 remote fractures. 21 patients had a single compression fracture - 3 patients had two concurrent fractures - 1 patient had three fractures - 1 patient had four factures Of these 26 patients, 23 patients elected to undergo further vertebral augmentation (no further detail given) Incidence of subsequent fracture was 15.1% per procedure, while the incident per patients was 22.6%. Incidence of postprocedure fracture in the primary osteoporotic patients was 11.2% (9/80ptaitns) and 48.6% (17/35) in patients with secondary osteoporosis (p<0.0001)	Primary aim of the paper is to assess the incidence of VCFs following kyphoplasty. Review of a database maintained by one of the authors. Procedures all performed at a single institution. Subsequent VCFs were identified based on changes from baseline imagine studies as either adjacent or remote fractures. Lack of information about duration of symptoms etc… Unclear about the generalisability of results – given experience of surgeon. Authors quote a natural history incidence of 24% for VCF

Abbreviations used: VCF – vertebral compression fractures; VAS – Visual analogue scale, EVOS – European Vertebral Osteoporosis Study group questionnaire; NASS – North American Spine Society armamentarium, ODI – Oswestry Disability Index, Sig - significant

Study Details	Key safety findings		Study Details
Nussbaum et al (2004) [14] Review of complications reported to the FDA for both vertebroplasty and kyphoplasty. 1999 – June 2003 58 reports of complications involving 52 patients. - 33 patients had kyphoplasty (21 major adverse events) - 5 lateral approach vertebroplasty (4 major adverse events) - 14 transpedicular vertebroplasty (4 major adverse events) Major adverse events are defined as any surgical complication requiring additional surgical interventions or resulting in permanent disability of death.	**Complications:** Kyphoplasty: Death (patient had a history of pulmonary and cardiac disease) 1 Canal intrusion with permanent paralysis, radiculopathy, paresthesias or loss of motor function 5 Epidural hematoma causing permanent muscle weakness resolving after decompression surgery 1 Canal intrusion with most symptoms resolving following decompression surgery 13 Epidural hematoma with most symptoms resolving following decompression surgery 1 Pulmonary embolism due to cement emboli-extended hospital stay, no long term problems 1 Ileus 1 Infection-discitis/osteomyelitis 2 Pneumothorax 1 Drop in blood pressure 1 Equipment breakage 6 33 Approx 40,000 – 60,000 total procedures performed between 1999-2003 Vertebroplasty with standard transpedicular approach Death 3 Canal intrusion/cord compression - paralysis n 1 Cardiac arrest (no clinical sequelae) 2 Anaphylaxis/blood pressure drop (no clinical sequelae) 2 Cement embolus (no clinical symptoms) 1 Equipment breakage (no clinical symptoms) 5 14 Approx 130,000 – 160,000 total procedures performed between 1999-2003 Vertebroplasty (lateral approach) Death 4 Equipment breakage (no clinical symptoms) 1 5 Approx 10,000 – 15,000 total procedures performed between 1999-2003		No efficacy outcomes reported as not the aim of the paper. Authors searched the FDA database and contacted manufactures to clarify information regarding outcomes. Authors note that at least five of the 20 spinal compressions were caused by breakage of the pedical during the insertion of the 8-gauge needle. Authors note the discrepancy between major events reported in the published literature and that report on the FDA database.

Validity and generalisability of the studies

- There is substantial variation among the studies in regards to methodological quality.
- Three comparative studies are included in the main data extraction table, two of these studies compare balloon kyphoplasty to conventional care and a third to vertebroplasty. In all three studies the procedure/control groups appear to be balanced at baseline, however allocation to treatment was typically made through discussion with the patient which may lead to some selection bias.
- In a number of studies there are inconsistencies in the reporting of results or a lack of reporting; for example in terms of outcomes and patient characteristics.
- Few studies have reported on quality of life (in comparison to self reported satisfaction)
- While papers reported on patients with both osteoporotic (secondary and primary) and multiple myeloma vertebral compression fractures, the majority of evidence published is in respect to patients with osteoporotic bone disease. It is unclear if efficacy and safety outcomes differ between these two groups.
- Mean duration of symptoms also varied among the study populations. This may be an important factor, as there is some suggestion that individuals with early fractures may benefit more from balloon kyphoplasty [7].
- In most studies it is difficult to gauge the experience of the surgeon(s) undertaking balloon kyphoplasty, and the possible learning curve associated with this procedure. The authors of several studies made note that adverse events occurred during the period in which the first few patients were treated.
- The authors of a report reviewing complications made to the FDA website [14], suggested that complications are possibly under-reported in the published literature as those publishing papers have greater experience.

Specialist Advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Mr Timothy Briggs Dr Malcome Crone, Mr Evan Davies Mr Jeremy Fairbank, Dr Tarun Sabharwal, Dr Martin Warren, Mr Lester Wilson and, Dr David Wilson.

- Comparators to balloon kyphoplasty are conservative therapy, surgical fixation and vertebroplasty.
- Most patients with osteoporosis fractures can be managed conservatively.
- Balloon kyphoplasty is an option for a small number of patients with vertebral compression fractures.
- Balloon kyphoplasty may have a role in pathological fractures - as yet this is uncertain but potentially more important.
- Surgical back up facilities and access to good imaging machines are needed when undertaking this procedure

Issues for consideration by IPAC

Balloon kyphoplasty was considered by the Committee in 2003. Since this time there has been a substantial number of papers published on balloon kyphoplasty, including three non randomised controlled trials.

There are a number of studies that specifically report on the use of balloon kyphoplasty in patients with pathological fractures. These studies have not been included in the main data extraction table but have been listed in Appendix A.

There is also a substantial pool of non-English literature on this procedure, with a number of papers listed in Appendix A.

There is a randomised controlled trial evaluating balloon kyphoplasty to conventional therapy. The patient enrolment was initiated in January 2003, with the aim of enrolling 300 patients (150 + 150). As of June 2005 about 250 patients have been enrolled as such the earliest that data (outcomes at 1 month) will be available will be the beginning of 2006 (personal communication 28th June 2005 Ms B Casteels).

European Registry is maintained by Kyphon http://www.kyphon-eu.com/

References

1 Blue Cross Blue Shield Association. (2004) Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy.

2 Ontario Ministry of Health and Long-Term Care. (2004) Balloon kyphoplasty.

3 Grafe I, Da Fonseca K, Hillmeier J et al. (2005) Reduction of pain and fracture incidence after kyphoplasty: 1 year outcomes of a prospective controlled trial of patients with primary osteoporosis. *Osteoporosis International* 10: (published online August 2005).

4 Kasperk C, Hillmeier J, Noldge G et al. (2005) Treatment of painful vertebral fractures by kyphoplasty in patients with primary osteoporosis: a prospective nonrandomized controlled study. *Journal of Bone & Mineral Research* 20: 604-612.

5 Grohs JG, Matzner M, Trieb K et al. (2005) Minimal invasive stabilization of osteoporotic vertebral fractures: a prospective nonrandomized comparison of vertebroplasty and balloon kyphoplasty. *Journal of Spinal Disorders & Techniques* 18: 238-242.

6 Komp, M., Ruetten, S. and Godolias, G. (2004) Minimally invasive therapy for functionally unstable osteoporotic vertebral fracture by means of kyphoplast: prospective comparative study of 19 surgically and 17 conservatively treated patients. *Journal of Miner.Stoffwechs (Metabolism)* 11: 13-15.

7 Hillmeier J, Grafe I, Da Fonseca K et al. (2004) [The evaluation of balloonkyphoplasty for osteoporotic vertebral fractures. An interdisciplinary concept]. [German]. *Orthopade* 33: 893-904.

8 Coumans JV, Reinhardt MK, and Lieberman IH. (2003) Kyphoplasty for vertebral compression fractures: 1-year clinical outcomes from a prospective study. *Journal of Neurosurgery* 99: 44-50.

9 Lieberman IH, Dudeney S, Reinhardt M-K et al. (2001) Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures. *Spine* 26: 1631-1637.

10 Crandall D, Slaughter D, Hankins PJ et al. (2004) Acute versus chronic vertebral compression fractures treated with kyphoplasty: early results. *Spine Journal: Official Journal of the North American Spine Society* 4: 418-424.

11 Majd ME, Farley S, and Holt RT. (2005) Preliminary outcomes and efficacy of the first 360 consecutive kyphoplasties for the treatment of painful osteoporotic vertebral compression fractures. *Spine Journal: Official Journal of the North American Spine Society* 5: 244-255.

12 Garfin S. (2003) A Multi-center post-marketing registry to assess outcomes of treatment of vertebral body compression fractures with an inflatable bone tamp. Final Report.

13 Harrop JS, Prpa B, Reinhardt MK et al. (2004) Primary and secondary osteoporosis' incidence of subsequent vertebral compression fractures after kyphoplasty. Spine 29: 2120-2125.

14 Nussbaum DA, Gailloud P, and Murphy K. (2004) A review of complications associated with vertebroplasty and kyphoplasty as reported to the Food and Drug Administration medical device related web site.[see comment]. [Review] [25 refs]. *Journal of Vascular & Interventional Radiology* 15: 1185-1192.

Appendix A: Additional papers on balloon kyphoplasty not included in the summary tables

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table. It is by no means an exhaustive list of potentially relevant studies.

Additional references on balloon kyphoplasty (general)

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Rhyne A, III, Banit D, Laxer E, Odum S, Nussman D. Kyphoplasty: report of eighty-two thoracolumbar osteoporotic vertebral fractures. Journal of Orthopaedic Trauma 2004; 18(5):294-299.	52 patients 9 month follow-up	Procedure safely improves vertebral body and heights and quality of life.	Study assessed a number of outcomes but had short term follow-up.
Berlemann U, Franz T, Orler R, Heini PF. Kyphoplasty for treatment of osteoporotic vertebral fractures: a prospective non-randomized study.[see comment]. European Spine Journal 2004; 13(6):496-501.	24 patients (27 procedures) 12 month follow-up	Reduction in pain at one year. A 50% average improvement of local kyphosis was possible	Study assessed a number of outcomes but only on reported on a small patient population.
Phillips FM, Ho E, Campbell-Hupp M, McNally T, Todd WF, Gupta P. Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. Spine 2003; 28(19):2260-2265.	29 patients 19 patients had 12 month follow-up	Procedure improves physical function, reduces pain and may correct kyphotic deformity	Short term follow-up
Masala S, Cesaroni A, Sergiacomi G, Fiori R, Massari F, Manenti G et al. Percutaneous kyphoplasty: new treatment for painful vertebral body fractures. In Vivo 2004; 18(2):149-153.	16 patients Enrolled: Jan – July 2003	Procedure was effective and safe.	Limited information. Mixed indications.
Feltes C, Fountas KN, Machinis T, Nikolakakos LG, Dimopoulos V, Davydov R et al. Immediate and early postoperative pain relief after kyphoplasty without significant restoration of vertebral body height in acute osteoporotic vertebral fractures. Neurosurgical Focus 2005; 18(3):e5.	13 patients 1 month follow-up	No increase in vertebral height however patients reported pain reduction and greater mobility.	Limited follow-up.
Gaitanis IN, Hadjipavlou AG, Katonis PG et al. (2005) Balloon kyphoplasty for the treatment of pathological vertebral compressive fractures. *European Spine Journal* 14: 250-260	32 patients Follow-up: 18 months (mean)	Procedure was effective and safe.	Limited outcomes
Lieberman IH, Dudeney S, Reinhardt M-K, Bell G. Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures. Spine 2001; 26(14):1631-1637.	30 patients (70 procedures) FU: 3 months	Kyphoplasty is associated with early clinical improvement of pain and function and vertebral body height	**Included in overview considered by IPAC in 2003** Later paper included in the main data extraction table[8]

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Ledlie JT, Renfro M. Balloon kyphoplasty: One-year outcomes in vertebral body height restoration, chronic pain, and activity levels. J Neurosurg 2003; 98(1):36-42.	96 patients 133 fractures, 104 procedures FU: 1 year (24patients)	Balloon kyphoplasty safely increases vertebral body height, decreases chronic back pain 4 new fractures and 12 cases of cement leakage	**Included in overview considered by IPAC in 2003**
Theodorou DJ, Theodorou SJ, Duncan TD, Garfin SR, Wong WH. Percutaneous balloon kyphoplasty for the correction of spinal deformity in painful vertebral body compression fractures. Clin Imaging 2002; 26(1):1-5.	15 patients FU: 6-8 months	Patients experienced pain relief	**Included in overview considered by IPAC in 2003**
Garfin SR, Yuan HA, Reiley MA. New technologies in spine: Kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. Spine 2001; 26(14):1511-1515.	340 patients (376 procedures, 603 fractures) Follow-up: Longest 18 months	The authors make the statement that kyphoplasty lead to 95% improvement in pain and significant function improvement	**Included in overview considered by IPAC in 2003.** Unpublished paper (submitted for publication)included in main summary table

Articles on balloon kyphoplasty for vertebral fractures due to malignancy

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Hentschel SJ, Burton AW, Fourney DR, Rhines LD, Mendel E. Percutaneous vertebroplasty and kyphoplasty performed at a cancer center: refuting proposed contraindications. Journal of Neurosurgery Spine 2005; 2(4):436-440.	53 patients Enrolled: Jan 2001 – July 2003.	Procedure seems to be of benefit to patients who are unresponsive to other therapies.	Group of patients chosen were those who have been considered contraindicated: therefore not generalisable. Heterogenous population
Lane JM, Hong R, Koob J et al. (2004) Kyphoplasty enhances function and structural alignment in multiple myeloma. *Clinical Orthopaedics & Related Research* 49	19 patients FU: 3 months	Kyphoplasty is a safe treatment. Efficacy in terms of pain relief and functional outcome is comparable with the results in osteoporosis	Small number of patients.
Dudeney S, Lieberman IH, Reinhardt M-K, Hussein M. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. J Clin Oncol 2002; 20(9):2382-2387.	18 patients FU: 7.4 months	Patients had improved pain and majority of patients had restoration of vertebrale height. Asymptomatic cement leakage occurred at two (4%) of 55 levels.	**Included in overview considered by IPAC in 2003**

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Fourney DR, Schomer DF, Nader R, Chlan-Fourney J, Suki D, Ahrar K et al. Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients. J Neurosurg 2003; 98(1):21-30.	15 patients FU median: 4.5 months	Percutaneous vertebro- and kyphoplasty provided significant pain relief in a high percentage of patients, and this appeared durable over time. No cement leaks in balloon kyphoplasty group	**Included in overview considered by IPAC in 2003**

Articles specifically reporting on safety aspects following balloon kyphoplasty

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Choe dH, Marom EM, Ahrar K, Truong MT, Madewell JE. Pulmonary embolism of polymethyl methacrylate during percutaneous vertebroplasty and kyphoplasty. AJR 2004; American Journal of Roentgenology. 183(4):1097-1102.	64 patients Mean follow-up 7 months	Pulmonary embolism of cement is seen in 4.6% of patients.	Primary aim: safety incidence of pulmonary embolism. Single outcomes of interest
Fribourg D, Tang C, Sra P, Delamarter R, Bae H. Incidence of subsequent vertebral fracture after kyphoplasty. Spine 2004; 29(20):2270-2276.	38 patients 2 months follow-up	Study found a higher rate of subsequent fracture after procedure compared to natural history data.	Primary aim: incidence of vertebral fracture. Similar paper [13] included in main summary table [13]
Phillips FM, Wetzel FT, Lieberman I et al. (2002) An in vivo comparison of the potential for extravertebral cement leak after vertebroplasty and kyphoplasty. *Spine* 27: 2173	20 procedures	The findings showed less vascular and transcortical extravasation of injected contrast with kyphoplasty than with vertebroplasty.	Technical paper
Elshinawy A Boland P and White DA. (2005) A patient with cement pulmonary embolus following kyphoplasty. *Journal of Respiratory*	One patient		Case report

Articles on balloon kyphoplasty from Non-English journals

Article title	Number of patients/ follow-up	Direction of conclusions	Comments/Reasons for non-inclusion
Hillmeier J, Meeder P-J, Noeldge G, Kasperk C. Minimally invasive reduction and interanl stabilization of osteoporotic vertebral body fractures (Ballon Kyphoplasty). Operative Orthopadie und Traumatologie 2003; 15:343-362.	95 patients 12 months follow-up	Symptom reduction in 89% patients, cement leakage (no complications) in 8% of patients.	Article in both English and in German. Review paper with study results . More recent paper [7] included in the main summary table

Weisskopf M, Ohnsorge JA, Wirtz DC, Niethard FU. Vertebroplasty/kyphoplasty—percutaneous stabilization of vertebrae. Zeitschrift fur Orthopadie und Ihre Grenzgebiete 2004; 142(6):R59-R69.	N/A	N/A	Non-English paper (German) – no English summary
Yang HL, Gu XH, Chen L, Lu J, Mao HQ, Meng B et al. Selectivity and individualization of transpedicular balloon kyphoplasty for aged osteoporotic spinal fractures. Chung-Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao Acta Academiae Medicinae Sinicae 2005; 27(2):174-178.	17 patients (22 procedures)	Pain, vertebral height and kyphosis angle was improved. No cases of cement leakage.	Non-English paper (Chinese)
Grohs JG, Krepler P. Minimal invasive stabilization of osteoporotic vertebral compression fractures. Methods and preinterventional diagnostics. Radiologe 2004; 44(3):254-259.	Unclear	Unclear	Non-English paper (German) Paper by authors included in the main summary paper.
Yang HL, Niu GQ, Liang DC, Wang GL, Meng B, Chen L et al. [The contrast study between single and double balloon bilateral dilatation of kyphoplasty.]. [Chinese]. Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery] 2004; 42(21):1299-1302.	58 patients (90 procedures)	Pain, vertebral height and kyphosis angle was improved.	Non-English paper (Chinese)
Wilhelm K, Stoffel M, Ringel F, Rao G, Rosseler L, Urbach H et al. Preliminary experience with balloon kyphoplasty for the treatment of painful osteoporotic compression fractures. Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin 2003; 175(12):1690-1696.	34 patients (56 fractures)	Pain, vertebral height and kyphosis angle was improved. Cement leakage occurred in 10 cases (all asymptomatic)	Non-English paper (German)
Weikopf M, Herlein S, Birnbaum K, Siebert C, Stanzel S, Wirtz DC. Kyphoplasty - A new minimal invasive treatment for repositioning and stabilising vertebral bodies. Zeitschrift fur Orthopadie und Ihre Grenzgebiete 2003; Vol. 141(4):-411.	22 patients (37 fractures)	Pain, vertebral height and kyphosis angle was improved.	Non-English paper (German)
Kasperk C, Hillmeier J, Noldge G, Libicher M, Kauffmann GW, Nawroth P et al. Kyphoplastie - Konzeot zur Behandlung schmerzhafter Wirbelkorperbruche. Deutsches Arzteblatt 2003; 100(25):1748-1752.	89 patients	Pain, vertebral height and kyphosis angle was improved.	Non-English paper (German)
Darius T, Vanderschot P, and Broos P. (2003) Balloon kyphoplasty: A new treatment option for painful osteoporotic vertebral body compression fractures. *Tijdschrift voor Geneeskunde* Vol. 59: 01	7 patients	Pain decreased. Cement leakage occurred twice. One case of retroperitoneal bleeding.	Non-English paper (German)

Appendix B: Related Reviews and NICE Guidance

Related Reviews

Review title	Review conclusions
Percutaneous kyphoplasty for Vertebral Fractures Caused by Osteoporosis and Malignancy [1]	Report Conclusions: 'The available evidence is not sufficient to permit conclusions of the effect of kyphoplasty on health outcomes. The published evidence describing the outcomes of kyphoplasty consists mostly of uncontrolled studies. These uncontrolled studies were mostly retrospective and enrolled heterogeneous patient populations. Such studies cannot eliminate placebo and natural history effects as explanation for the apparent effectiveness of kyphoplasty.' [1]
Balloon kyphoplasty: health technology literature review [2]	Report Conclusions: There is level 4 evidence that balloon kyphoplasty to treat pain association with VCFs due to osteoporosis is as effective as vertebroplasty at relieving pain. Furthermore the evidence suggests that it restores the height of the affected vertebra. It also results in lower fracture rates in other vertebrae compared with vertebroplasty, and in fewer neurological complications due to cement leaked compared with vertebroplasty. Balloon kyphoplasty is a reasonable alternative to vertebroplasty, although it must be reiterated that this conclusion is based on evidence from level 4 studies [2].

Related NICE guidance

Guidance	Recommendation
Interventional Procedures	**1 Balloon kyphoplasty (IPG020)** Current evidence on the safety and efficacy of balloon kyphoplasty for vertebral compression fractures does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Although the benefits and risks of this procedure appear similar to those for percutaneous vertebroplasty in the first few months after the procedure is carried out (see 2.6.1), there is insufficient long-term evidence to substantiate this at present. Clinicians wishing to undertake balloon kyphoplasty for vertebral compression fractures should inform the clinical governance leads in their Trusts. They should ensure that patients offered it understand the uncertainty about the procedure's safety and efficacy and should provide them with clear written information. Use of the Institute's Information for the Public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present. The following are recommended: This procedure should only be undertaken when there are arrangements for good access to a spinal surgery service, and with prior discussion between a specialist multidisciplinary team that includes a radiologist and a spinal surgeon. Clinicians should receive training to reach an appropriate level of expertise before carrying out this procedure. In particular, they must follow the manufacturer's instructions for making the cement, to reduce the risk of embolisation. The procedure should be limited to patients whose pain is refractory to more conservative treatment.

Interventional Procedures	**2 Verteoplasty (IPG0012)** Current evidence on the safety and efficacy of percutaneous vertebroplasty appears adequate to support the use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance. The following are recommended. This procedure should only be undertaken when there are arrangements for good access to a spinal surgery service, and with prior discussion between a specialist multidisciplinary team that includes a radiologist and a spinal surgeon. Clinicians should receive training to reach an appropriate level of expertise before carrying out this procedure. In particular, they must follow the manufacturer's instructions for making the cement, to reduce the risk of embolisation. The procedure should be limited to patients whose pain is refractory to more conservative treatment.
Technology Appraisals	None applicable
Clinical Guidelines	None applicable
Public Health	None applicable

Appendix C: Literature search for balloon kyphoplasty

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in EMBASE, Current Contents, PreMedline and all EMB databases.

For all other databases a simple search strategy using the key words in the title was employed.

Procedure number: 179	**Procedure Name: Balloon Kyphoplasty**	
Databases	**Version searched (if applicable)**	**Date searched**
The Cochrane Library	2005 Issue 2	23.6.2005
CRD	May 2005	23.6.2005
Embase	1980 to 2005 Week 25	22.6.2005
Medline	1966 to June Week 2 2005	22.6.2005
Premedline	June 21, 2005	22.6.2005
CINAHL	1982 to June Week 3 2005	23.6.2005
British Library Inside Conferences (limited to current year only)	2004-2005	23.6.2005
National Research Register	2005 Issue 2	23.6.2005
Controlled Trials Registry	N/A	23.6.2005

Search strategy used in Medline

1 kyphoplast$.tw.
2 kyphon.tw.
3 kyphx$.tw.
4 or/1-3
5 balloon$.tw.
6 tamp$.tw.
7 5 or 6
8 (bone$ adj3 cement$).tw.
9 exp Bone Cements/
10 PMMA.tw.
11 (methyl methacrylate or methylmethacrylate).tw.
12 exp Polymethyl Methacrylate/
13 vertebroplast$.tw.
14 or/8-13
15 7 and 14
16 4 or 15
17 limit 16 to yr=2002 - 2005
18 limit 17 to humans