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CAncer Patient Fracture Evaluation (CAFE) Study

Balloon Kyphoplasty versus Non-surgical Fracture Management for Treatment of Painful Vertebral Body Compression Fractures in Patients with Cancer: A Multicentre, Randomised Controlled Trial

THE LANCET Oncology

Berenson *et al*. 2011;**12**:225-35.
Published Online February 17, 2011

[speaker]
[title]

ClinicalTrials.gov NCT00211237

MICHELSON TECHNOLOGY AT WORK

Powerful Design: Level I Clinical Evidence

Prospective Randomized Controlled Trial (RCT)
Balloon Kyphoplasty (BKP) vs. Non-surgical Management (NSM)

Multicenter, Multinational
22 Sites (Europe, US, Canada, Australia)

Large Cohort, Well Matched
n = 134 patients: 70 BKP, 64 NSM

Long-term Follow-up
1, 3, 6, and 12 (optional crossover after 1 month for NSM group)

Multiple Validated Outcome Measures
Back Pain, Back Function, QOL, Karnofsky Performance Status, Activity Days

Independent Statistical & Radiographic Assessment

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Study Design: Patient Criteria

Major Inclusions

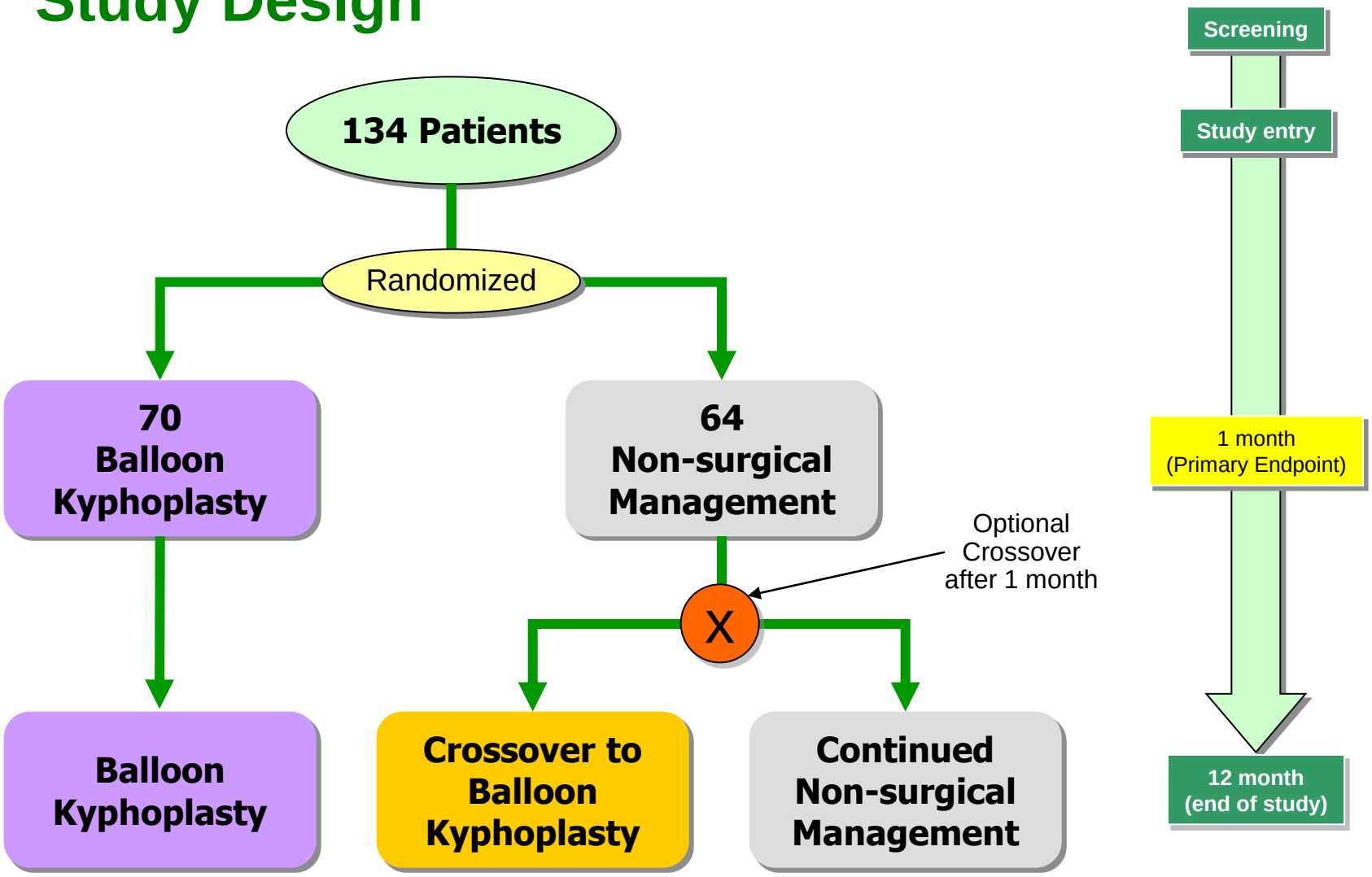
- Age ≥ 21 years old
- Diagnosed with cancer
- 1-3 painful VCFs (T5-L5) diagnosed in conjunction with MRI or plain radiographs
- Pain score ≥ 4 (on 0-10 scale)
- Roland-Morris Disability Questionnaire (RDQ) score ≥ 10 (on 0-24 scale)

Major Exclusions

- Spinal cord compression
- Primary bone tumor, osteoblastic tumor, or solitary plasmacytoma at index VCF
- Enrolled in Phase I investigational anti-cancer treatment
- BKP technically not feasible as determined by treating physician
- Required additional surgical treatment for VCF
- Use of high-dose steroids, IV pain meds, or nerve block to control chronic pain unrelated to VCF

CAFE Study (Lancet Oncology 2011)

Study Design



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Patient Baseline Characteristics*

	BKP n = 70	NSM (control) n = 64
Number patients evaluable	68	61
Number of patients not evaluable**	2	3
Patient age, mean (range)	64.8 (38-88)	63.0 (40-83)
Estimated Fx age, months, median	3.4	3.5
Underlying etiology		
Multiple myeloma	22 (32%)	27 (44%)
Breast cancer	16 (24%)	12 (20%)
Lung cancer	7 (10%)	4 (6.6%)
Prostate cancer	4 (5.9%)	4 (6.6%)
Other †	19 (28%)	14 (23%)
Bisphosphonate use	30 (44%)	33 (54%)
Steroid use	20 (29%)	25 (41%)
Fractures per patient		
1	24 (35%)	27 (44%)
2	18 (26%)	20 (33%)
3	26 (38%)	14 (23%)

* No differences in baseline characteristics between the groups

** Withdrew within a few days of randomization, had missing values for some characteristics and those randomized to BKP did not have the procedure.

† Other primary cancer types included colon/colorectal cancer, ovarian cancer, esophageal cancer, and bladder cancer.

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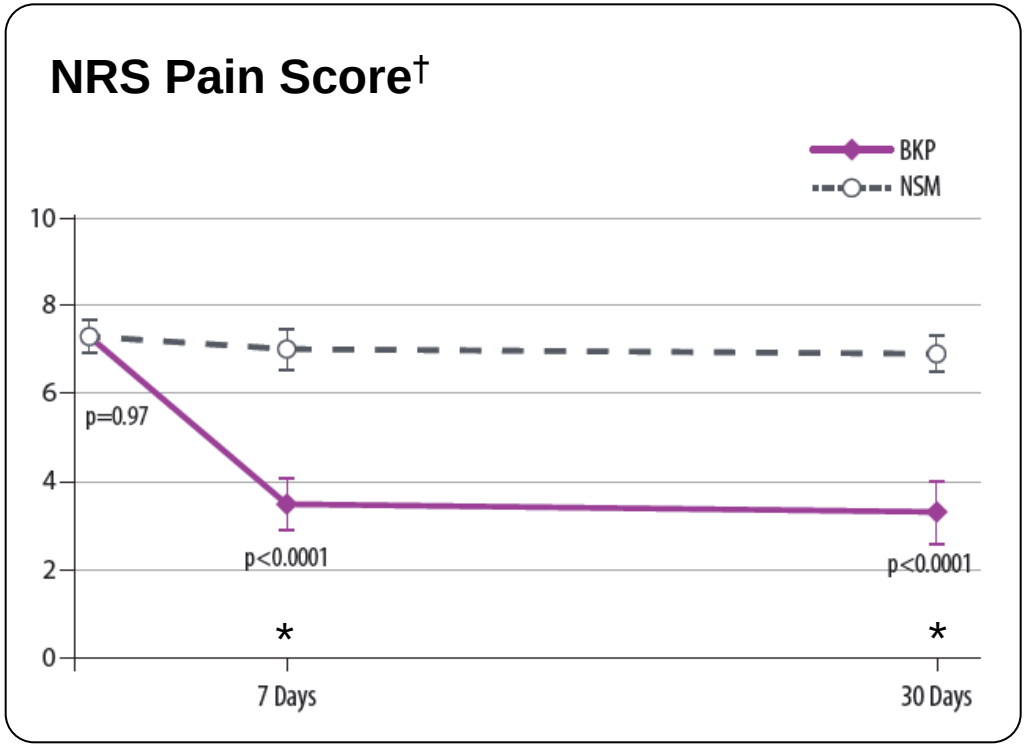
Back Pain @ 1 Month



† NRS = Numerical Rating Scale (0 to 10); Mean and 95% CI shown

§ Met MCID (Minimally Clinically Important Difference), 1.0-2.5 points for NRS

* p<0.0001 in comparison with NSM

** Decreased 0.6 points from baseline to 1 month (p=0.03)

Back Pain Relief at 7 days!

BKP

- Rapid (7 days) and sustained (1 mo) back pain relief
- Clinically § and statistically* significantly better than NSM
- Significantly fewer patients using analgesics for back pain than NSM (p=0.0018)

NSM

- Minimal change in back pain relief (no clinical improvement) **

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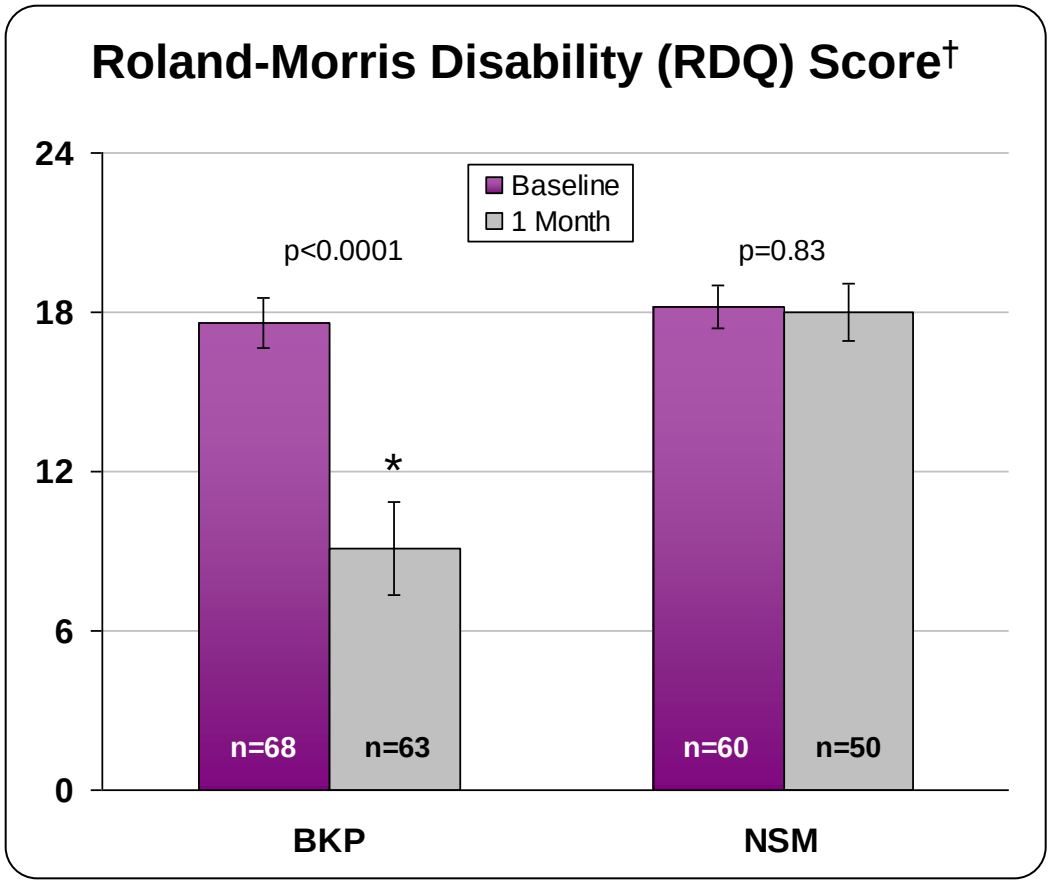
Back Function @ 1 Month



† Primary endpoint of study; Mean and 95% CI shown

§ met MCID (Minimally Clinically Important Difference), 2-points for RDQ

* p<0.0001 in comparison with NSM

8.3 point improvement!

BKP

- 8.3 point improvement
- Clinically § and statistically* significantly better than NSM
- 81% (51/63) patients had at least 2-point clinically significant improvement (MCID §)

NSM

- No significant change
- Only 28% (14/50) patients had at least 2-point MCID §

CAFE Study (Lancet Oncology 2011)

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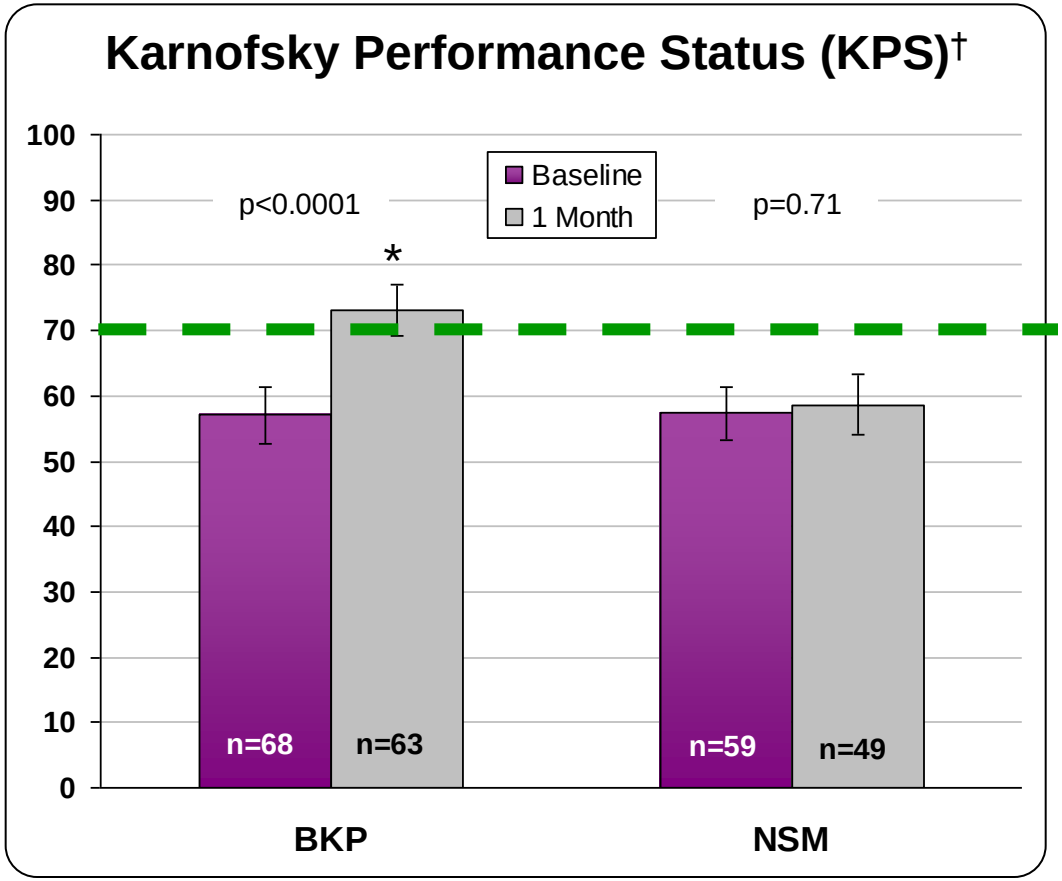
Performance Status @ 1 Month



16 point improvement!

BKP

- Clinically § and statistically* significantly better than NSM
- 75% (47/63) patients reached the meaningful self-care threshold (≥70 score)

NSM

- No significant change
- Only 39% (19/49) patients reached the self-care threshold (≥70 score)

† KPS is a standard way of measuring a cancer patient's ability to perform ordinary tasks (scale 0 to 100, higher score means the patient is better able to carry out daily activities); Mean and 95% CI shown.

§ met MCID (Minimally Clinically Important Difference), 5-points for KPS

* p<0.0001 in comparison with NSM

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Outcomes Summary @ 1 Month

		BKP	NSM (control)
Back-specific Function	RDQ	**Improved** * § ‡	**No Change**
QOL	Karnofsky	**Improved** * § ‡	
	SF-36 PCS	**Improved** * § ‡	
	SF-36 MCS	**Improved** *‡	
Activity	Limited Activity Days	**Improved** *‡	
	Bed Rest Days	**Improved** *‡	
Back Pain	NRS	**Improved** * § ‡	**Minimal Change** **
	Analgesic Use	**96% @ Baseline dropped to 60%** ‡	**84% @ Baseline dropped to 72%**

* Statistically significant ($p<0.0001$) improvement from baseline (data on file @ Medtronic Spine LLC in CAFE Final Clinical Study Report)

§ Clinically significant improvement from baseline, met minimally clinically important difference (MCID)

‡ Statistically significantly better than NSM ($p<0.0001$)

** Decreased 0.6 points from baseline to 1 month ($p=0.03$)

CAFE Study (Lancet Oncology 2011)

Results: Through 12 Months
(as treated analysis)

Crossover

- 73% (38/52) NSM patients that completed the 1 month evaluation eventually crossed over to BKP
- 55% (21/38) of the patients crossed over within 1 week after their 1 month visit

Outcomes (Article, Figure 4)

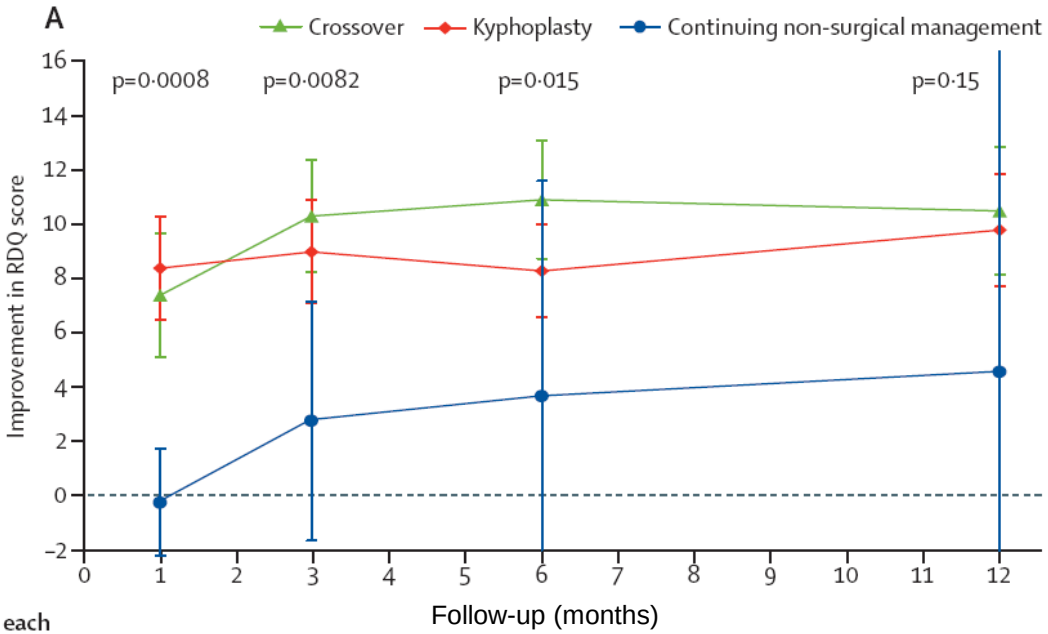
Improvements seen at 1 month post-BKP (patients randomized to immediate BKP and crossover) were generally maintained through the final 12-month assessment for:

- Back pain (NRS Pain Score)
- Back-specific function (RDQ)
- Quality of life (SF-36 Physical Component Summary)

Results: Through 12 Months

(as treated analysis)

Roland-Morris Disability Score (improvement from baseline)†



Number at each timepoint				
Crossover	38	36	33	27
Kyphoplasty	63	55	49	40
Continuing NSM	12	10	8	6

† Data represents improvement scores (change from baseline). Mean and 95% CI shown for treatment groups.

▲ Crossover = NSM patients that crossed over to BKP after 1 month. A new baseline was established just before the procedure and follow-up was done at 7 days (pain only), and 1, 3, 6 months after procedure, and the final assessment occurred at 12 months after study entry.

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Safety Outcomes Overview

1 Month (as randomized)

- Number of patients with
  - adverse events was similar between BKP and NSM
  - radiographic subsequent fractures was not different between BKP and NSM
- Most common adverse events
  - Back pain (4/70 BKP and 5/64 NSM control)
  - Subsequent symptomatic VCF (2 BKP and 3 NSM)
- BKP Related Serious Adverse Events
  - 1 patient experienced an intraoperative non-Q-wave myocardial infarction attributed to anesthesia and resolved
  - 1 patient with cement leakage to adjacent disc had an adjacent fracture determined device-related

12 months (as treated)

- Beyond the 1 month randomization period, original BKP group had no additional device-related serious medical complications
- BKP related serious adverse events for crossover group
  - 1 airway complication related to anesthesia (resolved)
  - 1 subsequent fracture possibly device-related
- Death rate among patients who had BKP (BKP group and crossover) was not different from those who had NSM (p=0.13; *webappendix p 1*)

CAFE Study (Lancet Oncology 2011)

Summary

- **Painful VCFs are common in cancer patients**
- **BKP provided** better results than NSM @ 1 month in all measures
  [pain, back function, QOL, activity, bed rest, patients using analgesics]
- **BKP treated patients** (original BKP and crossover) had their improvements seen at 1 mo generally sustained through 12 mo
  [pain, back function, QOL]
- **BKP is safe and minimally invasive**
  - BKP was found to be safe for treating VCFs in patients with cancer. Number of patients with adverse events was similar between BKP and NSM.
  - BKP is a percutaneous procedure and "typically requires minimal recovery time, and does not delay chemotherapy or radiation therapy." *

For painful VCFs in patients with cancer, balloon kyphoplasty is an effective treatment that rapidly reduces pain and improves function.

* Discussion, 3rd Paragraph

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Kyphon® Balloon Kyphoplasty

Important Safety Information

The complication rate with Kyphon® Balloon Kyphoplasty has been demonstrated to be low. There are risks associated with the procedure (*e.g.*, cement extravasation), including serious complications, and though rare, some of which may be fatal. For complete information regarding indications for use, contraindications, warnings, precautions, adverse events, and methods of use, please reference the devices' Instructions for Use included with the product.

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www.CompressionFractureStudy.com
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