NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

A vertebral compression fracture occurs when the main part of one of the bones in the spine (the vertebral body) is crushed. This can be caused by injury, osteoporosis (weakening of the bones) or the spread of cancer into the spine. In this procedure, metal implants are inserted through the skin and into the crushed vertebra. The implants are expanded to the desired size and surrounded with bone cement. The aim is to improve symptoms caused by the compression fracture.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make 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 IP overview was prepared in January 2016 and updated in August 2016.

Procedure name

- Percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

Specialist societies

- British Association of Spinal Surgeons (BASS).

Description

Indications and current treatment

Vertebral compression fractures usually occur when the front of the vertebral body collapses, and may be caused by trauma, cancer or osteoporosis.

Pain is the most common symptom in patients with vertebral compression fractures. Fractures can also cause progressive spinal deformity with abnormal curvature (kyphosis). This can lead to increased risk of further fracture at adjacent levels and progressive malalignment, deformity and pain.

Treating vertebral compression fractures aims to reduce pain, improve function and minimise the incidence of new fractures. Non-invasive treatment (such as pain medication, bed rest, and back braces) focuses on relieving symptoms and supporting the spine.

Surgery such as percutaneous vertebroplasty and balloon kyphoplasty may be considered in patients whose condition is refractory to medical therapy and when there is continued vertebral collapse and severe pain. Sometimes more invasive surgery with vertebral body realignment and instrumented fusion (bone grafts and spinal rods) may be needed.

What the procedure involves

Percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture aims to restore vertebral height and augment the fractured vertebral body to relieve pain and increase mobility.

Vertebral craniocaudal expandable implants are inserted under general, regional or local anaesthesia. With the patient in a prone position, using fluoroscopic guidance, trocars are inserted through the vertebral pedicles into the vertebral body, which is then cannulated. Unexpanded implants, mounted on a bespoke instrument, are placed inside the vertebral body and expanded to restore vertebral height. High-viscosity bone cement is injected into and around each implant, filling the space in the surrounding bone.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to the percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture. The following databases were searched, covering the period from their start to 8 August 2016: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also

searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection 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 were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with vertebral compression fracture.
Intervention/test	Percutaneous insertion of craniocaudal expandable implants.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
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 IP overview

This IP overview is based on 1,243 patients from 4 randomised controlled trials (RCTs)[1-3, 9], 2 comparative study[4,10], 4 case series[5-7, 11] and 1 observational study including registry data[8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

Study 1 Tutton S M (2015)

Details

Study type	**RCT**
Country	USA and Europe
Recruitment period	2010-2013
Study population and number	n= **300 (153 Kiva versus 147 balloon kyphoplasty [BK])** patients with 1 or 2 painful osteoporotic vertebral compression fractures
Age and sex	Kiva group: Mean 76 years; 73% (105/144) female BK group: Mean 75 years; 75% (106/141) female
Patient selection criteria	Inclusion criteria: minimum 50 years old, back pain visual analogue score (VAS) score ≥ 70 mm after 2–6 weeks of conservative care or a VAS score of ≥ 50 mm after 6 weeks of conservative care, Oswestry disability index (ODI) score ≥ 30%, radiographical evidence of 1 or 2 A 1.1, A 1.2, A 1.3. fractures as classified by the AO Spine Fracture classification, caused by primary or secondary osteoporosis in the thoracic and/or lumbar spine, central pain over the spinous process(es) upon palpation at the index level(s), acute or persistent index fracture(s), index fracture(s) has(have) failed conservative care of at least 2 weeks but no longer than 6 months, index fracture(s) shows (show) radiographical evidence of at least 5% vertebral collapse, the pedicle identified for access to the index fracture has a diameter of ≥ 6 mm, patient is mentally capable and willing to sign study-specific informed consent as documentation of the informed consent process prior to any study procedures, patient is willing and able to comply with all study requirements including follow-up visits and radiographical assessments. Exclusion criteria: index fracture(s) caused by high-energy trauma, index fracture(s) has (have) known tumour involvement, index fracture(s) diagnosed as osteonecrotic fracture(s), index fracture(s) is a (are) translational force fracture(s), index fracture(s) is a (are) burst fracture(s) or pedicle fracture(s) with posterior cortical wall disruption, index fracture(s) has (have) posterior vertebral wall displacement occupying >20% of the cross-sectional area of the spinal canal, index fracture(s) has (have) severe deformity with reduction of >75% in any height and accompanying area, index level(s) has (have) undergone previous surgical treatment of a vertebral body compression fracture or other surgical procedure at the index level(s), angulation of index fracture(s) makes treatment with the Kiva system impossible, pedicle identified for access to the index fracture has a diameter of < 6 mm, Paget's disease, body mass index (BMI) > 35 kg/m 2, uncontrolled diabetes, severe cardiopulmonary deficiencies, myelopathy, long-term steroid therapy, medical contraindication to spinal surgery or general anaesthesia, spinal canal compromise causing clinical manifestations of cord, neural foramen, or nerve root compression at the level(s) to be treated, neurological symptoms or deficits or radiculopathy related to the VCF, pain based on clinical diagnosis of herniated nucleus pulposus or severe spinal stenosis, indications of instability related to the index fracture, planned spine surgery during or up to 30 days after the procedure, spine surgery for any disorder in the 30 days before enrolment, documented active systemic or local infection, known allergy to the investigational device materials or acrylics/polymethylmethacrylate or a hypersensitivity to monomers, diagnosis of haemorrhagic diathesis, uncontrolled psychiatric illness or severe dementia, patient currently receiving anticancer or anti-HIV therapy, autoimmune or inflammatory rheumatic disease, patient's life expectancy is less than the study duration or undergoing palliative care, current alcohol or drug abuser, involvement in medical litigation including Workmen's Compensation, prisoner, participation in another investigational study that has the potential to affect the study treatment or the study end points, pregnancy or considering pregnancy during study participation.
Technique	Kiva system BK with the Kyphon inflatable bone tamps, bone filler devices, and cement (Medtronic).
Follow-up	**12 months**
Conflict of interest/source of funding	Benvenue Medical, Inc., funds were received in support of this study.

Analysis

Follow-up issues: 95% (285/300) of subjects met the criteria for the as-treated (AT) analysis population (Kiva: n=144; and BK: n=141). 84% (253/300) of patients (Kiva: n=127; and BK: n=126) completed the trial to the 12-month follow-up. In the Kiva group, 10 patients died within the 12-month follow-up, 5 withdrew from the study and 2 were lost to follow-up. In the BK group, 8 patients died and 7 withdrew from the study.

Study design issues:

- Multicentre study (21 centres)

- Blocked randomisation with blocks of randomly varying sizes; assignments were allocated via a secure web-based system administered by an independent data coordinating centre. Patients were blinded until after the procedure was completed.

- An independent imaging core laboratory did the assessment of all radiographical measurements and an independent physician adjudicator reviewed all safety events that occurred in the study, along with the associated imaging laboratory assessments.

- Efficacy analyses were done primarily on the AT population, consisting of randomised subjects having the intended procedure with technically successful procedures at all levels. Technical failure was defined as lack of Kiva implant placement or lack of bilateral bone tamp inflation. Additional analyses were done on the per protocol population, consisting of subjects with 12-month data and no major protocol deviations.

Study population issues: Kiva patients had a statistically higher percentage of former smokers (Kiva: 42%; and BK: 30%) and prior thoracolumbar junction fractures (Kiva: 29%; and BK: 19%).

Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **285 (144 Kiva versus 141 BK)**

Technical success

Kiva: 99%

BK: 98%

Bone cement usage (per treated level, cm^3)

Kiva: 2.37 ± 1.06 (n=177)

BK: 5.38 ± 2.17 (n=178)

Difference: − 3.01 (− 3.37, − 2.65)

Kiva system superior over BK.

Procedure success at 12 months[b]

	Kiva (n=144)	BK (n=141)	Difference (BCI)	Posterior probability non-inferiority*	Posterior probability superiority [a]
Success at 12 months	94% (120/127)	97.6% (123/126)	− 3.1% (-8.6%, 1.7%)	99.92%	9.55%

* The Kiva system was declared non-inferior to BK if posterior probability non-inferiority > 96.6%.

[a]The Kiva system was declared superior to BK if posterior probability superiority > 96.6%.

[b] The procedure success was defined as reduction in pain by 15 mm or more from baseline on the 100-mm VAS, maintenance (did not worsen by ≥ 10 points) or improvement in function from baseline on the 100-point ODI and absence of device-related serious adverse events.

Pain relief

	Kiva	BK
Reduction in VAS score of 15 mm or more at 12 months	95% (121/127)	98% (123/126)

VAS score change from baseline to	Kiva (n=144)	BK (n=141)	Difference (BCI)
30 days[c]	− 59.8 ± 28.93 (n=140)	− 61.1 ± 26.91 (n=135)	1.3 (−5.35, 7.97)
6 months[c]	− 68.6 ± 25.89 (n=135)	− 65.2 ± 27.37 (n=126)	− 3.4 (−9.94, 3.14)
12 months[c]	− 70.8 ± 26.31 (n=127)	− 71.8 ± 23.47 (n=126)	1 (−5.20, 7.21)

[c]Kiva system and BK superiority in improvement over baseline assessment.

Function

	Kiva	BK
Maintain or improve ODI score at 12 months	99% (126/127)	100% (126/126)

Safety

Rate of serious adverse events within 12 months

Kiva: 29%

BK: 35%

Device-related serious adverse events: none reported in either group.

Fractured pedicle: 1/144. It was associated with the use of the Kiva-Pilot in the setting of sclerotic bone. This resulted in back pain at the time of patient discharge, which was managed with analgesics.

Herpes zoster: 1/144

Pain after the procedure: 1/144

Pruritus: 1/144

Adjacent level fracture

	Kiva	BK	Difference (BCI)
Adjacent level fracture measured cumulatively at 12 mo (as- treated population)‡	21% (28/134)	22% (29/130)	−1% (−11 %, 8%)
Adjacent level fracture measured cumulatively at 12 mo (per protocol population) ‡	14% (16/116)	20% (23/114)	−6% (−16%, 3%)

‡ Kiva system statistically non-inferior to BK.

Extravasation of bone cement

	Kiva	BK	Difference (BCI)
Extravasation measured at the immediate postoperative time point (patients, CL/IPA)‡	64.6% (93/144)	64.5% (91/141)	0.1% (−10.96%, 11.04%)
Extravasation measured at the immediate postoperative time point (levels,	55.4% (98/177)	57.9% (103/178)	−2.5% (−12.73%, 7.76%)

ODI score change from baseline to	Kiva (n=144)	BK (n=141)	Difference (BCI)
30 days[c]	− 31.4 ± 21.93 (n=140)	− 34.6 ± 20.39 (n=135)	3.2 (−1.84, 8.25)
6 months[c]	− 37.7 ± 20.13 (n=135)	− 38.4 ± 20.41 (n=126)	0.7 (−4.27, 5.67)
12 months[c]	− 38.1 ± 19.81 (n=127)	− 42.2 ± 21.70 (n=126)	4.1 (−1.07, 9.28)

[c]Kiva system and BK superiority in improvement over baseline assessment.

CL/IPA) ‡			
Extravasation measured at the immediate postoperative time point (levels, site reported)**	16.9% (30/177)	25.8% (46/178)	−8.9% (−17.27%, −0.33%)

‡ Kiva system statistically non-inferior to BK.

**Kiva system superior over BK.

Abbreviations used: BCI, Bayesian credible interval; BK, balloon kyphoplasty; CL, core laboratory; IPA, independent physician adjudicator; ODI, Oswestry disability index; VAS, visual analogue scale.

Study 2 Vanni D (2012)

Details

Study type	**RCT**
Country	Italy
Recruitment period	From 2010
Study population and number	n=**300 (150 Spinejack versus 150 balloon kyphoplasty [BK])** patients with osteoporotic vertebral fractures
Age and sex	Age: range 65-85 years Sex: not reported
Patient selection criteria	Patients with osteoporotic vertebral fractures type A1 according to Magerl/AO spine classification.
Technique	Group A: percutaneous vertebral augmentation procedure with the Spinejack implant. Group B: Balloon kyphoplasty
Follow-up	**12 months**
Conflict of interest/source of funding	None.

Analysis

Follow-up issues:

- Patients had a clinical follow-up (using VAS and ODI) and postoperative standing plain radiogram of the spine at 1, 6, and 12 months. The radiographic parameters that were taken into account were: postoperative anterior vertebral body height, preoperative anterior vertebral body height, cephalic anterior vertebral body height, and caudal anterior vertebral body height.

Study design issues: Not reported.

Study population issues: The 2 groups were homogenous with regards to age, sex, and general clinical findings.

Other issues: Not reported.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 300 (150 Spinejack versus 150 BK)

Cement use
Spinejack: 4 ml per patient
BK: 5 ml per patient
p<0.005 for the comparison between groups.

Vertebral height restoration immediately after the procedure
<table>
<tr><th>Grade</th><th>Spinejack (% of patients)</th><th>BK</th></tr>
<tr><td>0 (no change)</td><td>3%</td><td>16%</td></tr>
<tr><td>1 (below 50%)</td><td>12%</td><td>26%</td></tr>
<tr><td>2 (more than 50%)</td><td>85%</td><td>58%</td></tr>
</table>
The postoperative increase in vertebral body height was greater in the Spinejack group than in the kyphoplasty group (p < 0.05).

Pain relief
There was no statistically significant difference in VAS pain scores between the 2 groups at any stage from the preoperative period, through the postoperative period, to the final follow-up.

Function
There was no statistically significant difference in ODI scores between the 2 groups at any stages from the preoperative period, through the postoperative period, to the final follow-up.</td><td>Cement leakage
Spinejack: None
BK: 20 not clinically significant leakage events</td></tr>
<tr><td colspan="2">Abbreviations used: BK, balloon kyphoplasty; ODI, Oswestry disability index; VAS, visual analogue scale.</td></tr>
</table>

Study 3 Korovessis P (2013)

Details

Study type	**RCT**
Country	Greece
Recruitment period	2010
Study population and number	n=**185 (92 Kiva versus 93 balloon kyphoplasty [BK])** consecutive patients with osteoporotic vertebral compression fractures
Age and sex	Kiva group: Mean 70 years; 68% (56/82) female BK group: Mean 72 years; 72% (63/86) female
Patient selection criteria	Inclusion criteria: history of low-energy recent trauma or acute onset of back pain without evident trauma, presence of associated back pain of no more than 3 months' duration, and the imaging evidence of presence of 1 or more (1–5) simultaneous vertebral fractures. Osteoporotic fractures were included if they were defined as vertebral collapse of grade 1 or higher according to the grading system of Genant and Jergas 23. Exclusion criteria: previous spinal operation, spinal infection, significant spinal deformity and bleeding disorders, patients with intraoperative biopsy positive for metastasis.
Technique	Implant group: Kiva system. BK with the Kyphon inflatable bone tamps, bone filler devices, and cement (Medtronic). Both procedures were done under biplane fluoroscopy in the operating room and under general anaesthesia and continuous neuromonitoring by a single experienced spine surgeon.
Follow-up	**Mean 14 months**
Conflict of interest/source of funding	No funds were received in support of this work.

Analysis

Follow-up issues:

- From the 185 patients who were eligible, 8 patients from the KIVA group and 4 from the BK group were lost to follow-up.
- During vertebral augmentation, metastasis was shown during needle biopsy in 2 patients of the KIVA group and 3 patients of the BK group. These 5 patients were excluded from the final analysis.

Study design issues:

- The participants, investigators (other than surgeons doing the procedures), and outcome assessors were unaware of the group assignments.
- Block randomisation with random block size was used.
- No *a priori* power analysis was conducted.

Study population issues:

- Only 2 burst fractures in the KIVA group and 1 in the BK group were included in the study.

Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **168 (82 Kiva versus 86 BK)**

Bone cement usage (per vertebrae)

Kiva: 1.8 ± 0.4 mL

BK**:** 2.8 ±0.5 mL

p<0.001

Radiological data

Anterior vertebral body height ratio (mean ± SD)

	Before the procedure	After the procedure	p	Correction (%)
KIVA	0.78 ±0.25	0.87 ±0.17	0.0014	24.3 ±45
BK	0.74 ±0.23	0.89 ±0.17	0.0019	23 ± 63
Intergroup p	0.38	0.67		0.97

Posterior vertebral body height ratio (mean ± SD)

	Before the procedure	After the procedure	p	Changes (%)
KIVA	0.92 ±0.12	0.95 ±0.11	0.082	5.92 ±16
BK	0.92 ±0.12	0.95 ±0.1	0.31	− 1.26± 8
Intergroup p	0.79	0.95		0.07

Midline vertebral body height ratio (mean ± SD)

	Before the procedure	After the procedure	p	Changes (%)
KIVA	0.74 ±0.25	0.88 ±0.18	0.000008	30.5 ±47
BK	0.70 ±0.23	0.89 ±0.14	0.00005	21.9 ±26
Intergroup p	0.42	0.82		0.45

Wedge angle (mean ± SD)

	Before the procedure	After the procedure	p	Changes (°)
KIVA	13.7± 7	7.80 ± 6	0.009	5 ± 3.5
BK	14.9± 8	11.5 ± 7	0.067	6 ± 5
Intergroup p	0.52	0.11		

84% (69/82) of spines in the KIVA group and 100% (86/86) of spines in the BK group, showed at the final observation a **residual kyphosis** of 5 ° or more (χ 2 = 14.6, p < 0.001).

Safety

Cement leakage

Kiva: 3% (4/133 vertebras)

BK**:** 10% (12/122 vertebras)

$\chi^2 = 5.05$, $p \leq 0.05$

Intracanal leakage

Kiva: None

BK**:** 2% (2/86)

New fractures

Kiva: 12% (10/82)

BK**:** 13% (11/86)

χ 2 = 0.014, p > 0.2

Adjacent vertebral body fractures

Kiva: 7% (6/82)

BK**:** 9% (8/86)

Remote fractures

Kiva: 5% (4/82)

BK**:** 3% (3/86)

Back pain relief (measured on VAS from 1 to 10)

	Before the procedure	1 year after the procedure	p
KIVA	8.2 ± 1.4	2.7 ± 3	0.001
BK	7.8 ± 1.2	2.5 ± 3	0.001
Between groups p		0.95	

Significant (> 5.5 points) back pain score (VAS) improvement was shown in 54% (44/82) and in 43% (37/86) of patients in KIVA and BK groups, respectively.

SF-36 (Physical functioning domain)

	Before the procedure	1 year after the procedure	p	Improve-ment (%)
KIVA	32 ± 11	65.8 ± 15.6	0.001	51
BK	28 ± 12	68 ± 19.8	0.001	59
Between groups p		0.72		

SF-36 (Mental health domain)

	Before the procedure	1 year after the procedure	p	Improve-ment (%)
KIVA	42 ± 10	64 ± 11	0.001	34
BK	41 ± 9	62 ± 9.7	0.001	34
Between groups p		0.64		

Functional impairment (Oswestry disability index)

	Before the procedure (%)	1 year after the procedure (%)	p
KIVA	64 ± 19	31.7 ± 19	0.001
BK	62 ± 14	26.3 ± 15.7	0.001
Between groups p		0.43	

Abbreviations used: BK, balloon kyphoplasty; SD, standard deviation; SF-36, 36-Item Short Form Health Survey; VAS, visual analogue scale.

Study 4 Otten LA (2013)

Details

Study type	**Retrospective matched-paired comparative study**
Country	Germany
Recruitment period	Kiva patients: 2010-2011 Balloon kyphoplasty (BK): 2004-2009
Study population and number	n= **52 (26 Kiva versus 26 BK)** patients with 68 vertebral compression fractures
Age and sex	Kiva: Mean 74 years; 77% (20/26) female BK: Mean 66 years: 58% (15/26) female
Patient selection criteria	Patients with 1 or two A1.1, A1.2, or A1.3 (AO Spine Fracture classification) painful osteoporotic vertebral fracture(s) at the thoracic and lumbar spine.
Technique	Implant group: pKiva VCF Treatment System (Benvenue Medical) The procedure was done under general anaesthesia, or local anaesthesia with fluoroscopic guidance. BK: The procedure was done with the KyphX-Systems (Kyphon) under general anaesthesia and biplanar fluoroscopy for control.
Follow-up	**6 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Not reported.

Study design issues:

- The criteria to match pairs across the 2 groups were defined by the cranial vertebral body treated, and the age.
- Back pain severity was evaluated with the 10-cm VAS in the Kiva group and with a numeric rating scale (0-100, from no pain to worst possible pain) for balloon kyphoplasty.

Study population issues: In each group 69 (18/26) of patients received treatment in only 1 vertebral body and 31% (8/26) of patients received treatment in 2 vertebral bodies.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **52 (26 versus 26)**

Pain relief (mean VAS score ± SD)

	Before the procedure	6 months after the procedure
KIVA	87.6 ± 12.8	10.8 ± 20.8
BK	83.1 ± 14.9	24.6 ± 11.0
Between groups p		<0.0001

In the Kiva group 96% of the patients and in the BK group 100% of the patients had pain relief 6 months after the treatment.

Functional impairment (mean Oswestry disability index score ± SD)

	Before the procedure (%)	6 months after the procedure (%)
KIVA	68.7 ±15.8%	24.8 ± 18.6%
BK	80.6 ± 8.6%	33.2 ± 6.3%
Between groups p		0.03

100% of patients in the Kiva group and 100% of patients in the balloon kyphoplasty group had an increased functional ability after the treatment.

Change of anterior and mid-vertebral height (mean±SD, mm)

		Pre-op	Post-op	3 months	6 months
Kiva	**Anterior**	21.06 ± 2.77 (n = 34)	22.41 ± 7.14 (n = 34)	22.40 ± 7.08 (n = 32)	22.28 ± 6.85 (n = 33)
	Mid	18.36 ± 5.64 (n = 34)	20.89 ± 6.00 (n = 34)	21.06 ± 5.90 (n = 32)	21.19 ± 6.08 (n = 33)
BK	**Anterior**	21.68 ± 2.08 (n = 34)	25.09 ± 2.54 (n = 34)	24.55 ± 2.25 (n = 33)	24.56 ± 2.27 (n= 34)
	Mid	21.97 ± 1.78 (n= 34)	25.29 ± 2.10 (n = 34)	25.00 ± 2.09 (n = 34)	24.91 ± 2.08 (n = 34)

A significant increase in the anterior and mid wall height was seen in both groups preoperatively compared with postoperatively (p< 0.001).

At 6-month follow-up the vertebral height did not change significantly in both groups.

Safety

Cement extravasation

Kiva: 23% (6/26)

BK**:** 31% (8/26)

No statistically significant difference between groups.

New fractures

	Kiva	BK
All	12% (3/26)*	54% (14/26)*
Adjacent	8% (2/26)	35% (9/26)
Non adjacent	4% (1/26)	19% (5/26)

*Significant difference between groups, p<0.0001.

No new fractures at the treated levels were reported in either group.

Abbreviations used: BK, balloon kyphoplasty; SD, standard deviation; VAS, visual analogue scale.

Study 5 Renaud C (2015)

Details

Study type	**Retrospective case series**
Country	France
Recruitment period	Not reported
Study population and number	n= **77** patients with 83 vertebral compression fracture(s)
Age and sex	Mean 60.9 years; gender not reported
Patient selection criteria	Patients with vertebral compression fracture(s) due to trauma or osteoporosis.
Technique	The Spinejack device was used.
Follow-up	**Mean 35 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The follow-up range was 6-67 months.

Study design issues: None.

Study population issues:

- Of the 83 fractures, 61% (51/83) were caused by trauma and 39% (32/83) by osteoporosis.
- The time to surgery was less than 15 days in 74% of patients.
- The procedure was done on a single vertebral body in 71 patients and on 2 vertebral bodies in 6 patients.
- The distribution of fracture types in the Magerl classification was: A1, 47% (A1.2, 30%); A2, 41% and A3.1, 11%).
- The most frequently affected levels were L1 (33%), L2 (23%) and T12 (17%).

Other issues: 2 generations of the Spinejack device were used (Spinejack G1 and Spinejack G2).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **77**

Mean **hospital length of stay** was 3.7 days.

Pain relief

	Before the procedure	Hospital discharge	1 month	3 months	12 months
Pain score (VAS)	7.9	1.8	1.8	1.4	1.1

Significant improvement from baseline at each time point, p<0.001.

Safety

Procedure-related complications: 4% (3/77)

Procedure-related complications	Patients (n/N)	Details
Device migration	1/77	This reflected a technical problem that occurred with an instrument prototype.
Secondary pedicular fracture line	1/77	
Infection	1/77	Nosocomial skin infection probably caused by contamination from an oral infection. It was treated with antibiotics.

Adjacent fractures: 3% (2/77) of patients. No reoperation was needed.

Recurrent compression fracture at the treated site: none.

Cement leakage identified by CT scan: 14% (11/77). All patients had post-traumatic fractures. Symptoms were present in a single patient who had nerve root pain caused by leakage of the cement along a secondary fracture line in the pedicle (reported above).

Abbreviations used: VAS, visual analogue scale.

Study 6 Rosales Olivarez L M (2011)

Details

Study type	**Case series**
Country	Mexico (3 sites) and Venezuela (1 site)
Recruitment period	Not reported.
Study population and number	n= **57** patients with painful osteoporotic vertebral compression fractures (VCFs)
Age and sex	Mean 72 years; 81% (46/57) female
Patient selection criteria	Age at entry of 50 years or greater, 1 to 3 symptomatic VCFs due to osteoporosis, a back pain visual analogue scale score of 5 or greater, fracture age of less than 6 months, and an Oswestry Disability Index (ODI) score of 30% or greater.
Technique	The Kiva device was used.
Follow-up	**Maximum 12 months**
Conflict of interest/source of funding	Not reported.

Analysis

Follow-up issues: 84% (48/57) of patients were available for 6-week follow-up, 72% (41/57) for 3-month follow-up and 63% (36/57) for 12-month follow-up.

Study design issues:

- Patient-reported outcomes were measured before device implantation and at 6 weeks, 3 months, and 12 months. Back pain severity was evaluated with a 100-mm VAS. Condition-specific functional impairment was evaluated with the ODI. Cement extravasation was evaluated from plain X-rays at an independent image analysis core laboratory by a musculoskeletal radiologist. Newly occurring adjacent and nonadjacent VCFs also were identified by the same radiologist.

- Overall clinical success was defined as a 30% improvement in VAS pain severity or greater and maintenance or improvement in the ODI.

Study population issues:

- There were 89% (51/57) single-level treatments, 9% (5/57) two-level treatments, and 2% (1/57) three-level treatment, representing 64 treated levels.

- Duration of symptoms was less than 6 weeks in 51% (29/57) of patients, 6 weeks to less than 3 months in 17% (10/57), 3 months to less than 6 months in 12% (7/57) and 6 to 12 months in 19% (11/57).

Other issues: None.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 57

Pain relief
<table>
<tr><th></th><th>Before the procedure (n=55)</th><th>6 weeks (n=48)</th><th>3 months (n=41)</th><th>12 months (n=36)</th></tr>
<tr><td>Mean back pain score (VAS)</td><td>79.3±17.2</td><td>21.9±21.3</td><td>21.9±24.6</td><td>23.2±23.3
(mean decrease at 12 months was 49.9±30.3mm, and the corresponding mean percentage improvement in VAS pain scores was approximately 66%).</td></tr>
</table>
Significant improvement from baseline at each time point, p<0.0001.

Functional impairment (Oswestry disability index)
<table>
<tr><th></th><th>Before the procedure (n=56)</th><th>6 weeks (n=48)</th><th>3 months (n=41)</th><th>12 months (n=36)</th></tr>
<tr><td>Mean ODI score</td><td>68.1%±16.9%</td><td>27.4%±17.2%</td><td>23.8%±18.7%</td><td>23.3%±15.5%
(mean change from baseline of 39.2±19.6 percentage points, or approximately 63%)</td></tr>
</table>
Significant improvement from baseline at each time point, p<0.0001.

Clinical success rates
<table>
<tr><th></th><th>6 weeks (n=47)</th><th>3 months (n=40)</th><th>12 months (n=35)</th></tr>
<tr><td>Clinical success rates</td><td>91% (43/47)</td><td>88% (35/40)</td><td>89% (31/35)</td></tr>
</table>
Cement usage (per vertebral body): mean of 2.2±0.12 mL</td><td>Cement extravasation identified radiographically: 8% (5/64)
None was symptomatic.

Fracture: In 30 patients (34 fractures) with adequate 12-month radiographs, 15% (5/34) adjacent-level fractures, 6% (2/34) nonadjacent fractures, and 3% (1/34) re-fracture at a previously treated index level were identified.

Dural tear: 1/57
It occurred during the initial pedicle access with the Jamshidi needle. A small quantity of Gelfoam was used at the site, the event resolved without incident, and there were no residual or permanent sequelae.</td></tr>
<tr><td colspan="2">Abbreviations used: ODI, Oswestry disability index; VAS, visual analogue scale; VCF, vertebral compression fractures.</td></tr>
</table>

Study 7 Ender SA (2014)

Details

Study type	**Prospective case series**
Country	Germany
Recruitment period	2010-2012
Study population and number	n= **32** consecutive patients with 46 vertebral compression fractures
Age and sex	Mean 71 years; 78% (25/32) female
Patient selection criteria	Inclusion criteria: Symptomatic new lumbar or thoracic osteoporotic or tumorous vertebral fracture and unsuccessful conservative therapy. Exclusion criteria: symptoms of neurological deficit, involvement of the posterior edge with relevant constriction of the spinal canal and a known allergy to the ingredients of the Osseofix® system or the bone cement.
Technique	The Osseofix implant was used. The procedure was done under intubation anaesthesia and the patients received perioperative intravenous antibiotics (1.5 g Cefuroxime or 600 mg clindamycin in case of allergy). Postoperative patient mobilisation was started on the first postoperative day with standing up of the patient under physiotherapeutic instruction and with physical therapy in the further course of recovery to strengthen the spine-stabilising musculature. All patients received postoperative thromboembolism prophylaxis with a low-molecular heparin derivative. Previously prescribed pain medication was continued postoperatively and reduced over time. In the case of an osteoporotic vertebral fracture, a special osteoporosis medication was continued if available or an oral medication with a bisphosphonate was started. In the case of a tumorous vertebral fracture, a previously prescribed bisphosphonate medication was continued or in the case of oncological recommendation bisphosphonate medication was started.
Follow-up	**12 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Clinical and radiological follow-up evaluation was performed 3 days postoperatively and after 12 months (12 to 15 months).

Study design issues: None.

Study population issues: The average duration of symptoms was 8.9 weeks (3 to 15 weeks).

Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **32**

Pain relief (VAS score, mean±SD)

	Before the procedure	3 days after the procedure	12 months after the procedure
All fractures (n=46)	7.8±1.6	2.1±1.2	1.6±0.95
Osteoporotic fractures (n=38)	7.6	1.8	1.5
Tumorous fractures (n=8)	8.6	3.8	2.1

Significant improvement from baseline compared against 12-month follow-up, p<0.001.

Functional impairment (Oswestry disability index score, mean±SD)

	Before the procedure	3 days after the procedure	12 months after the procedure
All fractures (n=46)	71%±4%	32%±5%	30%±4%
Osteoporotic fractures (n=38)	71%	30%	30%
Tumorous fractures (n=8)	74%	38%	33%

Significant improvement from baseline compared against 12-month follow-up, p<0.001.

Sagittal spine alignment (mean±SD)

	Before the procedure	3 days after the procedure	12 months after the procedure	p value for (comparison 12-month against baseline)
Vertebral kyphotic angle (α-angle)	9.0°± 5.8	8.3°± 5.6	8.3°± 5.5	p<0.05
Cobb angle (γ-angle)	12.3°± 16.4	10.8°± 16.4	10.8°± 16.3	p<0.05

Beck index (mean±SD)

	Before the procedure	3 days after the procedure	12 months after the procedure
Beck index	0.75± 0.14	0.77± 0.15	0.77± 0.14

Safety

Pronounced **haematoma**:1/32. Revision was not needed.

Symptomatic L2 **adjacent fracture:** 1/32.

It occurred during the stationary postoperative period. This was also stabilised with the Osseofix® system.

Minor **loss of height of the stabilized L2 vertebral body** in an osteoporotic fracture: 1/32

The Beck Index changed postoperatively from 1.0 to 0.96 and the Cobb angle (γ) changed from 11 degrees to 13 degrees. The VAS score remained unchanged.

No cement leakage was reported.

Abbreviations used: ODI, Oswestry disability index; SD, standard deviation; VAS, visual analogue scale.

Study 8 Noriega D (2015)

Details

Study type	**Observational study (registry data)**
Country	14 European sites
Recruitment period	2011-2012
Study population and number	n= **103** consecutive patients with 108 vertebral compression fractures (VCFs) of traumatic origin
Age and sex	Mean 62 years; 50% (51/103) female
Patient selection criteria	Inclusion criteria: All patients met the indication listed in the IFU of the device (over 18 years old, presenting a mobile spinal fracture that may result from trauma [Magerl group A1, A2, or A3.1] and/or osteoporosis, with a minimum internal pedicle diameter of more than 5.8 mm to allow placement of the device) and had acute fresh traumatic VCF. Exclusion criteria: severe osteoporosis.
Technique	The Spinejack (Vexim) implant was used. Patients were treated under general (94%), local (4%), by both local and general (1%) or by spinal (1%) anaesthesia. Postoperative rehabilitation was per standard of care at the treating institution.
Follow-up	**Mean 13 months**
Conflict of interest/source of funding	Relevant financial activities outside the submitted work include consultancy, expert testimony, payment for lecture and payment for the development of educational presentations.

Analysis

Follow-up issues:

- Data were collected at baseline, preoperatively, 48 hours after the surgery, at 3 and at 12 months. However, surgeons followed their own standard care practice follow-up so the patients analysed might have no complete datasets at 3 or 12 months.
- 22% (23/103) of patients withdrew from the study before the 12-month visit: 2 patients died of renal failure and acute respiratory syndrome, respectively; 11 patients refused medical follow-up because of complete relief of their symptoms; 1 patient was withdrawn because of severe aggravation of a pre-existing osteoporosis at inclusion, with 4 consecutive spontaneous fractures after surgery on Day 19, Day 49 and 2 fractures on Day 86; 9 patients were lost to follow-up.

Study design issues:

- Multicentre study.

Study population issues:

- 8% of patients (8/103) had previous traumatic VCF; 5 of them had already been treated surgically at a level different from the one treated in this study.
- For 75% (77/103) of patients, a previous treatment had been administered: bed rest (65%), bracing (10%) and walking aid (5%).
- A total of 108 VCF were treated (5 patients had 2 fractures treated).
- Most fractures were caused by high energy trauma (80% [86/108] concerning 81 patients) and the remaining were traumatic fractures with associated osteoporosis (20% [22/108], concerning 22 patients).

Other issues: Of the 108 treated vertebrae, 98% (106/108) were treated by a percutaneous approach, while 2% (2/108) were treated by open surgery.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **103 (108 fractures)**

Pain relief (VAS score)

	48 hours versus baseline (n=102)	3 months versus baseline (n=89)	12 months versus baseline (n=76)
Mean (SD) absolute changes	-5.2 (2.7)	-5.3 (2.9)	-5.5 (2.9)
Median absolute changes	-6.0	-6.0	-5.8
Within-group test	<0.001	<0.001	<0.001
Median relative changes	-81.5%	-88.0%	-91.5%

Analgesic intake

	Baseline (n=103)	48 hours (n=103)	3 months (n=91)	12 months (n=78)
Strong analgesics	20% (21/103)	1% (1/103)	1% (1/91)	0
Moderate analgesics	51% (53/103)	6% (6/103)	1% (1/91)	1% (1/78)
Mild analgesics	22% (23/103)	66% (68/103)	31% (28/91)	26% (20/78)
No treatment	6% (6/103)	27% (28/103)	67% (61/91)	73% (57/78)

Functional impairment (ODI)

	3 months versus baseline (n=89)	12 months versus baseline (n=77)
Mean (SD) absolute changes	-62.0 (24.9)	-65.7 (23.8)
Median absolute changes	-71.3	-73.3
Within-group test	<0.001	<0.001
Median relative changes	-91.3%	-94.9%

Quality of life (EQ-VAS, from worst to best)

	3 months vs baseline (n=86)	12 months vs baseline (n=75)

Safety

Total adverse events: 15% (15/103)

Adverse events	Patients (n/N)	Details
Procedure-related adverse events		
Asymptomatic adjacent vertebral fracture T11 at 99 days after surgery	1/103	No treatment was needed. The fracture remained stable at 12 months (ongoing).
Dislocation of posterior wall secondary to surgery which lead to sensorial deficit at 4 days	1/103	The hospitalisation (27 days) was prolonged in 1 obese, osteoporotic patient treated out of IFU indications at the time of this registry as he presented with a severe A3.3 fracture. He underwent decompression and posterior instrumentation at Day 4. At 12 months, this was resolved.
Collapse of treated vertebral body associated with canal compromise and haematoma leading to neurological symptoms at 16 days	1/103	The condition of the patient had improved within 12 months.
Other adverse events (not device- or procedure-related)		
Death at 52 and 204 days	2/103	Causes: acute kidney failure aggravation with vascular obliteration of leg and acute respiratory syndrome
Sigma diverticulitis aggravation at 8 days	1/103	Resolved within 12 months
Breakage of screws in L3 at 82 days.	1/103	Revision surgery was recommended but patient declined and was lost to follow-up.
Posterior articular conflict at 147 days	1/103	Caused by discopathy associated to a degenerative spondylolisthesis.Resolved at Day 455.
Algoneurodystrophic syndrome at 100 days	1/103	Caused by calcaneum fracture. Resolved by decompressive surgery.
Prostatic cancer at Day 257	1/103	Ongoing.
Bleeding at the point of skin incision just after	1/103	Resolved within 12 months.

Mean (SD) absolute changes	18.1 (30.2)	24.6 (27.2)
Median absolute changes	13.0	19.0
Within-group test	<0.001	<0.001
Median relative changes	21.1%	38.3%

Kyphotic angulation

Baseline: 14.5 ± 8.1◦

48 hours : 9.2 ± 5.8◦,

p < 0.001

Despite a lower reduction observed at 3 and 12 months, the improvement of kyphosis remained statistically significant compared to baseline (−2.5 ± 5.8 ◦ at 3 months, p = 0.012; −4.4 ± 6.0◦ at 12 months, p = 0.002).

Mean (±SD) hospital length of stay: 4.3±3.5 days

surgery		
Spontaneous adjacent fracture	2/103 (3 fractures)	2 fractures resolved; 1 fracture in patient who was discontinued.
Spontaneous new fracture	2/103 (4 fractures)	At 12 month, 1 patient discontinued (major osteoporosis) and condition resolved in other patient.
Hospitalisation in psychiatric department	1/103	Resolved within 12 months.
Lumbar pain at 418 days	1/103	Resolved within 12 months.
Shoulder fracture at 276 days	1/103	Ongoing. This was caused by a fall discovered lately and treated by physiotherapy.

Subsequent compression fractures: 8 in 3 osteoporotic patients.
Adjacent fractures: 4 in 3% (3/103) of patients.

Cement leakage: 40% (43/108) of treated vertebrae (no clinical consequences).

Abbreviations used: EQ, European quality of life score; IFU, instructions for use; ODI, Oswestry disability index; SD, standard deviation; VAS, visual analogue scale; VCF, vertebral compression fracture.

Study 9 Noriega D C (2016)

Details

Study type	**RCT**
Country	Spain
Recruitment period	2013
Study population and number	n= **30 (15 implant versus 15 balloon kyphoplasty)** patients with osteoporotic vertebral compression fractures (VCF)
Age and sex	Mean 68 years; 80% (24/30) female
Patient selection criteria	Inclusion criteria: male or female aged 21-75 years, 1 or 2 painful VCF(s) with at least 1 meeting the following criteria: fracture due to diagnosed or presumed underlying osteoporosis; VCFs between T7 and L3; aged<3 months; with a loss of height in the anterior, mid, or posterior third of the vertebral body (VB), from estimated pre-fracture configuration of at least 15% but not more than 40%; with hyperintense signal on STIR or T2 sequence MRI; patient who failed conservative medical therapy; target vertebral body suitable for Spinejack procedure and balloon kyphoplasty; ODI≥30 %; patient willing and able to comply with study requirements; patient signing informed consent form; and if women are post-menopausal, surgically sterile women, or agreeing to remain on contraceptives for the duration of their study participation for women with childbearing potential. Exclusion criteria: Target VCFs caused by underlying or suspected tumour, high-energy trauma or fall from significant height; segmental kyphosis of target VB over 30º; any prior surgical intervention on target VB or adjacent level; pre-existing or clinically unstable neurologic deficit; myelopathy or radiculopathy; not able to walk without assistance before fractures; pedicle fracture or inter-spinous process widening; spondylolisthesis>grade 1 at target VB(s); history of spine surgery in last year; any underlying systemic bone disease other than osteoporosis; irreversible coagulopathy and/or taking anticoagulant on regular basis; pregnancy and nursing; pain caused by any other condition that required daily narcotic medication; allergy to titanium; infection; BMI>40; severe cardiopulmonary disease; substance abuse; participation in any other investigational study; long-term steroid therapy; contraindications for MRI.
Technique	The procedures were done under general or spinal anaesthesia. • Implant group: the Spinejack (Vexim) implant was used. • Balloon kyphoplasty: the 20/3 KyphX Xpander inflatable bone tamp 20 mm and the KyphX HV-R Bone Cement (Medtronic) were used. All patients were treated for osteoporosis: denosumab 60 mg/ml subcutaneously every 6 months plus 1000 ng of calcium, plus 800 UI of vitamin D.
Follow-up	**12 months**
Conflict of interest/source of funding	3 of the authors received speaker honorariums from companies such as Vexim, Medtronic, Soteira, Biomed and/or DFine.

Analysis

Follow-up issues:

- Follow-up visits were planned at 5 days, 1, 3, 6 and 12 months.
- One patient from the implant group withdrew from the study 34 days after surgery because of remote location from the investigation site.

Study design issues:

- This was a single-centre study.
- After enrolment, patients were randomised and assigned to 1 treatment group with computer-generated block randomisation system and sealed sequential envelopes, according to a 1:1 allocation ratio.
- The allocated procedure was disclosed to the investigators before surgery. Patients remained blinded until the end of follow-up.
- In the implant group, 16 fractures were treated; 17 fractures were treated in the BK group.

Study population issues: Thoracolumbar vertebrae were the most frequently treated (T11, T12, L1).

Other issues: Not reported.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **30 (15 implant versus 15 BK)**

Pain relief (VAS score, mean change from baseline±SD)

Follow-up	5 days	1 month	3 months	6 months	12 months
Implant	-57.5±22.9	-67.7±15.5	-72.5±12.4	-72.8±10.7 (90% improvement)	-75.8±15.0 (94% improvement)
BK	-63.9±23.1	-64.2±26.0	-64.5±28.5	-68.2±21.3 (81% improvement)	-68.9±20.8 (82% improvement)

Statistically significant improvement from baseline at each follow-up visit in both groups (p<0.001). No statistically significant difference between groups at discharge (p=0.457).

Analgesic consumption

- Before surgery, all patients were taking paracetamol or acetylsalicylic acid or NSAID, 47% (7/15) of patients were prescribed central analgesics and 1 patient from the implant group needed morphine.
- At 5 days after surgery, no patient needed central analgesics or morphine.
- At 1 month after surgery, 33% (5/15) of patients in each group were taking analgesics (in the implant group these patients were taking paracetamol; in the BK group, 1 needed a central agent and the other 4 needed paracetamol only).

Ambulatory status

Throughout the 1-year follow-up period, no patient had worsening of ambulatory status and no patient needed walking aid.

Functional capacity (ODI score, mean change from baseline±SD)

Follow-up	5 days	1 month	3 months	6 months	12 months
Implant	-48.6±21.4	-59.2±18.5	-59.8±13.9	-61.2±15.8 (94% improvement)	-61.6±17.0 (94% improvement)
BK	-45.8±17.1	-47.8±20.8	-50.2±19.2	-53.7±19.6 (90% improvement)	-53.9±19.4 (90% improvement)

Statistically significant improvement from baseline at each follow-up visit in both groups (p<0.001). No statistically significant difference between groups (p=0.692).

Quality of life (EQ-VAS score, mean change from baseline±SD)

Follow-up	1 month	3 months	6 months	12 months
Implant	43.6±18.1	44.8±21.0	47.0±19.2 (94% improvement)	48.2±22.7 (94% improvement)
BK	38.8±25.7	34.5±21.4	40.1±26.8 (90% improvement)	40.1±28.3 (90% improvement)

No statistically significant difference between groups (p value not stated).

Radiological results at 12 months

	Implant	BK	p value (difference

Safety

Subsequent fractures: 4 in 3 patients

- Implant: 13% (2/15)
- BK: 7% (1/15)

3/4 fractures were adjacent fractures.

1 adjacent fracture in the implant group was caused by a fall at 55 days after the surgery.

Cement leakage:

- Implant: 7% (1/15)
- BK: none

The cement leakage presented at L1 level and was aymptomatic.

			between groups)
Mean correction of anterior height of VB	12±13%	0±7%	0.003
Mean correction of central height of VB	12±10%	2±6%	0.001
Vertebral kyphotic angle correction versus baseline	-4.4±5.8º	0.2±3.0º	0.012
Cobb angle correction versus baseline	-2.5±4.2º	0.3±4.1º	NS
Gardner angle correction versus baseline	-1.0±4.3º	0.95±4.26º	NS

Abbreviations used: BK, balloon kyphoplasty; BMI, body mass index; NS, not statistically significant; NSAID, non-steroidal anti-inflammatory drug; ODI, Oswestry disability index; SD, standard deviation; VB, vertebral body; VCF, vertebral compression fracture.

Study 10 Lin J-H (2016)

Details

Study type	**Retrospective comparative study**
Country	Taiwan
Recruitment period	2013-2015
Study population and number	n= **75 (36 intervertebral reduction device [IRD] versus 39 vertebroplasty [VP])** patients with severe osteoporotic vertebral compression fractures (VCF)
Age and sex	IRD group: Mean 73 years VP group: Mean 76 years 87% (65/75) female
Patient selection criteria	Inclusion criteria: age over 60; focal back pain without definite radicular signs and symptoms unresponsive to appropriate conservative treatment; back pain related to the location of the osteoporotic VCF; diagnosed with an apparent bone oedema in the fractured vertebra or with an enhanced area within the vertebral body; and revealed decreased bone mineral density. Exclusion criteria: spinal cord compression or stenosis of the vertebral canal, more than 30% of the local canal diameter; neurologic deficits; unmanageable bleeding disorders; systemic or local spine infections; or severe comorbidity in the heart, liver, kidney, or lung with intolerance to surgery.
Technique	In the IRD group, the Spinejack implant was used.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis
Follow-up issues:
- Follow-up rates for the IRD and VP groups were respectively 100% at 1 week, 92% and 95% at 3, 83% and 90% at 6 months, and 78% and 85% at 1 year.

Study design issues:
- All procedures were done by 3 neurosurgeons.
- All radiologic assessments were done by a researcher who was blinded to the clinical presentation and its outcome in the patients.
- Cement leakage was assessed by 2 investigators with an X-ray examination.

Study population issues: Not reported.
Other issues: Not reported.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **75 (36 IRD versus 39 VP)**

Pain relief (mean VAS score±SD)

	IRD	VP	p value (for the difference between groups)
VAS score before surgery	6.83±0.25	6.80±0.25	0.91
VAS score at 12 months	2.75±0.18	2.82±0.22	0.8137

Statistically significant improvement from baseline in both groups (p<0.001).

Radiologic outcomes

	IRD	VP	p value
KA			
Mean KA before surgery (±SD)	-10.07°±11.33°	-11.92°±11.38°	NS
Mean KA at 12 months (±SD)	-4.12°±8.07°	-13.79°±11.73°	<0.05
Mean KA restoration at 12 months (±SD)	4.88°±7.11°	-1.51°±5.76°	<0.05
Refracture rate of the KA	36% (10/28)	39% (13/33)	0.79
ABH			
Mean ABH before surgery (mm ±SD)	1.41±0.63	1.56±0.55	NS
Mean ABH at 12 months (mm ±SD)	1.89±0.49	1.52±0.55	NS
Mean ABH restoration at 12 months (±SD)	57%±74%	2%±24%	<0.05
Refracture rate of the ABH	32% (9/28)	85% (28/33)	0.03
MBH			
Mean MBH before surgery (mm ±SD)	1.26±0.50	1.45±0.46	<0.05
Mean MBH at 12 months (mm ±SD)	1.96±0.38	1.47±0.43	<0.05
Mean MBH restoration at 12 months (±SD)	73%±68%	5%±26%	<0.05
Refracture rate of the MBH	21% (6/28)	67% (22/33)	<0.001

Safety

Complications

	IRD	VP	p
Total	7	9	0.57
Pneumonia	1	2	
Urinary tract infection	17% (6/36)	21% (8/39)	
Adjacent fracture	11% (4/36)	15% (6/39)	0.74
Nonadjacent fracture	0	1	1.00

Abbreviations used: ABH, anterior body height; IRD, intervertebral reduction device; KA, kyphotic angle; MBH, middle body height; NS, not statistically significant ;ODI, Oswestry disability index; SD, standard deviation; VAS, visual analogue scale; VB, vertebroplasty; VCF, vertebral compression fracture.

Study 11 Noriega D C (2016)

Details

Study type	**Retrospective case series**
Country	Spain
Recruitment period	2009-2012
Study population and number	n= **32 (52 vertebral levels)** consecutive patients with malignant vertebral compression fractures (VCF)
Age and sex	Mean 73 years; 44% (14/32) female
Patient selection criteria	Patients with osteolytic malignant disease of the spine who had a VCF.
Technique	The Spinejack implant was used and the procedure was done under general anaesthesia.
Follow-up	**Mean 20 months**
Conflict of interest/source of funding	David Cesar NORIEGA and Francisco ARDURA are consultants for Vexim, Antonio KRÜGER is consultant for Vexim, Dfine, Biomet, and Medtronic.

Analysis
Follow-up issues: Not reported.
Study design issues: Not reported.
Study population issues:

- Mean time between cancer diagnosis and occurrence of the VCF: 26 months.
- 44% (14/32) of patients had a haematologic disease (9 had multiple myeloma and 5 had lymphoma. In the other 18 patients, the primary tumours were in the lung (1 case), gastrointestinal (7 cases), melanoma (1 case), in the breast (3 cases), seminoma (1 case), mesothelioma (1 case), in the bladder (1 case), and in the prostate (3 cases).
- The vertebral segments most frequently affected were T12 and L1.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **32 (52 vertebral levels)**

Pain relief

	Before surgery	Post-op	12 months	Final follow-up
Mean VAS score (all patients, n=32)	7.15	1.81	1.94	2,24
Mean VAS score (hematologic patients, n=14)	7.07	1.88	1.88	2.24 (at 23 months)
Mean VAS score (metastatic patients, n=18)	7.23	1.75	2.09	2.23

Statistically significant improvement from baseline at all time points in all groups (p<0.001).

Quality of life

	Before surgery	6 months	12 months
Mean EQ5-VAS score (n=32)	22.3	68.9	65.6

Statistically significant improvement from baseline at 6 months (p<0.005).

Mean survival time (95% CI)

All patients: 30.9 months (24.2-37.7).

Hematologic group: 38.3 months (29.6-47)

Metastatic group: 22.8 months (15.9-29.7)

3 patients died within the first 2-6 months after VCF. In total, 13 patients died across the period of study, and their average follow-up time was 14.9 (2-36) months. The remaining 19 patients had 33 VCFs and, at the time of publication were still alive and actively being followed up.

Radiologic outcomes

	Before surgery	Post-op	12 months
Mean ABH (mm)	19.6	25.8*	25.5*
Mean CBH (mm)	16.7	22.5*	22.5*
Mean PBH (change versus baseline)	NR	+2.4 mm (9%)	+2.4 mm (9%)
Mean regional Cobb Angle (range)	9.1° (5.1-11.1)	5.9°** (4.9-7.8)	6.1° ** (4.9-7.9)

***Statistically significant improvement from baseline for ABH and CBH (p<0.01).**

****Statistically significant improvement from baseline for regional Cobb Angle (p<0.05).**

Safety

Complications

	Number	Detail
Cement leakage	10% (5/52) of fractures	All asymptomatic. 2 were in the disc space ,3 in the paravertebral soft tissues.
Adjacent fractures	9% (3/32) of patients	All occurred in patients with metastatic disease.

Abbreviations used: ABH, anterior body height; CBH, central body height; CI, confidence interval; EQ5, EuroQol five dimensions questionnaire; NR, not reported; PBH, posterior body height; SD, standard deviation; VAS, visual analogue scale; VCF, vertebral compression fracture.

Efficacy

Procedure success (clinical)

In a randomised controlled trial (RCT) of 300 patients treated by a vertebral craniocaudal expandable implant (n=153) or by balloon kyphoplasty (n=147), procedure success at 12 months was 94% (120/127) in the implant group and 98% in the balloon kyphoplasty group (no statistically significant difference between groups; −3%, Bayesian credible interval 9% to 2%). Procedure success was defined as a reduction in pain by 15 mm or more from baseline on the 100 mm visual analogue scale (VAS), maintenance of function (did not worsen by 10 or more points) or improvement in function from baseline on the 100-point Oswestry disability index (ODI), and no device-related serious adverse events.[1]

In a case series of 57 patients, the clinical success rate was 91% (43/47) at 6 weeks, 88% (35/40) at 3 months and 89% (31/35) at 12 months.[6]

Pain relief

In the RCT of 300 patients treated by a vertebral craniocaudal expandable implant (n=153) or by balloon kyphoplasty (n=147), there was a statistically significant improvement from baseline in the mean VAS scores for pain (0 to 100 mm, from no pain to worst imaginable pain) in both groups at follow-up. In the implant group, the mean VAS score changes (± standard deviation, SD) from baseline were: −59.8±28.9 (n=140) at 30 days, −68.6±25.9 (n=135) at 6 months and −70.8±26.3 (n=127) at 12 months. In the balloon kyphoplasty group, the mean VAS score changes from baseline were −61.1±26.9 (n=135) at 30 days, −65.2±27.4 (n=126) at 6 months and −71.8±23.5 (n=126) at 12 months. No statistically significant differences between groups were seen at follow-up.[1]

In an RCT of 300 patients treated by a vertebral craniocaudal expandable implant (n=150) or by balloon kyphoplasty (n=150), there were no statistically significant differences in VAS pain scores between the 2 groups at any stage from the preoperative period, through the postoperative period, to the final follow-up.[2]

In an RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93), mean VAS scores improved statistically significantly in both groups from before the procedure to 1 year after the procedure: from 8.2±1.4 to 2.7±3 in the implant group and from 7.8±1.2 to 2.5±3 in the balloon kyphoplasty group (p=0.001 for both groups for the comparison with baseline). There was a statistically significant improvement (>5.5 points) of back pain score (VAS) in 54% (44/82) and 43% (37/86) of patients in the implant and balloon kyphoplasty groups, respectively. VAS scores 1 year after the procedure were not statistically significantly different between groups (p=0.95).[3]

In a retrospective matched-paired comparative study of 52 patients treated by a vertebral craniocaudal expandable implant (n=26) or by balloon kyphoplasty

(n=26), the mean VAS scores (±SD) improved in both groups from 87.6±12.8 before the procedure to 10.8±20.8 at 6 months in the implant group and from 83.1±14.9 to 24.6±11.0 in the balloon kyphoplasty group (p value within group not reported). VAS scores 6 months after the procedure were statistically significantly different between groups (p<0.0001).[4]

In a retrospective case series of 77 patients treated by a vertebral craniocaudal expandable implant, VAS scores statistically significantly improved from 7.9 before the procedure to 1.8 at hospital discharge and at 1 month, 1.4 at 3 months and 1.1 at 12 months (p<0.001 for the comparison from baseline with each follow-up visit).[5]

In the case series of 57 patients, mean VAS score (±SD) for back pain improved statistically significantly from 79.3±17.2 before the procedure to 21.9±21.3 at 6 weeks, 21.9±24.6 at 3 months, and 23.2±23.3 at 12 months (p<0.0001 for each follow-up time).[6]

In a prospective case series of 32 patients, mean VAS score (±SD) statistically significantly improved from 7.8±1.6 before the procedure to 2.1±1.2 at 3 days and 1.6±0.95 at 12 months (p<0.001 for the comparison from baseline against 12-month follow-up).[7]

In an observational study of 103 patients treated by a vertebral craniocaudal expandable implant, the median VAS scores were statistically significantly improved from baseline by 82% at 48-hour follow-up, 88% at 3-month follow-up and 92% at 12-month follow-up (p<0.001).[8]

In an RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), there was a statistically significant improvement from baseline in the mean VAS scores for pain in both groups at follow-up (p<0.001). In the implant group, the mean VAS score changes (± SD) from baseline were: -67.7±15.5 at 1 month, -72.8±10.7 at 6 months and -75.8±15.0 at 12 months. In the balloon kyphoplasty group, the mean VAS score changes from baseline were -64.2±26.0 at 1 month, -68.2±21.3 at 6 months and -68.9±20.8 at 12 months. No statistically significant differences between groups were seen at discharge.[9]

In a retrospective comparative study of 75 patients treated by a vertebral craniocaudal expandable implant (n=36) or by vertebroplasty (n=39), there was a statistically significant improvement from baseline in the mean VAS scores for pain in both groups at follow-up (p<0.001 in both groups). Mean VAS scores improved from 6.83±0.25 to 2.75±0.18 at 12 months in the implant group and from 6.80±0.25 to 2.82±0.22 in the vertebroplasty group. No statistically significant differences between groups were seen at follow-up (p=0.8).[10]

In a retrospective case series of 32 patients with malignant vertebral compression fractures treated with a vertebral craniocaudal expandable implant,

the mean VAS score statistically significantly improved from 7.15 before the procedure to 1.81 after the procedure, 1.94 at 12-month follow-up and 2.24 at final follow-up ($p<0.001$ for the improvement from baseline at all time points).[11]

Analgesic consumption

In the observational study of 103 patients, the rate of patients with no analgesic treatment improved from 6% (6/103) at baseline to 27% (28/103) at 48-hour follow-up, 67% (61/91) at 3-month follow-up and 73% (57/78) at 12-month follow-up (p value not reported). [8]

In the RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), all patients were taking paracetamol or acetylsalicylic acid or NSAID, 47% (7/15) of patients were prescribed central analgesics and 1 patient from the implant group needed morphine before the procedure. At 1 month after surgery, 33% (5/15) of patients in each group were taking analgesics (in the implant group these patients were taking paracetamol; in the BK group, 1 needed a central agent and the other 4 needed paracetamol only).[9]

Improvement in function

In the RCT of 300 patients treated by a vertebral craniocaudal expandable implant (n=153) or by balloon kyphoplasty (n=147), the mean ODI score (0 to 100, from no disability to maximum disability) changes from baseline were −31.4±21.9 (n=140) at 30 days, −37.7±20.1 (n=135) at 6 months and −38.1±19.8 (n=127) at 12 months in the implant group. In the balloon kyphoplasty group, the mean ODI score changes from baseline were −34.6±20.4 (n=135) at 30 days, −38.4±20.4 (n=126) at 6 months and −42.2±21.7 (n=126) at 12 months. There was a statistically significant improvement in ODI scores within groups but not between groups (level of statistical significance not reported). [1]

In the RCT of 300 patients treated by a vertebral craniocaudal expandable implant (n=150) or by balloon kyphoplasty (n=150), there were no statistically significant differences in ODI scores between the 2 groups at any stage from the preoperative period, through the postoperative period, to the final follow-up.[2]

In the RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93), mean ODI scores improved statistically significantly in both groups from before the procedure to 1 year after the procedure: from 64±19% to 31.7±19% in the implant group and from 62±14% to 26.3±15.7% in the balloon kyphoplasty group (p=0.001 for both groups for the comparison with baseline). ODI scores 1 year after the procedure were not statistically significantly different between groups (p=0.43).[3]

In the retrospective matched-paired comparative study of 52 patients treated by a vertebral craniocaudal expandable implant (n=26) or by balloon kyphoplasty (n=26), mean ODI scores improved in both groups from before the procedure to 6 months after the procedure: from 68.7±15.8% to 24.8±18.6% in the implant group and from 80.6±8.6% to 33.2±6.3% in the balloon kyphoplasty group (p value within group not reported). All patients in the implant group and all patients in the balloon kyphoplasty group had an increased functional ability after the treatment.[4]

In the case series of 57 patients, the mean ODI score (±SD) improved statistically significantly, from 68±17% before the procedure to 27±17% at 6 weeks, 24±19% at 3 months and 23±16% at 12 months ($p<0.0001$ for each follow-up time).[6]

In the prospective case series of 32 patients, the mean ODI score (±SD) improved statistically significantly from 71±4% before the procedure to 32±5% at 3 days and 30±4% at 12 months ($p<0.001$ for the comparison from baseline against 12-month follow-up).[7]

In the observational study of 103 patients, the median ODI scores statistically significantly improved from baseline by 91% at 3-month follow-up and 95% at 12-month follow-up ($p<0.001$).[8]

In the RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), there was a statistically significant improvement from baseline in the mean ODI scores in both groups at follow-up ($p<0.001$). In the implant group, the mean ODI score changes (± SD) from baseline were: -59.2±18.5 at 1 month, -61.2±15.8 at 6 months and -61.6±17.0 at 12 months. In the balloon kyphoplasty group, the mean ODI score changes from baseline were -47.8±20.8 at 1 month, -53.7±19.6 at 6 months and -53.9±19.4 at 12 months. No statistically significant differences between groups were seen.[9]

Quality of life

In the RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93), there was a statistically significant improvement in the mean short-form (SF)-36 (physical functioning domain) scores in both groups from 32±11 before the procedure to 65.8±15.6 at 1 year in the implant group and from 28±12 to 68±19.8 in the balloon kyphoplasty group ($p=0.001$ for both groups compared with baseline, but no statistically significant difference between groups at 1-year follow-up, $p=0.72$). There was also a statistically significant improvement in the mean SF-36 (mental health domain) scores in both groups, from 42±10 before the procedure to 64±11 at 1 year in the implant group and from 41±9 to 62±10 in the balloon kyphoplasty group ($p=0.001$ for both groups compared with baseline but no statistically significant difference between groups at 1-year follow-up, $p=0.64$). [3]

In the observational study of 103 patients, the median EQ-VAS scores statistically significantly improved from baseline by 21% at 3-month follow-up and 38% at 12-month follow-up ($p<0.001$).[8]

In the RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), there was an improvement from baseline in the mean EQ-VAS scores in both groups at follow-up (level of statistical significance not reported). In the implant group, the mean EQ-VAS score changes (± SD) from baseline were: 43.6±18.1 at 1 month, 47.0±19.2 at 6 months and 48.2±22.7 at 12 months. In the balloon kyphoplasty group, the mean EQ-VAS score changes from baseline were 38.8±25.7 at 1 month, 40.1±26.8 at 6 months and 40.1±28.3 at 12 months. No statistically significant differences between groups were seen.[9]In the retrospective case series of 32 patients, there was a statistically significant improvement from baseline in the mean EQ5-VAS score from 22.3 before the procedure to 68.9 at 6-month follow-up and 65.6 at 12-month follow-up ($p<0.005$). [11]

Restoration of vertebral height

In the RCT of 300 patients treated by a vertebral craniocaudal expandable implant (n=150) or by balloon kyphoplasty (n=150), there was a statistically significantly greater increase in vertebral body height after the procedure in the implant group than in the kyphoplasty group ($p<0.05$). In the implant group, vertebral height was restored by more than 50% in 85% of patients, by less than 50% in 12% of patients and there was no change in 3%. In the balloon kyphoplasty group, vertebral height was restored by more than 50% in 58% of patients, by less than 50% in 26% of patients and there was no change in 16%.[2]

In the RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93), mean (±SD) anterior vertebral body height ratio improved statistically significantly in both groups from before the procedure to after the procedure: from 0.78±0.25 to 0.87±0.17 in the implant group and from 0.74±0.23 to 0.89±0.17 in the balloon kyphoplasty group ($p=0.0014$ and 0.0019 for the implant and balloon kyphoplasty groups respectively). Anterior vertebral body height ratios after the procedure were not statistically significantly different between groups ($p=0.67$).[3]

In the same study, posterior vertebral body height ratio did not improve statistically significantly in both groups: 0.92±0.12 to 0.95±0.11 in the implant group and 0.92±0.12 to 0.95±0.1 in the balloon kyphoplasty group ($p=0.082$ and 0.31 respectively). Posterior vertebral body height ratios after the procedure were not statistically significantly different between groups ($p=0.95$).[3]

In the same study, midline vertebral body height ratio improved statistically significantly in both groups from before the procedure to after the procedure:

0.74±0.25 to 0.88±0.18 in the implant group and 0.70±0.23 to 0.89±0.14 ($p<0.0001$ for both groups). Midline vertebral body height ratios after the procedure were not statistically significantly different between groups ($p=0.82$).[3]

In the retrospective matched-paired comparative study of 52 patients treated by a vertebral craniocaudal expandable implant (n=26) or by balloon kyphoplasty (n=26), there was a statistically significant increase in anterior and mid-vertebral height (mean±SD) in both groups after the procedure. This increased from 21.06 ± 2.77 mm before the procedure to 22.41± 7.14 mm after the procedure (anterior) and from 18.36± 5.64 mm to 20.89± 6.00 mm (mid) in the implant group, and from 21.68 ± 2.08 mm to 25.09± 2.54 mm (anterior) and from 21.97± 1.78 mm to 25.29± 2.10 mm (mid) in the balloon kyphoplasty group ($p<0.001$ for the within-group comparison). At 6 months, vertebral height had not changed much from after the procedure in both groups: in the implant group, anterior vertebral height was 22.28 ± 6.85 mm and mid-vertebral height was 21.19± 6.08 mm, and in the balloon kyphoplasty group, anterior vertebral height was 24.56± 2.27 mm and mid-vertebral height was 24.91± 2.08 mm.[4]

In the prospective case series of 32 patients, the mean (±SD) Beck index (anterior edge height divided by posterior edge height) changed from 0.75± 0.14 before the procedure to 0.77± 0.14 at 12 months.[7]

In the RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), there was a statistically significantly greater correction of vertebral body anterior height 12 months after the procedure in the implant group than in the kyphoplasty group (12±13% versus 0±7%, $p=0.003$). In the same study, there was also a statistically significantly greater correction of central height of vertebral body in the implant group than in the kyphoplasty group (12±10% versus 2±6%, $p=0.001$).[9]

In the retrospective comparative study of 75 patients treated by a vertebral craniocaudal expandable implant (n=36) or by vertebroplasty (n=39), there was a statistically significantly greater restoration of the anterior body height 12 months after the procedure in the implant group than in the vertebroplasty group (57%±74% versus 2%±24%, $p<0.05$). In the same study, there was also a statistically significantly greater restoration of the middle body height in the implant group than in the vertebroplasty group at 12-month follow-up (73%±68% versus 5%±26%, $p<0.05$).[10]

In the retrospective case series of 32 patients with malignant disease of the spine, there was a statistically significant improvement in the mean anterior body height from 19.6 mm at baseline to 25.8 mm after the procedure and 25.5 mm at 12-month follow-up ($p<0.01$). In the same study, the central body height statistically significantly increased from 16.7 mm before the procedure to 22.5 mm after the procedure and at 12-month follow-up ($p<0.01$).[11]

Spine alignment

In the RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93) there was a statistically significant decrease in mean (±SD) wedge angle only in the implant group, from 13.7±7 degrees before the procedure to 7.80±6 degrees after the procedure (p=0.009). The mean wedge angle in the balloon kyphoplasty group decreased from 14.9±8 degrees to 11.5±7 degrees (p=0.067). Wedge angles after the procedure were not statistically significantly different between groups (p=0.11).[3]

In the prospective case series of 32 patients, there was a statistically significant decrease in the mean (±SD) vertebral kyphotic angle and in the mean Cobb angle from 9.0± 5.8 degrees before the procedure to 8.3± 5.6 degrees at 3 days and 8.3± 5.5 degrees at 12 months. For the mean (±SD) Cobb angle there was a statistically significant decrease from 12.3± 16.4 degrees before the procedure to 10.8± 16.4 degrees at 3 days and 10.8± 16.3 degrees at 12 months ($p<0.05$ for the comparisons at 12 months versus baseline). [7]

In the observational study of 103 patients, there was a statistically significant decrease in the mean (±SD) kyphotic angle from 14.5±8.1 degrees before the procedure to 9.2±5.8 degrees at 48-hour follow-up ($p<0.001$). The improvement of kyphosis remained statistically significant compared to baseline (−2.5± 5.8 degrees at 3 months, $p = 0.012$; −4.4 ± 6.0 degrees at 12 months, $p = 0.002$).[8]

In the RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15), there was a statistically significantly greater correction of vertebral kyphotic angle 12 months after the procedure in the implant group than in the kyphoplasty group (-4.4±5.8 degrees versus 0.2±3.0 degrees, p=0.012). In the same study, there was not statistically significant difference between groups in the correction of Cobb angle and Gardner angle 12 months after the procedure (-2.5±4.2 degrees versus 0.3±4.1 degrees for the Cobb angle and -1.0±4.3 degrees versus 0.95±4.26 degrees for the Gardner angle).[9]

In the retrospective comparative study of 75 patients treated by a vertebral craniocaudal expandable implant (n=36) or by vertebroplasty (n=39), the mean (±SD) restoration of the kyphotic angle at 12 months in the implant group was 4.88±7.11 degrees whilst the kyphotic angle was worse than baseline value in the vertebroplasty group (-1.51±5.76 degrees, $p<0.05$). [10]

In the retrospective case series of 32 patients with malignant disease of the spine, there was a statistically significant improvement in the mean regional Cobb angle from 9.1 degrees at baseline to 5.9 degrees after the procedure and 6.1 degrees at 12-month follow-up ($p<0.05$). [11]

Residual kyphosis

In the RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93), there was residual kyphosis of

5 degrees or more at the final observation in 84% (69/82) of spines in the implant group and in 100% (86/86) of spines in the balloon kyphoplasty group (p<0.001).[3]

Safety

Death

Death was reported in 2 patients in an observational study of 103 patients treated by a vertebral craniocaudal expandable implant. The first death occurred 52 days after the procedure and was caused by acute kidney failure; the other death occurred 204 days after the procedure and was caused by an acute respiratory syndrome. The authors stated that the deaths were neither implant- nor procedure-related.[8]

Pneumonia

Pneumonia was reported in 1 patient out of 36 in the vertebral craniocaudal expandable implant group and in 2 patients out of 39 in the vertebroplasty group in a retrospective comparative study of 75 patients, within 12-month follow-up (no further details provided).[10]

Cement extravasation

Cement extravasation measured immediately after the procedure and assessed on X-ray by an independent laboratory was reported in 55% (98/177) of vertebra levels in patients treated by a vertebral craniocaudal expandable implant and in 58% (103/178) of levels in patients treated by balloon kyphoplasty in an RCT of 300 patients treated by an implant (n=153) or by balloon kyphoplasty (n=147). There was no statistically significant difference between the groups (−3%, BCI −13% to 8%). However, in a secondary analysis, cement extravasation was reported statistically significantly less frequently in the implant group than in the balloon kyphoplasty group (17% [30/177] of levels compared with 26% [46/178] of levels, difference −9%, BCI −17% to −0.33%).[1]

Cement leaks were reported statistically significantly less frequently in the implant group (3% [4/133] of vertebras) than in the balloon kyphoplasty group (10% [12/122] of vertebras; p≤0.05) in an RCT of 185 patients treated by a vertebral craniocaudal expandable implant (n=92) or by balloon kyphoplasty (n=93). Intracanal leaks were reported in none of the patients treated by the implant and in 2% (2/86) treated by balloon kyphoplasty.[3]

Cement extravasation was reported in 23% (6/26) of patients in the implant group and in 31% (8/26) of patients in the balloon kyphoplasty group in a retrospective matched-paired comparative study of 52 patients treated by a vertebral craniocaudal expandable implant (n=26) or by balloon kyphoplasty (n=26); no statistically significant difference between groups. [4]

Cement leaks identified by CT scan were reported in 14% (11/77) of patients in a retrospective case series of 77 patients treated by a vertebral craniocaudal expandable implant. All patients had post-traumatic fractures. One patient had nerve root pain caused by the cement leaking along a secondary fracture line in the pedicle (reported below). [5]

Cement extravasation identified radiographically was reported in 8% (5/64) of vertebras in a case series of 57 patients. None of these were symptomatic.[6]

Cement leakage with no clinical consequences was reported in 40% (43/108) of treated vertebrae in the observational study of 103 patients. [8]

Cement leakage that was asymptomatic was reported in 1 patient in the implant group in an RCT of 30 patients treated by a vertebral craniocaudal expandable implant (n=15) or by balloon kyphoplasty (n=15). [9]

Cement leakage that was asymptomatic was reported in 10% (5/52) of fractures in a retrospective case series of 32 patients with malignant vertebral compression fractures treated with a vertebral craniocaudal expandable implant; two of the leaks were in the disc space and 3 were in the paravertebral soft tissues. [11]

Dural tear

Dural tear was reported in 1 patient in the case series of 57 patients. It occurred during the initial pedicle access with the Jamshidi needle. It was treated with Gelfoam and there were no residual or permanent sequelae.[6]

New fractures

Adjacent level fracture was reported in 21% (28/134) of the as-treated population in the implant group and in 22% (29/130) of the as-treated population in the balloon kyphoplasty group in the RCT of 300 patients treated by an implant (n=153) or by balloon kyphoplasty (n=147). There was no statistically significant difference between the groups (−1%, BCI −11% to 8%). In the same study, a fractured pedicle was reported in 1 patient in the implant group. It was associated with the use of the implant in the setting of sclerotic bone. This resulted in back pain at the time of discharge, which was treated with analgesics. [1]

New fractures were reported in 12% (10/82) of patients in the implant group and in 13% (11/86) of patients in the balloon kyphoplasty group in the RCT of 185 patients (no statistical significant difference between groups, p>0.2). Of these new fractures, 7% (6/82) were adjacent and 5% (4/82) were remote in the implant group and 9% (8/86) were adjacent and 3% (3/86) were remote in the balloon kyphoplasty group.[3]

New fractures were reported in 12% (3/26) of patients in the implant group and in 54% (14/26) of patients in the balloon kyphoplasty group in a retrospective matched-paired comparative study of 52 patients. The difference between the groups was statistically significant, p<0.0001. Adjacent fractures were reported in 8% (2/26) of patients in the implant group and in 35% (9/26) of patients in the balloon kyphoplasty group. [4]

Adjacent fractures were reported in 3% (2/77) of patients in the retrospective case series of 77 patients; no reoperation was needed. In the same study, a secondary pedicular fracture line was reported in 1 patient. [5]

Adjacent-level fracture was reported in 15% (5/34) of vertebras from 30 patients with adequate 12-month radiographs in the case series of 57 patients. Non-adjacent fractures were reported in 6% (2/34) of vertebras and re-fracture at a previously treated index level was reported in 3% (1/34). [6]

Symptomatic adjacent fracture at the L2 level was reported in 1 patient in a prospective case series of 32 patients. It occurred during the stationary postoperative period. This was also stabilised with the implant.[7]

Subsequent compression fractures were reported in 3% (3/103) of patients (8 fractures) in the observational study of 103 patients. There were 4 spontaneous new fractures, 3 spontaneous adjacent fractures, and 1 asymptomatic adjacent fracture (procedure-related) that did not need treatment. [8]

Subsequent fracture was reported in 13% (2/15) of patients in the implant group and in 7% (1/15) of patients in the balloon kyphoplasty group in the RCT of 30 patients treated by a vertebral craniocaudal expandable implant or by balloon kyphoplasty. Overall, 75% of fractures were adjacent fractures. One adjacent fracture in the implant group was caused by a fall 55 days after the procedure. [9]

New fractures were reported in 11% (4/36) of patients (all adjacent fractures) in the vertebral craniocaudal expandable implant group and in 18% (7/39) of patients (including 6 adjacent fractures) in the vertebroplasty group in the retrospective comparative study of 75 patients. [10]

New adjacent fractures were reported in 9% (3/32) of patients in the retrospective case series of 32 patients with malignant vertebral compression fractures. [11]

Pain after the procedure

Pain after the procedure was reported in 1 patient in the implant group in the RCT of 300 patients treated by an implant (n=153) or by balloon kyphoplasty (n=147).[1]

Lumbar pain was reported in 1 patient at 418 days in the observational study of 103 patients; the authors stated that it was neither implant- nor procedure-related. [8]

Infection

Skin infection that started in hospital was reported in 1 patient in the retrospective case series of 77 patients. The infection was probably caused by contamination from an oral infection and was treated with antibiotics.[5]

Urinary tract infection was reported in 17% (6/36) of patients in the vertebral craniocaudal explandable implant group and in 21% (8/39) of patients in the vertebroplasty group in the retrospective comparative study of 75 patients (no further details provided).[10]

Haematoma

Haematoma was reported in 1 patient in a prospective case series of 32 patients treated by a vertebral craniocaudal expandable implant; revision was not needed.[7]

Loss of height of the treated vertebral body

Minor loss of height of the stabilised L2 vertebral body in an osteoporotic fracture was reported in 1 patient in the prospective case series of 32 patients. The Beck Index changed after the procedure from 1.0 to 0.96 and the Cobb angle changed from 11 degrees to 13 degrees. The VAS score remained unchanged.[7]

Collapse of treated vertebral body

Collapse of the treated vertebral body resulting in canal compromise, haematoma and neurological symptoms was reported in 1 patient 16 days after the procedure in the observational study of 103 patients; the condition of the patient had improved at 12-month follow-up (no further details reported). [8]

Dislocation of posterior wall

Dislocation of posterior wall secondary to surgery and leading to a sensory deficit was reported in 1 patient 4 days after the procedure in the observational study of 103 patients. The patient had been treated outside of the device instructions for use and was subsequently treated by decompression and posterior instrumentation.[8]

Herpes zoster

Herpes zoster was reported in 1 patient in the implant group in the RCT of 300 patients treated by an implant (n=153) or by balloon kyphoplasty (n=147).[1]

Pruritus

Pruritus was reported in 1 patient in the implant group in the RCT of 300 patients treated by an implant (n=153) or by balloon kyphoplasty (n=147).[1]

Device migration

Device migration was reported in 1 patient in the retrospective case series of 77 patients; this reflected a technical problem that occurred with an instrument prototype. [5]

Validity and generalisability of the studies

- In the studies included in table 2, 3 different types of vertebral expandable implants were used: Spinejack[2,5,8, 9, 10, 11], Kiva[1,3,4,6] and Osseofix[7].
- Studies involving vertebral expandable devices that were not left in situ were excluded.
- Two of the 4 RCTs[1, 3] included involved the use of the Kiva implant. In the other 2 RCTs, the Spinejack implant was used.[2, 9]
- The longest follow-up was 35 months.[5]
- Most evidence comes from patients with osteoporotic and trauma fractures. In the Ender (2014) study [7] the procedure was used for treating tumour-associated vertebral collapse in 8 patients. In the Noriega (2016)[11] study added after the consultation period, the procedure was used to treat 32 consecutive patients with 52 malignant vertebral compression fractures.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

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

Interventional procedures

- Balloon kyphoplasty for vertebral compression fractures. NICE interventional procedure guidance 166 (2006). Available from http://www.nice.org.uk/guidance/IPG166
- Percutaneous vertebroplasty. NICE interventional procedure guidance 12 (2003). Available from http://www.nice.org.uk/guidance/IPG12

Technology appraisals

- Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for treating osteoporotic vertebral compression fractures. NICE technology appraisal guidance 279 (2013). Available from http://www.nice.org.uk/guidance/TA279

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Specialist Advisor Questionnaires for percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 20 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 0 completed questionnaire.

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- Ongoing studies:
    - NCT02461810: Prospective comparative study to compare safety and effectiveness of two vertebral compression fracture reduction techniques (SAKOS); study type, randomised controlled trial; location, multicentre (France, Germany, Spain, Switzerland); estimated enrolment, 160; estimated completion date, December 2017.

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11. Noriega DC, Krüger A, Ramajo RH et al. (2016) Long-term benefits of percutaneous anatomical restoration of vertebral compression fractures linked to malignancy. Turkisk Neurosurgy, DOI: 10.5137/1019-5149.JTN.12294-14.1.

Appendix A: Additional papers on percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Anselmetti GC, Tutton SM, Facchini FR et al. (2012) Percutaneous vertebral augmentation for painful osteolytic vertebral metastasis: a case report. International Medical Case Reports Journal 5:13-17.	Single case report (kiva implant) FU= 4 months	The Kiva system represents a novel and effective minimally invasive treatment option for patients suffering from severe pain caused by osteolytic vertebral metastasis.	Studies with more patients or longer follow-up are already included. No new safety event reported.
Baeesa SS, Krueger A, Aragon FA et al. (2015) The efficacy of a percutaneous expandable titanium device in anatomical reduction of vertebral compression fractures of the thoracolumbar spine. Saudi Medical Journal 36:52-60	Prospective case series n=27 FU= minimum 12 months	This new percutaneous technique for VCF has shown good clinical results in pain control and the possibility to reduce both vertebral kyphosis angles and fractured endplates seen in 3D-CT scans assessment method. Further studies are needed to confirm those results on larger cohorts with long-term follow up.	Studies with more patients or longer follow up are already included. No new safety event reported.
Berjano P, Damilano M, Pejrona M et al. (2014) KIVA VCF system in the treatment of T12 osteoporotic vertebral compression fracture. European Spine Journal 23:1379-1380.	Single case report (Kiva implant) FU= 3 months	Back pain improved from 1 day after the procedure. At 3 months, ODI score=8% and VAS=3/10.	Studies with more patients or longer follow up are already included. No new safety event reported.
Ender SA, Eschler A, Ender M et al. (2015) Fracture care using percutaneously applied titanium mesh cages (OsseoFix) for unstable osteoporotic thoracolumbar burst fractures is able to reduce cement-associated complications-results after 12 months. Journal of Orthopaedic Surgery 10:175.	Prospective case series (Osseofix implant) n=15 FU=12 months	As a safe and effective procedure, the use of intravertebral expandable titanium mesh cages presents a valuable alternative to usual intravertebral stabilisation procedures for incomplete osteoporotic burst fractures and bears the potential to reduce cement-associated complications.	Same patient population as in Ender (2014) which is included in Table 2.
Eschler A, Ender SA, Ulmar B et al. (2014) Cementless fixation of osteoporotic VCFs using titanium mesh implants (OsseoFix): preliminary results. BioMed Research International 2014:853897.	Prospective case series (Osseofix implant) n=4 FU=28 months	Preliminary results in a small, selected patient collective indicate the ability of bony healing for osteoporotic vertebral compression fractures. Cementless fixation using intravertebral titanium mesh cages revealed substantial pain relief, adequate reduction, and reduction	Studies with more patients or longer follow up are already included. No new safety event reported.

		maintenance without complications.	
Korovessis P, Repantis T, Miller LE et al. (2011) Initial clinical experience with a novel vertebral augmentation system for treatment of symptomatic vertebral compression fractures: a case series of 26 consecutive patients. BMC Musculoskeletal Disorders 12:206.	Prospective case series (Kiva implant) n=26 FU=6 months	The initial clinical experience with the Kiva system demonstrated significant improvements in back pain and function with minimal and clinically insignificant procedural cement leakage	Studies with more patients or longer follow up are already included. No new safety event reported.
Noriega D, Kruger A, Ardura F et al. (2015) Clinical outcome after the use of a new craniocaudal expandable implant for vertebral compression fracture treatment: one year results from a prospective multicentric study. BioMed Research International :927813.	Prospective case series n=32 patients FU=12 months	This observational study demonstrates promising and persistent results consisting of immediate and sustained pain relief and durable clinical improvement after the procedure and throughout the 1-year follow-up period.	Studies with more patients or longer follow up are already included. No new safety event reported.

Appendix B: Related NICE guidance for percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

Guidance	Recommendations
Interventional procedures	**Balloon kyphoplasty for vertebral compression fractures. NICE interventional procedure guidance 166 (2006)** 1.1 Current evidence on the safety and efficacy of balloon kyphoplasty for vertebral compression fractures appears adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 The following are recommended. • This procedure should only be undertaken with prior discussion by a specialist multidisciplinary team that includes a radiologist and a spinal surgeon, and when there are facilities for good imaging, and arrangements for good access to a spinal surgery service. • 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. **Percutaneous vertebroplasty. NICE interventional procedure guidance 12 (2003)** 1.1 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. 1.2 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	**Percutaneous vertebroplasty and percutaneous balloon**

	kyphoplasty for treating osteoporotic vertebral compression fractures. NICE technology appraisal guidance 279 (2013) 1.1 Percutaneous vertebroplasty, and percutaneous balloon kyphoplasty without stenting, are recommended as options for treating osteoporotic vertebral compression fractures only in people: • who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management **and** • in whom the pain has been confirmed to be at the level of the fracture by physical examination and imaging.

Appendix C: Literature search for percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	08/08/2016	Issue 8 of 12 August 2016	12
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	08/08/2016	Issue 8 of 12 August 2016	0
HTA database (Cochrane Library)	08/08/2016	Issue 8 of 12 August 2016	0
MEDLINE (Ovid)	08/08/2016	1946 to July Week 4 2016	88
MEDLINE In-Process (Ovid)	08/08/2016	August 05, 2016	145
EMBASE (Ovid)	08/08/2016	1974 to 2016 Week 32	126
PubMed	08/08/2016	-	0
JournalTOCS	08/08/2016	-	0

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Database: Medline
Strategy used 1 Spinal Fractures/ (11655) 2 Spin* injur*.tw. (6134) 3 ((spin* or vertebral*) and (fractur* or trauma* or metastas** or compress*)).tw. (55650) 4 (trauma* or mylema* or osteoporo*).tw. (295152) 5 3 and 4 (25738) 6 fractures, compression/ or osteoporotic fractures/ (3752) 7 (fractur* adj3 (compress* or osteoporot*)).tw. (9538) 8 vcf.tw. (695) 9 1 or 2 or 5 or 6 or 7 or 8 (42681) 10 (vertebr* adj3 cranio caudal).tw. (2) 11 (craniocaud* adj3 implant*).tw. (2) 12 (spin* adj4 fract* adj4 reduc*).tw. (156) 13 (Compress* fract* adj4 reduct*).tw. (18) 14 (vertebr* adj4 fract* adj4 reduct*).tw. (293) 15 (vertebr* adj4 (augument* or implant*)).tw. (276) 16 PVP.tw. (4155) 17 PKP.tw. (583) 18 Bone Cements/ (9443) 19 (bone adj4 (cement* or glue* or paste* or adhesiv*)).tw. (6769) 20 or/10-19 (17812)

21	9 and 20 (1787)
22	spinejack.tw. (3)
23	Osseofix*.tw. (6)
24	22 or 23 (9)
25	21 or 24 (1791)
26	Animals/ not Humans/ (4137434)
27	25 not 26 (1740)
28	limit 27 to yr="2005 -Current" (0808)
29	limit 28 to english language (1077)