

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### **Interventional procedure overview of radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases**

Cancer from elsewhere in the body can spread to the spine (spinal metastases), causing severe pain and weakness in the vertebrae (bones of the spine). This leads to instability or fractures and spinal cord compression. In this procedure a needle-like probe containing an electrode is inserted into the spinal metastases. It produces an electrical current that heats the cancer cells and destroys them (radiofrequency ablation). The aim is to shrink the spinal metastases to relieve pain and other symptoms (palliation). During the same procedure, bone cement is injected into the resultant cavity (percutaneous vertebroplasty) or a balloon is put into the vertebral cavity to lift the bone into position and then cement is injected (balloon kyphoplasty).

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## Abbreviations

Abbreviation	Word or phrase
BPI	Brief pain inventory
EBRT	External beam radiation therapy
FACT-BP	Functional assessment of cancer therapy – bone pain
FACT-G7	Functional assessment of cancer therapy – general 7
HRQoL	Health-related quality of life
HTA	Health technology assessment
NM	Not measured
NRS	Numerical rating scale
ODI	Oswestry disability index
RF	Radiofrequency
RFA	Radiofrequency ablation
SBRT	Stereotactic body radiation therapy
SMD	Standardised mean difference
VAS	Visual Analog Scale
WHO	World Health Organization

## Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure 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 professional opinion. It should not be regarded as a definitive assessment of the procedure.

## Date prepared

This overview was prepared in August 2022.

## Procedure name

- Radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases

## Professional societies

- British Society of Interventional Radiology
- Faculty of Clinical Oncology, Royal College of Radiologists
- Faculty of Clinical Radiology, Royal College of Radiologists
- British Association of Spinal Surgeons (BASS)
- Society of British Neurological Surgeons (SBNS)
- British Society of Skeletal Radiologists (BSSR)
- Faculty of Pain Medicine, The Royal College of Anaesthetists.

## Description of the procedure

### Indications and current treatment

Spinal metastases can affect quality of life by causing severe pain, functional impairment, vertebral fractures, nerve root impingement, spinal cord compression and hypercalcaemia.

Treatment for spinal metastases is mainly palliative. It aims to reduce pain, improve and maintain function, provide mechanical stability, and prevent further local tumour progression. Current treatment options include a combination of medical therapies (such as analgesics, systemic therapies including osteoclastic inhibitors such as bisphosphonates and denosumab, chemotherapy or hormone therapy), orthotic support, radiation therapy (external beam radiotherapy or stereotactic body radiotherapy), and minimally invasive localised percutaneous procedures such as cryoablation, photodynamic therapy, microwave ablation, and radiofrequency ablation. These techniques may also be used with kyphoplasty or vertebroplasty to improve structural or mechanical stabilisation after tumour ablation. Open surgery (or surgery combined with radiotherapy) may be suitable for some patients with spinal cord compression and vertebral fractures.

## What the procedure involves

Radiofrequency ablation is a procedure for palliative treatment of spinal metastases. It is usually done in a day-case setting using a transpedicular or parapedicular approach under general anaesthesia or local anaesthesia with sedation. The approach is either percutaneous, endoscopic or surgical.

Under imaging guidance (fluoroscopy, CT or MRI) a radiofrequency probe is inserted into the spinal tumour. The radiofrequency probe is attached to a radiofrequency generator, which creates high frequency alternating current pulses that heat and destroy the tumour. This creates a cavity in the vertebral body. In this procedure, percutaneous vertebroplasty or balloon kyphoplasty is done at the same time with the aim of preventing subsequent fractures in the treated vertebrae.

Radiofrequency ablation is not usually done if the spinal metastases are close to neurological structures because of the risk of neurological injury.

## Efficacy summary

### Pain reduction

In a systematic review of 15 studies on RFA with cement augmentation for spinal metastases, pooled analyses indicate that RFA treatment reduced pain in the short term. VAS scores reduced at 3 to 5 weeks (SMD 2.24, 95% CI 1.55 to 2.93; 8 studies, n=286) at medium term (3 to 4 months: SMD 3.00, 95% CI 1.11 to 4.90; 4 studies, n=98) and long-term follow up (5 to 6 months: SMD 3.54, 95% CI 1.96 to 5.11; 4 studies, n=144; Murali 2021).

In a systematic review of 9 studies (4 prospective and 5 retrospective) on RFA as a palliative treatment in 583 patients with painful metastatic spinal lesions, all studies reported that patients experienced a reduction in pain (72% [437/583] of these patients had an additional vertebroplasty treatment). Pain was measured using instruments such as VAS and NPRS, in which higher scores represented worst pain. In the 4 prospective studies, 1 study (Bagla 2016) reported a statistically significant decrease in pain from baseline NPRS score of 5.9 to 2.6 at 1 month and 2.1 at 3 months (a decrease of 3.3 and 3.8 points, respectively;  $p < 0.0001$ ). Similar results (decrease in baseline VAS mean score from 7.5 to 2.7,  $p < 0.0005$  after 1 week) were reported in another study (Nakatsuka 2009). Local pain relief was reported in 87% (13/15) of patients at 2 to 4 weeks (Georgy 2009) and sustained in 90% (9/10) of patients during survival period (Nakatsuka 2009). In another study (Proschek 2009), pain at baseline (mean VAS score 7.6 in RFA group [n=8] and 7.9 in RFA plus vertebroplasty group [n=8]) decreased to 4.0 ( $p < 0.008$ ) in the RFA group and 3.5 ( $p < 0.005$ ) in the RFA plus vertebroplasty group, respectively, at 15 to 36 months follow up (Rosian 2018).

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A systematic review of 8 studies (4 prospective and 4 retrospective) of RFA plus additional cement augmentation in 239 patients with painful spinal metastases reported statistically significant pain relief compared with baseline (mean baseline VAS scores ranged between 5.9 and 8; mean baseline NRS scores ranged between 5.9 and 8). Five studies reported more than 4 points of pain reduction (mean score ranged from 4 to 5.7) and 2 studies reported more than 2 points of pain reduction (mean score 3.3 and 3.8) between baseline and last follow up (range 1 week to 6 months). Two studies reported results separately for the group having RFA plus cement augmentation compared with the group having RFA alone. One study (Nakatsuka 2009) reported that at 1-week follow up, VAS decreased from baseline 4.3 to 1.7 ( $p=0.0004$ ) in the RFA alone group ( $n=4$ ) and from 6.6 to 1.7 ( $p=0.003$ ) in the RFA plus cement augmentation group ( $n=6$ ). Similarly, in another study (Proschek 2009) between 15 to 36 months of follow up, VAS decreased from 7.9 to 4 ( $p=0.008$ ) in the RFA alone group ( $n=8$ ), and from 7.6 to 3.5 ( $p=0.005$ ) in the RFA plus cement augmentation group ( $n=8$ ; Cazzato 2018).

A systematic review of 8 retrospective studies on combined RFA and vertebral stabilisation techniques for palliative treatment of vertebral metastases reported a decrease in pain VAS scores from baseline. RFA followed by percutaneous kyphoplasty (in 3 studies) resulted in decreased pain scores from baseline and between 1 week to 6 months of follow up (VAS scores at baseline ranged from 7.2 to 7.9 and at last follow up ranged from 2.96 to 3.82). RFA followed by vertebroplasty (in 4 studies) resulted in decreased pain scores from baseline and between 3 days to 15 months of follow up (VAS scores at baseline ranged from 6.3 to 8.5 and at last follow up ranged from 2.4 to 3.5; Greif 2019).

A prospective case series of 100 patients with painful metastases who had RFA plus additional cement augmentation (in 97%) reported that the mean worst pain score (measured using the Brief Pain Index) decreased from 8.2 at baseline to 3.5 at 6 months follow up ( $n=22$ ;  $p<0.001$  for all visits). Patients experienced significant improvement in average pain for all visits (from 6.0 at baseline to 2.9 at 6 months,  $p<0.001$ ) and pain interference (from 6.1 at baseline to 2.5 at 6 months,  $p<0.001$ ; Levy 2020).

A retrospective comparative case series of 87 patients with spinal metastatic tumours (125 vertebral bodies) compared RFA combined with bone cement (35 patients with 47 vertebral segments) with bone cement alone (52 patients with 78 vertebral segments). This reported that pain scores (measured using VAS) and disability scores (measured using ODI scores) for the 2 groups improved significantly at 3 days and at 1 month compared with baseline. But no significant difference was seen between the groups. At 6-month follow up, pain scores and disability scores were statistically significantly lower in the RFA combined with bone cement group than those in bone cement alone group (Lv 2020).

A retrospective analysis of 64 patients comparing RFA plus vertebral augmentation (n=34) with kyphoplasty alone (n=30) reported an overall decrease in pain scores for all treatment groups from baseline and between 7 to 14 days (RFA with SpineStar system 6.9 to 3.3; RFA with OsteoCool system 6 to 3.28; kyphoplasty alone 6.3 to 3.69). However, a difference of square means analysis showed no statistical difference in pain scores at each time interval between the 2 RFA systems, and there was no statistical difference in pain scores when each RFA system was compared with kyphoplasty alone (Jain 2020).

A retrospective analysis of 26 patients (with 28 spinal metastases) who had RFA plus cement augmentation (n=17) or RFA plus radiotherapy (n=10) reported that there was a significant decrease in the pain scores in both the groups (RFA plus cement augmentation group VAS score decreased from baseline 4.2 to 2.7 at 3 weeks and 2.1 at 12 weeks,  $p<0.0001$ ; RFA plus radiotherapy group VAS score decreased from baseline 4.5 to 2.7 at 3 weeks and 1.6 at 12 weeks,  $p<0.0001$ ). However, there was no significant difference in pain scores between the 2 groups at these follow-up periods ( $p=0.96$ ; Prezzano 2019).

In a retrospective analysis of 169 patients with spinal metastases comparing combined percutaneous vertebroplasty with radiofrequency ablation, 125I seed implantation, zoledronic acid or radiotherapy, there was no statistically significant difference in VAS, ODI scores or WHO pain relief during the follow-up periods (24 hours, 1 month or 6 months, all  $p<0.05$ ). Patients who had PVP plus 125I seed implantation (n=49) reported significantly decreased VAS scores from a baseline of 8.16 to 2.39 at 6-month follow up ( $p<0.005$ ), and WHO pain relief was reported in only 67% patients (6 months after treatment). Patients who had PVP plus radiotherapy (n=31) reported decreased VAS scores (from baseline 7.91 to 4.63 at 6 months,  $p<0.005$ ) and had better pain relief, with the highest WHO pain relief reported by 84% of patients. The PVP plus zoledronic acid group (n=38) reported decreased VAS scores (from baseline 8.02 to 3.99 at 6 months,  $p<0.05$ ) but only 66% of patients had WHO pain relief at 6 months. The PVP plus RFA group (n=51) also reported decreased VAS scores from baseline 8 to 4.3 at 6 months ( $p<0.05$ ; Lu 2019).

A retrospective cohort study of 166 patients with spinal osseous metastases (266 tumours) who had RFA combined with vertebral augmentation reported a statistically significant improvement in pain (measured using BPI scores) from baseline 8 to 3 at all follow-up periods ( $p<0.001$  for all; Tomasian 2021).

### **Progression or recurrence of vertebral metastases**

In the systematic review of 15 studies, 13% (51/387) of patients with different tumour histologies reported failure of local tumour control or tumour recurrence between 2.5 months and 5 years follow up (Murali 2021).

In the systematic review of 9 studies, 1 study (Proschek 2009) reported that none of the patients had a local relapse after treatment with RFA alone or RFA in combination with vertebroplasty (Rosian 2018).

In the systematic review of 8 studies (Cazzato 2018), 3 studies reported local tumour control and progression outcomes. One study (Anchala 2004) reported stable disease in 77% of patients at an average 82-day follow up, and local progression was noted in 23% of patients at an average 82-day follow up. Another study (Greenwood 2015) reported locally stable disease in 92% (12/13) of patients at 3 months and 100% at 6-month follow up. In another study (Yang 2017), 67% of patients did not have tumour progression at 2-year follow up.

The retrospective comparative case series of 87 patients with spinal metastatic tumours (125 vertebral bodies) compared RFA combined with bone cement (35 patients with 47 vertebral segments) with bone cement alone (52 patients with 78 vertebral segments). It reported that the tumour recurrence rate in RFA combined with bone cement group was significantly lower than those in the bone cement alone group (11% compared with 31%,  $p < 0.05$ ; Lv 2020).

The retrospective analysis of 26 patients (with 28 spinal metastases) who had RFA plus cement augmentation ( $n=17$ ) or RFA plus radiotherapy ( $n=10$ ) reported that at a median follow up of 8.2 months, local failure (recurrence or progression within the treated vertebral level) was noted in 47% (8/17) of metastases treated with RFA plus cement augmentation compared with 9% (1/11) of metastases treated with RFA plus radiotherapy ( $p=0.049$ ). Time to local failure was 44 weeks in patients who had RFA plus cement augmentation but was not yet reached in those treated with RFA plus radiotherapy ( $p=0.016$ ). There was no difference in distant failure (any disease progression outside of the treated vertebral level) between the 2 groups ( $p=0.70$ ). Time to distant failure was not statistically significantly different between the 2 groups (RFA plus cement augmentation: 11.3 weeks compared with RFA plus radiotherapy: 36.3 weeks,  $p=0.15$ ; Prezzano 2019).

### **Health-related quality of life (HRQoL)**

In the systematic review of 15 studies, 5 studies reported outcomes on HRQoL using different measures (FACT-G7, FACT-BP and ODI). Four studies reported a significant reduction in disability and improvement in HRQoL in the short term (within 3 months follow up). Mid-term (at 3 to 12 months) and long-term outcomes (over 12 months follow up) were not consistent across studies and remained clear (Murali 2021).

In the systematic review of 9 studies, HRQoL was assessed in 2 studies using different measures (FACT-G7, FACT-BP and ODI). In 1 prospective study of 50 patients treated with RFA plus cement augmentation (Bagla 2016), significant

improvements in mean scores for disability and cancer-specific HRQoL from baseline to 3 months were reported (ODI improved from 52.9 to 37.0,  $p < 0.01$ ; FACT-G7 improved from mean 11 to 16.2,  $p = 0.0001$ ; FACT-BP improved from 22.6 to 38.9,  $p < 0.0001$ ). In a study of 16 patients (Proschek 2019), 8 who had RFA alone and 8 who had RFA plus vertebroplasty, improved quality of life was reported (mean ODI scores improved from 64% at baseline to 33%,  $p = 0.06$  at 3 to 6 months follow up in the RFA group; and from 66% at baseline to 35%,  $p = 0.071$  at 15 to 36 months follow up in the RFA plus vertebroplasty group; Rosian 2018, Cazzato 2018).

In the retrospective analysis of 169 patients, the PVP plus RFA group ( $n = 51$ ) reported the lowest ODI scores (decreased from baseline score 71 to 37 at 6 months,  $p < 0.05$ ) whereas the PVP plus zoledronic acid group ( $n = 38$ ) reported the highest ODI scores (from baseline score 68 to 49 at 6 months,  $p < 0.05$ ; Lu 2019).

The prospective case series of 100 patients with painful metastases who had RFA reported a significant improvement for all visits in quality of life measured using European Quality of Life questionnaires (from 0.48 at baseline to 0.69 at 6 months,  $p < 0.006$ ; Levy 2020).

### **Medication use**

The retrospective analysis of 64 patients comparing RFA plus vertebral augmentation ( $n = 34$ ) with kyphoplasty alone ( $n = 30$ ) reported that the 2 RFA groups and the kyphoplasty alone group had similar opioid usage during the first month after the procedure ( $p = 0.82$ ; Jain 2020).

### **Survival**

The retrospective analysis of 26 patients (with 28 spinal metastases) who had RFA plus cement augmentation ( $n = 17$ ) or RFA plus radiotherapy ( $n = 10$ ) reported that median survival in the RFA plus cement augmentation group was 31.9 weeks, compared with 55.3 weeks for the RFA plus radiotherapy group ( $p = 0.0045$ ; Prezzano 2019).

### **Vertebral height**

The retrospective comparative case series of 87 patients with spinal metastatic tumours (125 vertebral bodies) compared RFA combined with bone cement (35 patients with 47 vertebral segments) with bone cement alone (52 patients with 78 vertebral segments). It reported that the postoperative vertebral body height of the 2 groups significantly increased compared with baseline. The difference was statistically significant ( $p < 0.001$ ) but no significant difference was seen between the 2 groups ( $p > 0.05$ ; Lv 2020).

## Safety summary

### RFA-related adverse events

Procedure-related adverse events occurred in 3% (16/583) of patients (range 0% to 11%) in the systematic review of 9 studies. All 9 studies reported complications. Increased pain and numbness (n=6) and post-procedure radicular symptoms and pain (n=5) were the most frequently described procedure-related adverse events. Procedure-related adverse events were not reported in 4 of the studies (Rosian 2018).

Immediate onset of lower extremity paralysis, diminished sensation, and bowel and bladder dysfunction after the RFA procedure was reported in 1 patient. Radiology reports indicated suspicion for thermal injury to the ventral nerve roots at L1. Authors state that this might have been caused by inaccurate placement of the RFA probe or more extensive zones of thermal ablation. The patient had prolonged inpatient rehabilitation, and sensation in the lower extremities was noted at 1-year follow up, but severe neurogenic bladder and bowel dysfunction continued. Electromyography study showed severe membrane instability with no active motor units in L1, L2, L3, L4 and L5, consistent with a conus medullaris or cauda equina injury (Huntoon 2020).

Four adverse events were reported in the case series of 100 patients, of which 2 resulted in hospitalisation for pneumonia and respiratory failure (Levy 2020).

In the retrospective cohort study of 166 patients (266 tumours), the total complication rate related to RFA was 3% (8/266). Major complication (bilateral lower extremity weakness, difficulty in urination, lack of erection, attributed to spinal cord thermal injury during the procedure) was reported in 1 patient. This was treated with high-dose intravenous steroids that only gave slight improvement. Minor complications were reported in 7 patients. These included periprocedural transient radicular pain in 4 patients (resolved after transforaminal steroid injections), delayed secondary lumbar vertebral fracture where vertebral augmentation was not done in 1 patient (treated with analgesics) and asymptomatic spinal cord oedema in 2 patients seen on imaging (resolved without treatment; Tomasian 2021).

### Pain and numbness

Increased pain and numbness were reported in 1% (6/583) of patients in the systematic review of 9 studies with 583 patients (Rosian 2018).

Contralateral lower limb pain and numbness during the procedure was reported in 16% (4/25) of patients in a case series (Yang 2017) included in the systematic review of 8 studies. These symptoms spontaneously resolved with temperature

decrease after RFA (grade 1 complication) in 2 patients, and the other 2 patients needed steroids. One of them experienced heaviness in the legs 1 day after RFA without any subsequent consequence at 1-week follow up (grade 2 to 3a complications; Cazzato 2018).

### **Post-procedure radicular symptoms and pain**

Post-procedure radicular symptoms and pain were reported in 1% (5/583) of patients in the systematic review of 9 studies with 583 patients (Rosian 2018).

Post-procedure radicular pain needing selective nerve block (grade 3a complication) was reported in 1 patient in a case series included in the systematic review of 8 studies (Cazzato 2018).

Postoperative radicular pain was reported in 4 patients in a study (Wallace 2015) included in the systematic review of 8 studies on combined RFA and vertebral stabilisation techniques for patients with palliative treatment of vertebral metastases (Greif 2019).

### **Neural damage**

Transient neural damage related to the high temperature rise during RFA treatment was reported in 1 patient (Nakatsuka 2009) in a systematic review of 8 studies. This resolved 2 days after the procedure with intravenous administration of steroids (Cazzato 2018).

### **Vertebroplasty-related adverse events**

Cement extravasation was reported in 10% of patients in the systematic review of 15 studies. Only 1 patient reported moderate pain and needed surgical removal (Murali 2021).

The rate of vertebroplasty-related adverse events ranged from 4% to 73% in the systematic review of 9 studies with 583 patients. Cement extravasation after vertebroplasty was the most frequently reported adverse event, occurring in 15% (67/437) of patients. It is not clear if these events resulted in any clinically relevant episodes (Rosian 2018).

Bone cement leakage outside the vertebral body occurred in 71% (26/37) of patients at 31 levels in a case series (Gregory 2009) included in the systematic review of 8 studies (Cazzato 2018).

Extravasation after RFA followed by kyphoplasty was reported in 19 patients and anterior leaks were reported in 2 patients in a case series (Lane 2011) included in the systematic review of 8 studies on combined RFA and vertebral stabilisation techniques for patients with palliative treatment of vertebral metastases. Cement

leakage (in 7 and 8 patients) was reported in 2 studies (Munk 2009, Madaeil 2016) included in the same systematic review (Greif 2019).

The retrospective comparative case series of 87 patients with spinal metastatic tumours (125 vertebral bodies) compared RFA combined with bone cement (35 patients with 47 vertebral segments) with bone cement alone (52 patients with 78 vertebral segments). It reported that the permeability of bone cement in the RFA combined with bone cement group was significantly lower than those in the bone cement alone group (6% compared with 21%,  $p < 0.05$ ; Lv 2020).

### **Haematoma**

Haematoma at the site of treatment was reported in 6 patients from 3 studies (Burgard 2014, Toyota 2005, Hoffman 2008) included in the systematic review of 8 studies on combined RFA and vertebral stabilisation techniques for patients with palliative treatment of vertebral metastases (Greif 2019).

### **Mortality**

24% (109/462) of patients died at a median follow up of 1 year across 10 studies in the systematic review of 15 studies. One death was related to postoperative sepsis and 2 studies reported that 13 deaths were unrelated to the RFA procedure. The cause of death was not mentioned in other studies (Murali 2021).

Deaths (5 and 10) were reported in 2 studies in the systematic review of 9 studies (Rosian 2018). There were 30 deaths (attributed to the underlying malignancy and not related to the study procedure) reported in the case series of 100 patients (Levy 2020). There were 27 deaths (related to other causes without spinal cord compression) reported in the retrospective cohort study of 166 patients (Tomasian 2021).

### **Anecdotal and theoretical adverse events**

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts listed the following anecdotal adverse events: cement extravasation into spinal canal or vasculature with pulmonary embolism, thermal burns of spinal cord or nerve root, spinal cord or nerve compression and lung infarction. They considered that the following were theoretical adverse events: visceral damage as a result of inaccurate positioning of needle or RFA probe, adverse effects of anaesthesia and effect on pacemaker function.

## The evidence assessed

### Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases. The following databases were searched, covering the period from their start to 04.05.2021: 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 the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The [inclusion criteria](#) 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.

### Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	<p>Clinical studies were included. Emphasis was placed on identifying good quality studies.</p> <p>Abstracts were excluded when no clinical outcomes were reported, or when the paper was a review, editorial, or a laboratory or animal study.</p> <p>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.</p>
Patient	Patients with painful spinal metastases.
Intervention/test	Radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation.
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 2,447 patients from 4 systematic reviews, 1 prospective case series, 5 retrospective cohort studies and 1 case report. There is an overlap of studies included in the systematic reviews.

Other studies that were considered to be relevant to the procedure but were not included in the main [summary of the key evidence](#) are listed in the [appendix](#).

## Summary of key evidence on radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases

### Study 1 Murali N (2021)

#### Study details

<b>Study type</b>	Systematic review and metanalysis
<b>Country</b>	UK
<b>Study period</b>	Databases searched (Ovid MEDLINE, Embase, CENTRAL) until July 2020. Reference lists of included studies for additional records was also done. Trial registries were also searched.
<b>Study population and number</b>	n= 15 studies (non-randomised: 5 prospective and 10 retrospective studies) 2 of these were comparative studies ( RFA + cement augmentation compared with RFA + radiotherapy; RFA alone versus RFA + cement augmentation) with 725 adult patients with spinal metastases.
<b>Age and sex</b>	Mean age across studies ranged from 59 to 69.6 years. 50% (364/361) female
<b>Patient selection criteria</b>	Inclusion criteria: both randomised and non-randomised comparator study designs with patients aged over 18-years-old; presenting with spinal metastases and have undergone treatment with RFA alone or RFA combined with another modality; reporting pain, disability, HRQoL, complications, tumour control and mortality. Exclusion criteria: Studies that only included data for primary spinal tumours, animals and RFA assisted open surgery were excluded.
<b>Technique</b>	Patients were treated with radiofrequency ablation (RFA) and majority had an additional vertebroplasty treatment. Variety of ablation systems were used in the studies; most commonly used was the STAR® Tumor Ablation System (temperature used for ablation 50 degrees), other

	system used were the CAVITY SpineWand (cold energy temperature 42 degrees), OsteoCool ablation device, RFA-I type multipolar cancer ablation system, Radionics system, Cool-Tip RF ablation system, and CelonPower system.
<b>Follow up</b>	mean follow-up periods varied across studies (range of 24–48 hours [1 study], 2-4 weeks [2 studies] to 60 months)
<b>Conflict of interest/source of funding</b>	None

## Analysis

Follow-up issues: varied follow up across studies. Loss to follow up ranged from 0 to 61%.

Study design issues: systematic review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Sample size was low in included studies and study characteristics were heterogenous in most. Data extraction, study quality and risk of bias was assessed by 2 reviewers using the Risk of Bias In Non-randomised Studies of Interventions (ROBINS-1) tool. Any disagreements were resolved by a third researcher. Studies were considered to be a serious risk of bias because of confounding factors, high dropout rate and subjective measurement of outcomes. Meta-analysis was done for homogenous results, and other results were synthesised narratively..

Study population issues: patients with different tumour histologies were included. Other clinical characteristics were similar in the studies. Most common primary tumours in the studies included were breast, renal and lung neoplasms.

Other issues: There is an overlap of studies between the 4 systematic reviews (Murali 2021, Rosian 2018, Cazzato 2018, Greif 2019). Vertebral cement augmentation was common across all included studies.

## Key efficacy findings

Number of patients analysed: 725

**Pain reduction (n=14 studies)** Assessed using different instruments: VAS and NPRS. Higher scores represented worst pain. Time points short, medium and long-term outcomes were adjusted to 3-5 weeks, 3-4 months and 5-6 months for pooling pain data.

Studies	Follow up	SMD	95% ci	I <sup>2</sup>
8 studies (n=286)	3-5 weeks	2.24	1.55–2.93	89%
4 studies (n=98)	3-4 months	3.00	1.11–4.90	95%
4 studies (n=144)	5-6 months	3.54	1.96–5.11	88%

## RFA in combination with radiotherapy (n=2 studies)

Patients received radiotherapy to the same spinal level within 4 weeks after RFA. A significant reduction in pain was reported in both studies. One study (Prezzano 2019) reported that there was no

significant difference in VAS scores between the RFA plus cement augmentation group versus the RFA plus radiotherapy group ( $p=0.96$ ).

### Progression or recurrence of vertebral metastases/tumour control (n=10)

Overall 13.2% (51/387) patients reported recurrence or failure of local tumour control at 2.5 months to 5 years follow up. In one study (Prezzano 2019) RFA plus radiotherapy group showed better local tumour control (1/11 patients had local failure in RFA plus radiotherapy group versus 8/17 in RFA plus cement augmentation group).

### Survival

In 1 study (Prezzano 2019) median survival was also longer in the RFA plus radiotherapy group compared with RFA plus cement augmentation group (55.3 weeks versus 31.9 weeks).

### HRQoL, n=5 studies)

Assessed across studies using different measures: Functional Assessment of Cancer Therapy-General 7 (FACT-G7) and the Functional Assessment of Cancer Therapy Quality of Life Measurement in Patients with Bone Pain (FACT-BP) and Oswestry Disability Questionnaire (ODI)

Results indicate that RFA is effective in reducing disability/improving HRQoL in the short term but longer-term efficacy is unclear.

Studies	HRQoL measures	Baseline	1 month	3 months
Bagla 2016 (n=50)	FACT-G7 (0-28)	Mean score 11	15.8 ( $p<0.0001$ )	16.2 ( $p<0.0001$ )
Bagla 2016 (n=50)	FACT-BP (0-60)	Mean score 22.6	37.3 ( $p<0.0001$ )	38.9 ( $p<0.0001$ )
Bagla 2016 (n=50)	Modified Oswestry Disability Index (0-100)	Mean score 52.9%	40% ( $p<0.01$ )	37% ( $p<0.01$ )
Sayed	FACT-G7		NS	
–	–	<b>Baseline</b>	<b>3-6 months</b>	<b>15-36 months</b>
Proschek 2009 (n=16)	Oswestry Disability Questionnaire score	RFA group 64% (range 38-84%) RFA plus vertebroplasty group 66% points (range 39-86%)	33%, range 23-38%; $p=0.06$ (RFA group)	35%, range 26-38%; $p=0.071$ (RFA plus vertebroplasty group)
Gervagez	Pain disability index score		% decrease at 6 weeks ( $p<0.015$ )	4% decrease ( $p=0.002$ ) 10% decrease over 6 months ( $p=0.003$ )
Zhao	EORTC QLQ-C30 scale		Physical function ( $p=0.03$ )	

			Emotional function (p=0.003)	
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## Key safety findings

### Adverse events

	% (n)
Cement extravasation after vertebroplasty	10.3% (72 occurrences) In 1 patient it caused pain and needed surgical removal.
All-cause mortality* (in 10 studies) at mean 1 year follow up	23.6% (109/462)
Postoperative sepsis resulting in death (RFA done despite having a subclinical paravertebral abscess which was misdiagnosed)	n=1
Deaths unrelated to the procedure (in 2 studies)	n=13

\*cause of death was not mentioned in many studies. Temporary paraplegia, radicular pain and transient neural damage was reported in some patients.

## Study 2 Rosian K (2018)

### Study details

<b>Study type</b>	Systematic review
<b>Country</b>	Austria
<b>Study period</b>	Databases searched (Ovid MEDLINE, Embase, the Cochrane Library, CRD and PubMed); until December 2016. Manual search for additional records done.
<b>Study population and number</b>	n= 9 studies (4 prospective and 5 retrospective studies) with 583 patients with painful vertebral metastases.
<b>Age and sex</b>	Mean age across studies ranged from 61 to 69.6 years. Sex not reported.
<b>Patient selection criteria</b>	Inclusion criteria: patients with solitary fracture-related vertebral metastases unresponsive to previous curative or symptomatic treatments; RFA with or without vertebroplasty or other add-on therapies (for example, radiation); randomised controlled trials, non-randomised controlled trials, prospective and retrospective case series (with more than 30 patients); published in English or German. Exclusion criteria: multiple publications including subgroup analysis published by the same investigator in a previous article were excluded from the final analysis.
<b>Technique</b>	Patients were treated with radiofrequency ablation (RFA) and 72% (437/583) had an additional vertebroplasty treatment. Vertebroplasty was done if there was a risk of fracture and instability of the bone structure because of tumour removal. Variety of ablation systems were used in the studies; most commonly used were the STAR® Tumor Ablation System (temperature used for ablation 50degrees) and the CAVITY SpineWand (cold energy temperature 42 degrees)
<b>Follow up</b>	mean follow-up periods varied across studies (range of 24–48 hours [1 study], 2-4 weeks [2 studies] to 60 months)
<b>Conflict of interest/source of funding</b>	None

### Analysis

Follow-up issues: Loss to follow up ranged from 0 to 61%. One study of patients with a severe progression of cancer and a long follow-up period reported high losses to follow up.

Study design issues: systematic review was done according to the PRISMA statement. Sample size was low in included studies and study characteristics were heterogenous in most. The review methodology was based on the HTA Core Model and data were analysed according to Grading of Recommendations, Assessment, Development and Evaluation (GRADE). The strength of evidence was found to be “very low” for safety outcomes and could not be assessed for efficacy outcomes because of lack of comparative studies. Data extraction, study quality and risk of bias was done by 2 reviewers using the Institute of Health Economics (IHE) risk of bias checklist for case series. Studies were categorised as having a moderate (n=4) to high risk of bias (n=5). Any disagreements were resolved by a third researcher.

Study population issues: overlap of patients in 2 studies. Adjuvant therapies were given in 2 studies.

Other issues: authors state that comparison of the effectiveness of RFA alone to RFA in combination with vertebroplasty was not done in this review because of low number of patients.

There is an overlap of studies between the 3 systematic reviews (Rosian 2018, Cazzato 2018, Greif 2019).

## Key efficacy findings

Number of patients analysed: 583

**Pain reduction (n=4 studies)** Assessed using different instruments: VAS and NPRS. Higher scores represented worst pain.

Study	Measures	Baseline	1 month	3 months
Bagla 2016 (n=50)	NPRS (0-100)	Mean score 5.9	2.6 (p<0.0001) (n=40)	2.1 (p<0.0001) (n=33)
Nakatsuka 2009 (n=10)	VAS (0-10)	Mean score 7.5 ± 2.7	<b>1 week</b> 2.7 ± 2 (P=.00005)*	
Proschek 2009 (n=16)	VAS (0-10)	<u>RFA group</u> Mean score 7.6 <u>RFA+ cement</u> Mean score 7.9	<b>After treatment</b> <u>RFA group [n=8]</u> 5.5 (p=0.018) <u>RFA+ cement</u> (n=8) <u>5.0</u>	<b>15-36 months</b> <u>RFA group [n=8]</u> 4.0 (p<0.008) <u>RFA+ cement</u> (n=8) 3.5 (p<0.005)
Georgy 2007 (n=15)	VAS (0–10-point scale)	Pain scores range 6 to 10	Range 0-5	Pain relief in 87% (13/15) <b>at 2-4 weeks</b>

\*in all patients who had RFA alone (n=4) or RFA+ cement (n=6). Local pain relief lasted in 90% (9/10) of patients during survival period.

## Progression or recurrence of vertebral metastases

One study (Proschek 2009) reported that none of the patients had a local relapse after treatment with RFA or RFA in combination with vertebroplasty.

## HRQoL, n=2 studies)

Assessed across studies using different measures: Functional Assessment of Cancer Therapy-General 7 (FACT-G7) and the Functional Assessment of Cancer Therapy Quality of Life Measurement in Patients with Bone Pain (FACT-BP) and Oswestry Disability Questionnaire (ODI)

Studies	HRQoL measures	Baseline	1 month	3 months
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Bagla 2016 (n=50)	FACT-G7 (0-28)	Mean score 11	15.8 (p<0.0001)	16.2 (p<0.0001)
Bagla 2016 (n=50)	FACT-BP (0-60)	Mean score 22.6	37.3 (p<0.0001)	38.9 (p<0.0001)
Bagla 2016 (n=50)	Modified Oswestry Disability Index (0-100)	Mean score 52.9%	40% (p<0.01)	37% (p<0.01)
–	–	<b>Baseline</b>	<b>3-6 months</b>	<b>15-36 months</b>
Proschek 2009 (n=16)	Oswestry Disability Questionnaire score	<u>RFA group</u> 64% (range 38-84%) <u>RFA plus vertebroplasty group</u> 66% points (range 39-86%)	33%, range 23-38%; p=0.06 (RFA group)	35%, range 26-38%; p=0.071 (RFA plus vertebroplasty group)

## Key safety findings

### Complications

Adverse events	% (n)
Major complications (procedure related)	0
Overall complications	30.2 (78/583) Ranged from 4.3 to 40%
Adverse events (procedure-related or non-procedure-related)	18 (105/583) ranged from 5.6% to 11.1% in each study.
Procedure-related adverse events	2.74 (16/583) range 0 to 11%
Non-procedure-related adverse events	15.2 (89/583) range 4.3 to 73%
Increased pain and numbness	1 (6/583)
Post-procedure radicular symptoms and pain	0.8 (5/583)
Rate of adverse events not RFA-related (but vertebroplasty-related)	ranged from 4.3% to 73.0%
Cement extravasation after vertebroplasty	15.3% (67/437)
Mortality (reported in 2 studies)	5 to 10 deaths

Procedure-related adverse events were not reported in 4 studies. 1 study did not report any adverse events.

## Study 3 Cazzato (2018)

### Study details

<b>Study type</b>	Systematic review
<b>Country</b>	France
<b>Study period</b>	Databases searched (Ovid MEDLINE, Embase, the Cochrane CENTRAL and PubMed); until March 2017. conference abstracts were also searched.
<b>Study population and number</b>	n= 8 studies (4 prospective and 4 retrospective studies) with 261 patients with painful spinal metastases (340 vertebral lesions) Lesions were located mainly in lumbar or thoracic area. <u>Metastases origin</u> from breast, lung, and renal cancers. <u>previous treatments</u> (n=4) chemotherapy, radiation therapy, surgery, or a combination.
<b>Age and sex</b>	Mean age across studies ranged from 59 to 69.6 years. Sex not reported.
<b>Patient selection criteria</b>	Inclusion criteria: randomised controlled or non-randomised studies with a prospective or retrospective design; adults with spinal metastasis; treated with RFA alone or in combination/ comparison with other treatments; studies reporting patients' pain before and after RFA; and English-language studies. Exclusion criteria: multiple publications were excluded.
<b>Technique</b>	Patients were treated with radiofrequency ablation (RFA) and 239 had cement augmentation (during RFA in 40-60%, or in 95.8% of treated vertebrae in the same treatment session). 4 patients underwent cement augmentation after a few days or months. Variety of ablation systems were used in the studies (STAR Tumor Ablation System, the CAVITY SpineWand, RITA, CELON Power System, Cool-Tip RF) Lumbar ones were the most commonly treated. Mean ablation time ranged between 6 and 9.75 min. across 4 studies. Ablation zone ranged from 1-8 cm. Bipolar RFA was applied in 4 out of the 8 studies.
<b>Follow up</b>	mean follow-up periods varied across studies (ranged from 2-4 weeks [2 studies] to mean 20 months)
<b>Conflict of interest/source of funding</b>	Authors are proctors for Medtronic and Galil Medical.

### Analysis

Study design issues: systematic review was done following the guidelines of the Cochrane Collaboration for systematic reviews of interventions. Studies were small case series with different treatment strategies. 2 reviewers selected studies and extracted data; any disagreements were resolved by consensus. Study quality and risk of bias was not assessed because of heterogeneity in study designs and authors also thought there was no single suitable critical appraisal tool for all studies.

Study population issues: sample size ranged between 10 and 92 patients across studies. Overlap of patients in 2 studies.

IP overview: Radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases

Other issues: There is an overlap of studies between the 3 systematic reviews (Rosian 2018, Cazzato 2018, Grief 2019).

## Key efficacy findings

Number of patients analysed: 261

**Pain assessment** Assessed using different instruments: VAS and NPRS. Higher scores represented worst pain.

Study	Intervention	Pain scale	Baseline	Postoperative	Mean difference (p value)	Mean pain reduction %	Pain relief %
Bagla 2016 (n=50)	RFA + cement augmentation	NRS (0-100)	5.9	3.7 (discharge)	2.2 (<0.0001)	37	-
Bagla 2016 (n=50)	RFA + cement augmentation	NRS (0-100)	5.9	2.6 (1 month, n=40)	3.3 (<0.0001)	56	-
Bagla 2016 (n=50)	RFA + cement augmentation	NRS (0-100)	5.9	2.1 (3 months, n=34)	3.8 (<0.0001)	64	-
Gronemeyer 2002 (n=10)	RFA+ cement augmentation	VAS (0-10)	5.9	2.6 (mean 5.8 months)	3.3	56	-
Nakatsuka 2009 (n=10)	RFA (all patients)	VAS	7.5	2.7 (1 week)	4.8 (0.00005)	64	-
Nakatsuka 2009 (n=10)	RFA alone (n=4)		4.3	1.7 (1 week)	2.6 (0.0004)	60	
Nakatsuka 2009 (n=10)	RFA + cement augmentation (n=6)		6.6	1.7 (1 week)	4.9 (0.003)	74	-
Proschek 2009 (n=16)	RFA alone (n=8)	VAS	7.9	4 (15-36 months)	3.9 (0.008)	49	-
Proschek 2009 (n=16)	RFA +cement augmentation (n=8)		7.6	3.5 (15-36 months)	4 (0.005)	52	-
Greenwood 2015 (n=21)	RFA +cement augmentation	NRS	8	2.9 (4 weeks)	5.1 (<0.0003)	63	-
Anchala 2004 (n=92)	RFA+ vertebral augmentation	VAS	7.5	2.2 (1 month, n=83)	5.26 (<0.0001)	70	-

Anchala 2004 (n=92)	RFA+ vertebral augmentation	VAS	7.5	1.7 (6 months, n=9)	5.7 (0.009)	76	-
Georgy 2009 (n=37)	RFA+ vertebral augmentation	VAS	8	4 (2-4 weeks)	4	50	89.5
Yang 2017 (n=25)	RFA+ cement augmentation	VAS					100 Mean 7.8 months

## Pain medication

Pain medication intake following RFA was reported by 2 studies. In 1 study (Greenwood 2015) reported that 62% of patients reduced their intake, 19% increased intake and 19% kept it stable compared with baseline. Another study (Anchala 2004) reported that 54% of patients reduced their intake, 16% increased it and 30% kept it stable at the 4-week follow up.

## Local tumour control (n=3 studies)

-	Stable disease	Progression
Anchala 2004	76.9% (70/92) at average 92 days after RFA	23.1% (22/92) at average 82 days
Greenwood 2015	92.3 (12/13) at 3 months 100% (at 6 months)	-
Yang 2017	66.67% (at 2 years)	-

## HRQoL, n=2 studies

Assessed across studies using different measures: Functional Assessment of Cancer Therapy-General 7 (FACT-G7) and the Functional Assessment of Cancer Therapy Quality of Life Measurement in Patients with Bone Pain (FACT-BP) and Oswestry Disability Questionnaire (ODI)

Studies	HRQoL measures	Baseline	1 month	3 months
Bagla 2016 (n=50)	FACT-G7 (0-28)	Mean score 11	15.8 (p<0.0001)	16.2 (p<0.0001)
Bagla 2016 (n=50)	FACT-BP (0-60)	Mean score 22.6	37.3 (p<0.0001)	38.9 (p<0.0001)
Bagla 2016 (n=50)	Modified Oswestry Disability Index (0-100)	Mean score 52.9%	40% (p<0.01)	37% (p<0.01)
Proschek 2009 (n=16)	Oswestry Disability Questionnaire score	<b>Baseline</b>	<b>3-6 months</b>	<b>15-36 months</b>
Proschek 2009 (n=16)	Oswestry Disability Questionnaire score	<u>RFA group</u> 64% (range 38-84%)	33%, range 23-38%; p=0.06 (RFA group)	35%, range 26-38%; p=0.071 (in both RFA alone and RFA plus

		<u>RFA plus vertebroplasty group</u> 66% points (range 39-86%)		vertebroplasty groups)
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## Key safety findings

### Complications

-	% (n)
Grade IV-V complications	0
Transient neural damage (grade II) related to high temperature rise during RFA (resolved 2 days after the procedure with intravenous administration of steroids)	n=1 (Nakatsuka 2009)
Contralateral lower limb pain and numbness during RFA -grade I (2 spontaneously resolved with temperature decrease and 2 needed steroids, but 1 developed heaviness in legs 1 day after treatment which resolved at 1 week [grade II-IIIa])	16% (4/25) (Yang 2017)
Bone cement leakage outside the vertebral body (Gregory 2009)	70.5% (26/37) 31 levels
Radicular pain because of cement leakage needing selective nerve block (grade IIIa)	(1/26)

## Study 4 Greif (2019)

### Study details

<b>Study type</b>	Systematic review
<b>Country</b>	USA
<b>Study period</b>	PubMed was searched and bibliographies of selected articles were examined for additional studies. Search dates not reported.
<b>Study population and number</b>	n= 8 retrospective studies with 265 patients with palliative treatment of vertebral metastasis. Combined tumour treatment with vertebral stabilisation techniques <ol style="list-style-type: none"> <li>1. RFA followed by percutaneous kyphoplasty [PKP] (n=4 studies, 110 patients, 142 vertebrae),</li> <li>2. RFA followed by vertebroplasty (n=4 studies, 155 patients, 172 vertebrae)</li> </ol>
<b>Age and sex</b>	not reported.
<b>Patient selection criteria</b>	Inclusion criteria: randomised controlled trials and retrospective studies in English using a multidisciplinary approach of tumour treatment and vertebral stabilisation. Exclusion criteria: nonhuman studies, case reports, narrative reviews, clinical reports without technical outcomes, and studies involving patients with osteoporotic, traumatic, or metastatic vertebral compression fractures were excluded.
<b>Technique</b>	<u>RFA followed by PKP</u> (n=4 studies, 110 patients, 142 vertebrae) Mean RFA procedure time ranged from 9 to 47 minutes. Mean ablation temperature 95°C Mean cement used ranged from 6.1 to 7.9 ml. <u>RFA followed by vertebroplasty</u> (n=4 studies, 155 patients, 172 vertebrae) Mean RFA time ranged from 4.1 to 8.6 minutes. Mean ablation temperature ranged 71.8°C to 95°C. Mean cement used ranged from 2.9 to 9.1 ml
<b>Follow up</b>	mean follow-up periods varied across studies (3 days to 15 months).
<b>Conflict of interest/source of funding</b>	No conflicts of interest.

### Analysis

Follow-up issues: majority of the studies had a limited follow up.

Study design issues: systematic review was done PRISMA guidelines for retrospective studies. There is a lack of standard protocol, outcomes assessed among studies within combined treatments, including different ranges of follow-up times. Quality assessment of studies was not done.

Other issues: outcomes from studies related to radiotherapy combination techniques: radiotherapy followed by PKP (n =1), radiotherapy followed by vertebroplasty (n = 3), PKP followed by radiotherapy (n = 4), and vertebroplasty followed by radiotherapy (n =2) were not reported in this overview as it is outside the remit. There is an overlap of studies between the 3 systematic reviews (Rosian 2018, Cazzato 2018, Greif 2019).

## Key efficacy findings

Number of patients analysed: 265

### Pain assessment

#### RFA followed by percutaneous kyphoplasty (PKP; 4 studies)

Study	Preoperative pain	Postoperative pain	Last follow up	Change in VAS
Zheng 2014 (n=26)	7.69 ±1.12	6.62 ±1.02	2.96± 0.92 (6 months)	4.73
Lane 2011 (n=36)	7.2±1.69	NM	3.4±1.6 (1 week)	3.8
Munk 2009 (n=19)	7.9±1	NM	3.82±3.82 (6 weeks)	4.08
Burgard 2014 (n=29)	NM	NM	NM	NM

#### RFA followed by vertebroplasty (4 studies)

Study	Preoperative pain	Postoperative pain	Last follow up	Change in VAS
Wallace 2015 (n=105)	8.0	3.9	2.9 (4 weeks)	5.1
Toyota 2005 (n=17)	6.3	NM	2.4 (3 days)	3.9
Madaelil 2016 (n=11)	8	NM	3 (1 month)	5
Hoffman 2008 (n=22)	8.5	5.5	3.5 (15 months)	5

## Key safety findings

### RFA followed by percutaneous kyphoplasty (PKP; 4 studies)

-	n
Extravasation	19 (Lane 2011)
Anterior leaks	2 (Lane 2011)
Cement leakage	7 (Munk 2009)
Local hematoma	2 (Burgard 2014)
Pain	2 (Burgard 2014)
Oxygen saturation decrease	1 (Burgard 2014)
Increased paresis	1 (Burgard 2014)

### RFA followed by vertebroplasty (4 studies)

-	n
Postoperative radicular pain	4 (Wallace 2015)
Hematoma	4 (2 in Toyota 2005, 2 in Hoffman 2008)
Cement leaks	8 (Madaelil 2016)

## Study 5 Levy 2020

### Study details

<b>Study type</b>	Prospective case series (NCT03249584: OPuS One Study)
<b>Country</b>	Global multicentre study (USA, Canada, Europe)
<b>Recruitment period</b>	October 2017- March 2019
<b>Study population and number</b>	n=100 patients with painful metastatic bone disease <u>metastatic tumour location</u> : 87 involving thoracolumbar spine and 13 around pelvis and/or sacrum.
<b>Age and sex</b>	Mean age 64.6 years (range 30-89 years); 56% (56/100) female
<b>Patient selection criteria</b>	<u>Inclusion criteria</u> : patients at least 18 years of age with metastatic tumours of the thoracic and/or lumbar vertebral body/bodies, peri-acetabulum, iliac crest, and/or sacrum and were candidates for radiofrequency ablation (RFA); had osteolytic bone metastases confirmed by imaging or biopsy. <u>Exclusion criteria</u> : pure osteoblastic tumours, worst pain rated as < 4 on a scale from 1 to 10 in the past 24 hours, more than 2 painful sites requiring treatment, or Karnofsky performance score < 40.
<b>Technique</b>	Radiofrequency ablation (RFA) for palliative treatment with the OsteoCool RF Ablation System done using manufacturer algorithm. In the thoracolumbar spine, the vertebral bodies were accessed by a transpedicular or parapedicular approach. A total of 134 ablations were done under imaging guidance. 68 patients had a single target site treated and 32 had multiple sites treated. 85% of RFA approaches were bilateral (2 probes) in the thoracic and lumbar vertebrae. Polymethyl methacrylate [PMMA] augmentation was done in the majority of cases (97%; 130/134). After RFA patients received chemotherapy (43%), steroids (39%), and osteoporosis medications (38%).
<b>Follow up</b>	6 months
<b>Conflict of interest/source of funding</b>	Medtronic sponsored the study and analysed the data collected by individual sites. Few authors were paid consultants for different companies and received personal fees or research funding.

### Analysis

Follow-up issues: Follow up was done after RF ablation, 3 days, 1 week, and 1, 3, and 6 months. Around 40 patients discontinued the study within 6-month follow up and 2 patients after 6 months. The reasons for this included deaths (n=30), withdrawal by patients (n=9), loss to follow up (n=2), and biopsy diagnosis of non-malignant bone tumour (n=1).

Study design issues: study was done in 14 centres, patient outcomes (pain, function and quality of life) were measured before and after RFA using validated self-administered 12 item Brief Pain Inventory and European QOL 5 dimension questionnaires. Oral opioid agent use and adverse events were collected. The primary objective was to achieve a minimal clinically important difference in pain, as measured by the BPI, (defined by a 2-point change from baseline to postprocedural follow up).

Study population issues: 71 patients had concurrent treatments (medications, steroids, chemotherapy) at baseline and only 5 patients received radiation at baseline.

Other issues: PMMA augmentation was used with RFA ablation as the procedure was done in locations where mechanical stabilisation is important.

## Key efficacy findings

Number of patients analysed: 100

All ablations were technically successful (RFA was delivered to the targeted tumour), and 97% were followed by cementoplasty.

## Clinical outcomes

	Baseline (n=100)	Day 3 (n=94)	1 week (n=89)	1 month (n=64)	3 months (n=46)	6 months (n=22)
BPI worst pain (mean score $\pm$ SD), 95% CI, p value	8.2 $\pm$ 1.7	5.6 $\pm$ 2.7 (-3.1 to -1.9, p<0.001)	4.7 $\pm$ 2.9 (-3.9 to -2.7, p<0.001)	3.9 $\pm$ 3.0 (-4.7 to -3.1, p<0.001)	3.7 $\pm$ 2.9 (-5.1 to -3.1, p<0.001)	3.5 $\pm$ 3.2 (-6.2 to -3.5, p<0.001)
Subjects with $\geq$ 2-point change (%)	-	59	66	75	83	86
BPI average pain (mean score $\pm$ SD), 95% CI, p value	6.0 $\pm$ 2.1	4.0 $\pm$ 2.3 (-2.5 to -1.4, p<0.001)	3.3 $\pm$ 2.3 (-3.3 to -2.1, p<0.001)	2.8 $\pm$ 2.2 (-3.4 to -2.1, p<0.001)	2.8 $\pm$ 2.4 (-3.6 to -2.1, p<0.001)	2.9 $\pm$ 2.5 (-4.4 to -2.1, p<0.001)
Subjects with $\geq$ 2-point change (%)	-	51	62	67	74	77
BPI pain interference score (mean score $\pm$ SD), 95% CI, p value	6.1 $\pm$ 2.3	4.1 $\pm$ 2.8 (-2.4 to -1.4, p<0.001)	3.1 $\pm$ 2.7 (-3.5 to -2.3, p<0.001)	2.9 $\pm$ 2.5 (-3.5 to -2.2, p<0.001)	2.8 $\pm$ 2.7 (-3.9 to -2.1, p<0.001)	2.5 $\pm$ 2.5 (-4.7 to -2.6, p<0.001)
EQ-5D index (mean score $\pm$ SD), 95% CI, p value	0.48 $\pm$ 0.32	0.58 $\pm$ 0.33 (0.03-0.15, p=0.0018)	0.64 $\pm$ 0.28 (0.10-0.21, p<0.001)	0.69 $\pm$ 0.21 (0.10-0.24, p<0.001)	0.66 $\pm$ 0.26 (0.05-0.25, p=0.0021)	0.69 $\pm$ 0.24 (0.09-0.34, p=0.0006)

## Key safety findings

4 adverse events were reported, of which 2 resulted in hospitalisation for pneumonia and respiratory failure, respectively. 30 deaths were reported during the study (with 29 within 6 months). All deaths were attributed to underlying malignancy and not related to RFA.

## Study 6 Tomasian 2021

### Study details

<b>Study type</b>	Retrospective cohort study
<b>Country</b>	USA (single centre)
<b>Recruitment period</b>	January 2012 to August 2019
<b>Study population and number</b>	N=166 patients with spinal osseous metastases (266 tumours). <u>Location of treated tumours:</u> lumbar 51.5% (137/266), thoracic 41.3% (110/266), sacral 6.8% (18/266), and cervical 0.4% (1/266) <u>Radiotherapy before RFA:</u> 69 patients (108/266 tumours) had EBRT or SBRT ranging from 17 months to 1 month before RFA
<b>Age and sex</b>	Median age 61 years (range 52-69); 53.6% (89/166) female
<b>Patient selection criteria</b>	<u>Inclusion criteria:</u> patients unable to undergo radiation therapy, or tumour progression at sites previously treated with radiation therapy, resistance to chemoradiotherapy, and substantial pain (brief pain inventory score of at least 4); selected by a multidisciplinary team (of radiation and medical oncologists, interventional musculoskeletal radiologists, and oncologic spine surgeons) and treated to achieve local tumour control and pain palliation. <u>Exclusion criteria:</u> correctable coagulopathy, active infection, entirely osteoblastic metastases, pathologic compression fracture with spinal instability, or metastases resulting in spinal cord compression.
<b>Technique</b>	Percutaneous image guided radiofrequency ablation (RFA) combined with or without vertebral augmentation of vertebral metastases was done mainly using conscious sedation. STAR Tumor ablation system used. Vertebral body was accessed by a bipedicular approach. RFA was done according to a sequential bipedicular protocol (in 71% [189/266]) or a simultaneous bipedicular protocol (in 28.9% [77/266]). For both, the ablations were done anteriorly and then the posterior vertebral body and pedicles were treated aligning with the international spinal radiosurgery consortium consensus recommendation. Vertebral augmentation was done with the StabiliT vertebral augmentation system. Cement was injected using the same working cannulas used for RFA in 91% (242/266) of tumours. Vertebral augmentation was not done if they were small sacral tumours (<2-3 cm) or involved only in the posterior vertebral elements or lower sacral segments. Passive thermal protection with a decrease of moderate to mild sedation during ablation along the posterior vertebral body was applied in cases done under conscious sedation
<b>Follow up</b>	6 months (median imaging follow up was 202 days, IQR 142-466 days)

<b>Conflict of interest/source of funding</b>	One author received consultation fees and the other authors declared that there are no conflicts of interest
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## Analysis

Study design issues: Retrospective, single-centre, observational large cohort study. Electronic medical and telephone records, postprocedural imaging records were retrospectively reviewed. Local tumour control rate (agreed by 2 radiologists using imaging records) and pain (using Brief pain inventory scores) were assessed at 1 week, 1, 3, and 6 months follow up. Complications were categorised as major (3-4) or minor (1-2) according to common terminology criteria for adverse events (CTCAE) version 5.0. Complications were also further classified as immediate (within 24 hours), periprocedural (within 30 days) or delayed (after 30 days).

Study population issues: heterogenous patient population with various tumour histologies, sizes, and location were included in the study.

Other issues: a subgroup of patients in this study have been included in other primary studies included in the systematic reviews added to the overview.

## Key efficacy findings

- Number of patients analysed: 166 (266 tumours)
- All procedures were technically successful.

## Clinical outcomes

<b>Overall local tumour control rate</b>	<b>78.9% (180/228 tumours)</b>
Sequential RFA group	76.% (126/165 tumours)
Simultaneous RFA	85.7% (54/63 tumours)*
<b>BPI score</b>	
Pre-procedural score (median)	8±1
Postprocedural score (median, at 1 week, 1,3, 6 months)	3±1^

\*Compared with sequential RFA the difference was not significant (p=0.27).

^ Compared with baseline the difference was significant for all follow-up periods (p<0.001).

## Key safety findings

### Complications

<b>Complications related to RFA</b>	<b>–</b>
<b>Total complication rate</b>	<b>3% (8/266)</b>

<b>Major complication rate</b>	<b>0.4% (1/266)</b>
Bilateral lower extremity weakness, difficulty in urination, inability to have an erection 3 days after the procedure (grade 3, attributed to spinal cord thermal injury during the procedure, treated with high-dose intravenous steroids resulting in only slight improvement of symptoms)	n=1
<b>Minor complication rate</b>	<b>2.6% (7/266)</b>
Periprocedural transient radicular pain in the adjacent nerve distribution (grade 2, resolved after transforaminal steroid injections)	n=4
Delayed secondary lumbar vertebral fracture (because of osseous weakening in which vertebral augmentation was not done, grade 2, treated with analgesics)	n=1
Asymptomatic spinal cord oedema along treated area (noted on MRI at 3-4 months, resolved without treatment)	n=2
<b>Other complications not related to RFA</b>	
Deaths (related to other causes without spinal cord compression)	27
Progression of metastatic disease (entered hospice care)	5
Surgery (posterior spinal fusion) after RFA	3% (5/166)

## Study 7 Lv N 2020

### Study details

<b>Study type</b>	Retrospective comparative case series
<b>Country</b>	China
<b>Recruitment period</b>	January 2016 to December 2018
<b>Study population and number</b>	N=87 patients with spinal metastatic tumours (125 vertebral bodies). Group A (treated with RFA combined with bone cement PVP/PKP) n=35 (with 47 vertebral segments [26 thoracic and 21 lumbar]) Group B (treated with bone cement only) n=52 patients (with 78 vertebral segments [42 thoracic and 36 lumbar])
<b>Age and sex</b>	Group A: mean age 51.4 ± 9.3 years; 40% (14/35) female Group B: mean age 52.2 ± 8.5 years; 38% (20/52) female
<b>Patient selection criteria</b>	<u>Inclusion criteria</u> : definite diagnosis of spinal metastatic cancer (pathological or cytological); structurally intact posterior margin of the vertebral body without nerve root symptoms; thoracic and lumbar vertebral body lesions (of osteolytic or mixed destruction); willingness to undergo the procedure and relatively treatment compliance. <u>Exclusion criteria</u> : incomplete structure of the posterior margin of the vertebral cortex or infiltration of tumour into the dura, accompanied by nerve root symptoms; osteogenic lesions; terminal patients; severe cardiopulmonary disease or coagulation dysfunction.
<b>Technique</b>	<u>Group A (Radiofrequency ablation (RFA) combined with PKP or PVP)</u> : RFA was done on the anterior half of the vertebral body at 90°C, and on the posterior part at 75°C and the treatment time was 4–6 min. It was done from different angles, and the electrode was removed slowly. After RFA, PVP or PKP was done. <u>Group B (Bone cement alone)</u> : directly performed PVP or PKP surgery and injected bone cement into the diseased vertebra.
<b>Follow up</b>	6 months
<b>Conflict of interest/source of funding</b>	The authors declared that there are no conflicts of interest.

### Analysis

Follow-up issues: short-term follow up.

Study design issues: Retrospective, single-centre, small observational cohort study. Retrospectively analysed medical records. Outcomes such as pain (on a visual analogue scale), function (on an Oswestry disability index), quality of life, vertebra height and bone cement leakage (on X rays), postoperative tumour recurrence, and complications were assessed 3 days and 1 and 6 months.

Study population issues: primary cancer and tumour location was not similar in both groups. No statistically significant difference was observed between the 2 groups in terms of age, gender, and disease types.

## Key efficacy findings

- Number of patients analysed: 87 patients with spinal metastatic tumours (125 vertebral bodies).

### Clinical outcomes

–	Group A RFA plus bone cement (n=35)	Group B Bone cement alone (n=52)	P value
<b>VAS scores</b>	–	–	–
Baseline	7.52 ± 1.44	7.63 ± 1.52	0.736
3 days	2.79 ± 0.53*	2.88 ± 0.51*	0.429
1 month	2.14 ± 0.40*	2.28 ± 0.43*	0.130
6 months	2.23 ± 0.46*	3.15 ± 0.52*	<0.001
<b>ODI scores</b>	–	–	–
Baseline	77.52 ± 8.84	76.65 ± 8.12	0.638
3 days	48.79 ± 6.45*	49.42 ± 6.94*	0.671
1 month	43.23 ± 5.69*	45.08 ± 6.43*	0.172
6 months	46.46 ± 6.46*	52.15 ± 7.52*	< 0.001
<b>Anterior height of vertebral body</b>	–	–	–
Baseline	18.53 ± 3.84 <sup>^</sup>	18.66 ± 3.24	0.840
Postoperative	24.23 ± 4.25 <sup>^</sup>	23.89 ± 4.34	0.670
<b>Intermediate height of vertebral body</b>	–	–	–
Baseline	24.12 ± 3.88 <sup>^</sup>	24.32 ± 3.52	0.768
Postoperative	28.18 ± 4.25 <sup>^</sup>	27.33 ± 4.39	0.291

\*Compared with baseline the difference was p<0.05.

<sup>^</sup> Compared with baseline the difference was p<0.001.

## Key safety findings

### Complications

–	Group A RFA plus bone cement (n=35)	Group B Bone cement alone (n=52)	P value
Bone cement leak	6.4% (3/35)	20.5% (16/52)	0.033
Tumour recurrence	11.4% (4/35)	30.8% (16/52)	0.036

## Study 8 Jain S (2020)

### Study details

<b>Study type</b>	Retrospective cohort study
<b>Country</b>	USA (one centre)
<b>Recruitment period</b>	2011-2017
<b>Study population and number</b>	n= 64 patients with painful spinal metastases RFA (Spine star) with vertebral augmentation (n=22) RFA (OsteoCool) with vertebral augmentation (n=12) Kyphoplasty alone (n=30)
<b>Age and sex</b>	Mean age 62.6 years; male 56% (36/64)
<b>Patient selection criteria</b>	Inclusion criteria: patients greater than 18 years old having metastatic vertebral compression fracture involving the thoracolumbar spine. Exclusion criteria consisted of non-pathologic osteoporotic compression fractures, metastasis in cervical spine, or previous radiofrequency ablation (RFA) treatment. patients with coagulopathy greater than 1.4 and platelet count less than 50,000, or an active infection either systemically or locally.
<b>Technique</b>	Patients were treated with radiofrequency ablation (RFA) using 2 ablation systems (STAR Tumor Ablation System, the CAVITY SpineWand). RFA was done at 70°C for 5–15 min with subsequent cement injection. Kyphoplasty alone was done in 30 cases.
<b>Follow up</b>	2 weeks
<b>Conflict of interest/source of funding</b>	Authors declare that they have no conflict of interest.

### Analysis

Follow-up issues: very short follow-up period limited to 2 weeks.

Study design issues: small retrospective analysis of medical records, pain scores (using VAS score) immediately and between 7-14 days and opioid use after 1 month were assessed and compared between RFA systems and kyphoplasty alone.

Study population issues: The demographic characteristics between the treatment arms were similar. Mean age of diagnosis 62 years, diseases leading to vertebral metastases were multiple myeloma (20.3%) and lung adenocarcinoma (12.5%). The most common previous treatment modality was chemotherapy and radiotherapy.

### Key efficacy findings

Number of patients analysed: 64 (RFA systems 34 versus kyphoplasty alone 30)

**Pain scores (assessed on a VAS 0 to 10) and opioid use**

–	RFA SpineStar	RFA OsteoCool	Kyphoplasty alone
Preoperative pain score	6.9	6	6.3
Postoperative pain score	2.7	1.7	2.3
Between 7-14 days pain score	3.3	3.28	3.69
Opioid use	50% (11/22)	41.7 (5/12)	30% (9/30)

**Difference of square means analysis between kyphoplasty and the 2 RFA systems (SpineStar and OsteoCool)**

–	T value (SE)	P value
Postoperative day 0	–	–
Kyphoplasty versus OsteoCool	0.49 (1.08)	0.99
Kyphoplasty versus SpineStar	1.63 (0.49)	0.79
OsteoCool versus SpineStar	0.86 (1.12)	0.99
Day 1-14	–	–
Kyphoplasty versus OsteoCool	0.17 (1.12)	1
Kyphoplasty versus SpineStar	1.76 (1.02)	0.72
OsteoCool versus SpineStar	1.67 (1.12)	0.76
30 days and above	–	–
Kyphoplasty versus OsteoCool	1.07 (1.33)	0.98
Kyphoplasty versus SpineStar	2.76 (1.17)	0.14
OsteoCool versus SpineStar	1.23 (1.48)	0.95

Chi-squared analysis reveals no statistical difference in opioid usage among the 3 groups ( $p = 0.82$ ).

## Study 9 Prezzano KM (2019)

### Study details

<b>Study type</b>	Retrospective cohort study
<b>Country</b>	USA (one centre)
<b>Recruitment period</b>	2016-2017
<b>Study population and number</b>	n= 26 patients with 28 painful spinal metastases (in thoracic/lumbar spine) treated with RFA plus cement augmentation (n=17 [17 lesions]) versus combined RFA with radiation therapy (RT, n=10 [11 lesions])
<b>Age and sex</b>	Median age 63 years (no significant difference between 2 groups; p=0.57); male
<b>Patient selection criteria</b>	Inclusion criteria: all patients who underwent RFA for painful spinal metastases, regardless of metastatic disease burden. Exclusion criteria: patients treated with RT alone.
<b>Technique</b>	<u>RFA (n=11 lesions)</u> OsteoCool ablation device was used at more than 60 C. Vertebral augmentation was done after RFA using balloon-assisted techniques with the Kyphon system. Polymethyl methacrylate was injected. At a median of 11 months post-RFA, 3 lesions were treated with radiotherapy for local progression. <u>Radiotherapy (n=11 lesions)</u> majority of the patients were treated using 3-dimensional conformal radiotherapy (3D-CRT, with a median dose of 30 Gy in 3 Gy daily fractions). Some were treated using volumetric-arc therapy, or stereotactic body radiotherapy (SBRT) (in 2 cases at 28 days post-RFA, both having 35 Gy in 5 fractions). 10 lesions were treated at a median of 28 days and 1 lesion was treated 1 day before RFA.
<b>Follow up</b>	12 weeks
<b>Conflict of interest/source of funding</b>	Authors declare that they have no conflict of interest.

### Analysis

Study design issues: small retrospective analysis. Patients were treated with varying treatment schedules (the dose, radiotherapy techniques used, and the treatment timing; that is, during or after RFA). Some patients were treated with concurrent systemic therapy. Local failure, distant failure, and overall survival were compared and Kaplan-Meier statistics were calculated.

Study population issues: There was uneven allocation of primary tumour histologies between the 2 groups (more patients with lung primaries were treated with RFA alone and more patients with breast primaries were treated with combination RFA plus RT). The majority of patients had narcotic analgesics (of varying doses) at initial treatment and were similar between groups (p=0.70).

### Key efficacy findings

Number of patients analysed: 27 (28 lesions)

**Pain scores (assessed on a VAS 0 to 10)**

–	Baseline (mean±SD)	3 weeks (mean±SD)	12 weeks (mean±SD)
RFA plus cement augmentation	4.2	2.7±2.9 (p<0.0001)	2.1
RFA plus radiotherapy	4.5±3.07	2.7±2.9 (p<0.0001)	1.6±2.6 (p<0.0001)

There is no significant difference in pain scores between groups (p=0.96).

**Local failure, distant failure, and survival (median follow up 8.2 months; Kaplan-Meier statistics)**

–	RFA plus cement augmentation	RFA plus RT	P value
Local failure <sup>^</sup> %	47 (8/17)	9 (1/11)*	0.049
Time to local failure (weeks)	44	Not reached	0.016
Distant failure	NR	NR	0.70
Time to distant failure (weeks)	11.3	36.3	0.15
Survival (median, weeks)	31.9	55.3	0.0045

\* in a patient treated with 30 Gy in 10 fractions, 6 days after RFA.

Of the 3 lesions treated with RT for local progression after RFA alone, there was no local failure.

<sup>^</sup> All local failure occurred in the setting of prior or simultaneous distant failure.

## Study 10 Lu CW (2019)

### Study details

<b>Study type</b>	Retrospective cohort study
<b>Country</b>	China
<b>Recruitment period</b>	2010-2013
<b>Study population and number</b>	n= 169 patients with painful spinal metastases (in thoracic/lumbar spine) treated with Group A: percutaneous vertebroplasty (PVP) combined with <sup>125</sup> I seed implantation (n=49) Group B: PVP combined with RFA (n=51) Group C PVP combined with Zoledronic acid (n=38) and Group D: PVP combined with radiotherapy (n=31).
<b>Age and sex</b>	Median age 56.9 years. (95/169) male
<b>Patient selection criteria</b>	not reported
<b>Technique</b>	<u>Group A: underwent PVP combined with <sup>125</sup>I seed implantation (n=49)</u> Based on patient condition the dose and distribution of <sup>125</sup> I seed implantation was done and further evaluated using the dosimetry protocol. Then, bone cement was injected into the patient's diseased vertebra. <u>Group B: underwent PVP combined with RFA (n=51)</u> radiofrequency ablation (RFA) was done and bone cement in a semi-solidified state was injected. <u>Group C: underwent PVP combined with Zoledronic acid (n=38)</u> PVP procedure was under local anaesthesia, then bone cement was slowly injected into the vertebral body until reaching the edge. The patients were then treated with intravenous drip of 4 mg zoledronic acid for 15 minutes and once every 3–4 weeks. <u>Group D: underwent PVP combined with radiotherapy (n=31)</u> PVP was done under local anaesthesia and then bone cement was separately injected into the thoracic and lumbar region, respectively. Three or 4 days after PVP, patients had radiotherapy, with the diseased vertebra as the central point of radiotherapy, 10 times in 2 weeks and total radiation dose of 30 Gy. All patients were supervised for 24 hours after operation. CT was done to investigate the distribution of bone cement in the diseased vertebra, and antibiotics were given to prevent postoperative infection.
<b>Follow up</b>	6 months
<b>Conflict of interest/source of funding</b>	Authors state that they have no conflict of interest to declare.

### Analysis

IP overview: Radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases

Follow-up issues: complete clinical follow up.

Study design issues: retrospective analysis was done, all patients diagnosed with spinal metastases were randomly assigned to 4 groups to have 4 different combinations treatments. Pain and function scores were assessed using measures such as VAS (score 0-10, higher values representing worse scores), ODI (score of 0-10), and WHO pain relief (scored as complete, partial, mild or pain relief). These were collected through telephone after 24 hours, 1 month, and at 6 months follow up.

Study population issues: All patients underwent routine examinations before operation.

## **Key efficacy findings**

Number of patients analysed: 169

## Pain and function scores

–	VAS	ODI	WHO pain relief
<b>PVP combined with 125 I seed implantation</b>	–	–	–
Baseline	8.16±1.06	68.19±0.89	-
24 hours	3.91±1.01 <sup>^</sup>	49.92±1.01 <sup>^*</sup>	73.47%+
1 month	3.15±1.16 <sup>^</sup>	48.26±0.99 <sup>^</sup>	71.43%
6 months	2.39±0.89 <sup>^</sup>	47.99±0.89 <sup>^</sup>	67.35%
<b>PVP combined with RFA</b>	–	–	–
Baseline	8.07±0.79	71.04±0.83	–
24 hours	4.61±0.75 <sup>^#</sup>	37.03±0.76 <sup>^</sup>	76.47%+
1 month	4.38±0.61 <sup>^</sup>	36.84±0.91 <sup>^</sup>	74.51%
6 months	4.34±0.31 <sup>^</sup>	36.61±1.04 <sup>^</sup>	72.55%
<b>PVP combined with zoledronic acid</b>	–	–	–
Baseline	8.02±0.93	67.85±0.88	–
24 hours	4.43±1.19 <sup>^#</sup>	49.21±0.87 <sup>^*</sup>	73.68%+
1 month	4.27±0.76 <sup>^</sup>	48.94±0.44 <sup>^</sup>	71.05%
6 months	3.99±0.41 <sup>^</sup>	48.87±0.54 <sup>^</sup>	65.79%
<b>PVP combined with radiotherapy</b>	–	–	–
Baseline	7.91±0.92	70.22±0.92	–
24 hours	4.72±0.21 <sup>^#</sup>	41.01±0.37 <sup>^*</sup>	90.32%
1 month	4.66±0.31 <sup>^</sup>	40.83±0.43 <sup>^</sup>	87.10%
6 months	4.63±0.10 <sup>^</sup>	40.74±0.54 <sup>^</sup>	83.87%

<sup>^</sup>P<0.05 compared with baseline values.

<sup>#</sup>P<0.05 when the VAS of 4 different combination treatments was compared.

<sup>+</sup>P<0.05 when the WHO pain relief of 4 different combination treatments was compared.

<sup>\*</sup>P<0.05 when the ODI of 4 different combination treatments was compared.

## Key safety findings

### Adverse events: PVP combined with RFA

**Rate of bone cement extravasation was 16% (8/51):** 2 cases into paravertebral soft tissues, 3 into paravertebral veins, 2 into spinal epidural, and 1 into upper intervertebral disc through bone breaks.

## Study 11 Huntoon K (2020)

### Study details

<b>Study type</b>	Case report
<b>Country</b>	USA
<b>Recruitment period</b>	Not reported
<b>Study population and number</b>	N=1 patient with spinal metastases
<b>Age</b>	61-year-old woman
<b>Patient selection criteria</b>	
<b>Technique</b>	RFA and kyphoplasty using polymethylmethacrylate for spinal metastases using a bipolar cooled RFA system to treat lesions at L1 and L3
<b>Follow up</b>	1 year
<b>Conflict of interest/source of funding</b>	Not reported

### Key efficacy findings

Number of patients analysed: 1

### Key safety findings

Immediate onset of lower extremity paralysis, diminished sensation and bowel and bladder dysfunction after the procedure was reported. Patient was unable to move legs. No evidence of new fractures or evidence of polymethylmethacrylate extravasation into the spinal canal or spine foramina was noted. Imaging findings did not reveal any pathologic changes in the spinal cord at any level (no focal stenosis or spinal cord compression/injury). Radiology reports indicated suspicion for thermal injury to the ventral nerve roots at L1. Authors state that this might have occurred because of inaccurate placement of the RFA probe or more extensive zones of thermal ablation.

She underwent a prolonged inpatient rehabilitation stay and was discharged with follow up. At 4 months follow up, neurological examination revealed a power strength of 4 of 5 plantar flexion bilaterally, but otherwise 0 of 5 in her legs. At 1 year follow up, she has sensation in the lower extremities, but continued to have severe neurogenic bladder and bowel dysfunction. electromyography study showed severe membrane instability with no active motor units in L1, L2, L3, L4, and L5, consistent with a conus medullaris/cauda equina injury.

## Validity and generalisability of the studies

- Evidence included in systematic reviews was mainly from small prospective and retrospective studies.
- RFA systems with different ablation methods (bipolar RF electrodes) and temperatures, protocols were used in studies.
- The majority of the patients or treated vertebrae (94 to 96%) had vertebral augmentation with RFA
- Most of the outcomes were variable patient reported outcomes and are subject to high risk of bias.
- Follow-up periods varied across studies.
- Limited studies show that RFA is likely to provide effective short to mid-term (1 week to 6 months) pain relief.

## Existing assessments of this procedure

CIRSE standards of practice guideline recommends that '*RFA is indicated for osteolytic or mixed osteolytic– osteoblastic lesions with no, or a small, extra-osseous component. Where an extra-osseous soft tissue component exists, ablation of the soft tissue–bone interface can achieve pain palliation*' (Ryan 2022).

The National Comprehensive Cancer Network [NCCN] guideline states that radiofrequency ablation of bone lesions may be done to reduce pain and prevent skeletal related events. Radiofrequency ablation of bone lesions has proven successful in pain management, especially for those who do not attain adequate analgesia without intolerable effects (Swarm 2020).

European Society for Medical Oncology (ESMO) guidelines states that 'RFA can also relieve pain from bone metastases and reduce the tumour burden in bone. Minimally invasive RFA and vertebroplasty or kyphoplasty are used in combination to reduce tumour mass, create a cavity and stabilise the vertebral body' (Coleman R 2020).

A recently published guideline on percutaneous vertebral augmentation recommends treatment with vertebroplasty after different tumour treatments (like RFA) in patients with painful vertebrae because of metastases to achieve pain relief and the consolidation of vertebra (Tsoumakidou G 2017).

NICE guideline on 'metastatic spinal cord compression in adults: risk assessment, diagnosis and management' in section 1.5.1.8 recommends to 'consider vertebroplasty or kyphoplasty for patients who have vertebral metastases and no evidence of metastatic spinal cord compression or spinal

instability if they have: mechanical pain resistant to conventional analgesia, or vertebral body collapse' (NICE clinical guideline CG75, 2008).

## Related NICE guidance

Below is a list of NICE guidance related to this procedure.

### Interventional procedures

- Percutaneous insertion of craniocaudal expandable implants for vertebral compression fracture. Interventional procedures guidance IPG568 (November 2016) Available from <https://www.nice.org.uk/guidance/ipg568>
- Percutaneous cementoplasty for palliative treatment of bony malignancies. Interventional procedures guidance IPG179 (June 2006) Available from <https://www.nice.org.uk/guidance/ipg179>
- Balloon kyphoplasty for vertebral compression fractures. Interventional procedures guidance IPG166 (April 2006) Available from <https://www.nice.org.uk/guidance/ipg166>
- Percutaneous vertebroplasty. Interventional procedures guidance IPG12 (September 2003) Available from <https://www.nice.org.uk/guidance/ipg12>

### Technology appraisals

- Denosumab for the prevention of skeletal-related events in adults with bone metastases from solid tumours. NICE technology appraisal TA265 (October 2012). Available from <http://www.nice.org.uk/guidance/TA265>
- Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for treating osteoporotic vertebral compression fractures. NICE technology appraisal TA279 (April 2013). Available from <http://www.nice.org.uk/guidance/TA279>

### NICE guidelines

- Metastatic spinal cord compression in adults: risk assessment, diagnosis, and management. Clinical guideline CG75 (November 2008). Available from <http://www.nice.org.uk/guidance/CG75>

## **Additional information considered by IPAC**

### **Professional experts' opinions**

Expert advice was sought from consultants who have been nominated or ratified by their professional 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 professional experts, 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. 3 professional expert questionnaires for radiofrequency ablation as an adjunct to balloon kyphoplasty or percutaneous vertebroplasty for palliation of painful spinal metastases were submitted and can be found on the [NICE website](#).

### **Patient commentators' opinions**

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

### **Company engagement**

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

## **Issues for consideration by IPAC**

### **NCT02419703 The STAR™ Tumor Ablation Registry**

A prospective observational study of 65 patients with painful spinal metastases in the thoracolumbar spine (T1-L5) following targeted radiofrequency ablation (t-RFA) treatment with the STAR™ Tumor Ablation System, follow up 12 months, outcome measures are pain relief and quality of life improvement; location USA,

study completion date March 2017; status: study was terminated due to difficulty enrolling.

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## Literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	15/08/22	1946 to August 12, 2022
MEDLINE In-Process (Ovid)	15/08/22	1946 to August 12, 2022
MEDLINE Epubs ahead of print (Ovid)	15/08/22	August 12, 2022
EMBASE (Ovid)	15/08/22	1974 to August 12, 2022
EMBASE Conference (Ovid)	15/08/22	1974 to August 12, 2022
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	15/08/22	Issue 8 of 12, August 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	15/08/22	Issue 7 of 12, July 2022
International HTA database (INAHTA)	15/08/22	-

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

### Medline search strategy

Number	Search term
1	Catheter Ablation/
2	(Catheter* adj4 Ablat*).tw.
3	((needle* or electrode* or heat*) adj4 ablat*).tw.
4	exp Radiofrequency Ablation/
5	(Radiofrequen* adj4 (ablat* or therap* or treatment* or intervent* or program* or procedure*)).tw.
6	(Radio-frequen* adj4 (ablat* or therap* or treatment* or intervent* or program* or procedure*)).tw.
7	(rf adj4 ablat*).tw.
8	RFA.tw.
9	target* radiofreq* ablat*.tw.
10	t-rfa.tw.
11	(radio* adj4 frequen* adj4 ablat*).tw.
12	or/1-11

13	exp Spinal Neoplasms/
14	((spine* or spina* or vertebra* or lumbar*) adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinoma* or tumour* or tumor* or malignan* or dysplasia* or disease* or lesion* or metasta*)).tw.
15	exp Spinal Cord Neoplasms/
16	((spine* or spina* or vertebra* or lumbar*) adj4 cord* adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinoma* or tumour* or tumor* or malignan* or dysplasia* or disease* or lesion* or metasta*)).tw.
17	(thoracolumb* adj4 (spine* or spina* or vertebra* or lumbar*)).tw.
18	osseous metastatic disease.tw.
19	Bone Neoplasms/
20	((bone* or osseous*) adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinoma* or tumour* or tumor* or malignan* or dysplasia* or disease* or lesion* or metasta* or osteoma*)).tw.
21	(vertebral adj4 tumor*).tw.
22	(Radio adj4 resistan* adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinoma* or tumour* or tumor* or malignan* or dysplasia* or disease* or lesion* or metasta* or osteoma*)).tw.
23	or/13-22
24	exp Neoplasm Metastasis/
25	metastas*.tw.
26	(secondar* adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinoma* or tumour* or tumor* or malignan* or dysplasis* or disease* or lesion* or metasta*)).tw.
27	or/24-26
28	23 and 27
29	CAVITY spineWand.tw.
30	cool-tip RF ablation system.tw.
31	osteoCool RF spinal tumor ablation.tw.
32	STAR tumor ablation.tw.
33	Radioion* system.tw.
34	RITA medical system.tw.

35	celonpro power system.tw.
36	celon* power system.tw.
37	or/29-36
38	12 and 28
39	37 or 38
40	Animals/ not Humans/
41	39 not 40
42	limit 41 to ed=20220815

## Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the [summary of the key evidence](#). It is by no means an exhaustive list of potentially relevant studies.

### Additional papers identified

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Anchala PR, Irving WD, Hillen TJ et al. (2014). Treatment of metastatic spinal lesions with a navigational bipolar radiofrequency ablation device: A multicenter retrospective study. Pain Physician; 17:317-327.	Retrospective study N=92 patients with 128 spinal metastatic osseous lesions radiofrequency ablation (RFA) STAR tumour ablation system used (96 procedures were done). Cement augmentation was done when needed. Follow up 6 months	RFA was successful in all. Significant ( $p < 0.01$ ) decreases in the VAS scores noted at follow up. 54% patients experienced a decrease and 30% had no change in their pain medications.	Study included in systematic review added to table 2.
Angileri, SA, Granata G, Savoldi, AP et al. (2020) Cooled radiofrequency ablation technology for painful bone tumors Acta bio-medica : Atenei Parmensis; 91 (10s); e2020007	Case report	Osteocool RF Ablation System (Medtronic) on a patient with a painful bone metastasis localized in the 5th lumbar vertebra showed encouraging results. The radiofrequency ablation of bone metastases with palliative aim represents an excellent treatment option, as it is	Case report

		a minimally invasive and safe procedure, and can be repeated multiple times.	
Bagla S, Sayed D, Smirniotopoulos J et al. (2016). Multicenter prospective clinical series evaluating radiofrequency ablation in the treatment of painful spine metastases. Cardiovasc Intervent Radiol; 39:1289-1297.	Prospective study N=50 patients with vertebral body metastases. Radiofrequency ablation (RFA) STAR tumour ablation system used (69 treatments). Cement augmentation was done in 96%. Follow up 3 months	Significant improvement in scores for pain, disability, and cancer-specific health-related quality of life from baseline was seen. NRPS improved from 5.9 to 2.1 (p<0.0001). ODI improved from 52.9 to 37.0 (p<0.08). FACT-G7 improved from 10.9 to 16.2 (p = 0.0001). FACT-BP improved from 22.6 to 38.9 (p<0.001). No complications related to the procedure were reported.	Study included in systematic review added to table 2.
Cazzato RL, GarnonJ, CaudrelierJ, Prabhakar RaoP, Koch G, Gangi, A. Low-power bipolar radiofrequency ablation and vertebral augmentation for the palliative treatment of spinal malignancies. Int. J. Hyperthermia. 2018, VOL. 34, NO. 8, 1282–1288. <a href="https://pubmed.ncbi.nlm.nih.gov/29347855/">https://pubmed.ncbi.nlm.nih.gov/29347855/</a>	N=11 patients with painful spinal tumours treated with bipolar RFA and vertebral augmentation.	Low-power bipolar RFA performed with internally cooled electrodes and coupled to vertebral augmentation provides safe and effective early analgesia in patients affected by painful spinal malignancies.	Larger studies added to the overview.
David E, Kaduri S, Yee A, et al. Initial single center experience: radiofrequency ablation assisted vertebroplasty and osteoplasty using a bipolar device in the palliation of bone metastases. Ann Palliat Med. 2017;6(2):118-124.	Retrospective study N=26 patients. bipolar-RFA system with standard (70 °C) target temperature and vertebroplasty in 35 vertebral levels.	RFA assisted VP and OP using a bipolar device is safe and allows for controlled injection of cement into a preformed thermal cavity with a significant decrease in venous and posterior cement leaks. Rate of cement	Larger studies included in the overview summary.

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doi:10.21037/apm.2016.12.02.		leakage into the disc spaces was unaffected	
Dupuy De, Hong R, Oliver B et al. (2000). Radiofrequency ablation of spinal tumors: temperature distribution in the spinal canal. Technical Innovation. AJR:175, 1263-66.	Review	This innovative new approach provides not only pain palliation but also local tumour control, thus avoiding additional therapy such as radiation or surgery.	Review
Dabravolski D, Lahm A, Eser J, Merk H (2015). Tumours and metastases of the spine: Cavity/coblation surgery and vertebroplasty/kyphoplasty. Orthopade; 44:806-819.	Retrospective study N=250 patients with spinal tumours or metastases Radiofrequency ablation done with CAVITY SpineWand followed by kyphoplasty. Follow up 60 months	Significant pain reduction, satisfaction, early mobilization, and improvement in quality of life were demonstrated in all patients. Lower complication rates reported.	Study included in systematic review added to table 2.
Filippiadis D, Kelekis A (2021) Percutaneous bipolar radiofrequency ablation for spine metastatic lesions. European Journal of Orthopaedic Surgery and Traumatology <a href="https://doi.org/10.1007/s00590-021-02947-9">https://doi.org/10.1007/s00590-021-02947-9</a>	Review on imaging guided percutaneous bipolar radiofrequency ablation.	Percutaneous radiofrequency ablation of vertebral lesions is a reproducible, successful and safe procedure. Ablation should be combined with vertebral augmentation in all cases. In order to optimize maximum efficacy a patient and a lesion-tailored approach should both be offered focusing upon clinical and performance status along with life expectancy of the patient as well as upon lesion characteristics.	Review
Gazis AN, Beuing O, Franke J et al. (2014).	Prospective study	The extent of the ablation zones was	Study included in

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Bipolar radiofrequency ablation of spinal tumors: Predictability, safety, and outcome. Spine J; 14:604-608.	N=36 patients with advanced spine tumour (39 lesions) had radiofrequency ablation. CelonLab Power and Celon Aquaflow III Follow up not reported.	predictable to the millimetre because it did not cross planned dorsal and ventral boundaries. No complications were observed.	systematic review added to table 2.
Gazis A, Beuing O, Jollenbeck B et al. (2012). Bipolar radiofrequency ablation of spinal neoplasms in late stage cancer disease. A report of three cases. SPINE 37, 1, pp E64–E68.	Case series N=3 patients with metastases of the spine had bipolar radiofrequency ablation.	Ablation of tumours adjacent to neural structures is feasible. Spinal cord damage can be avoided by planning.	Larger studies with longer follow up included in table 2.
Georgy BA, Wong W. Plasma-mediated radiofrequency ablation assisted percutaneous cement injection for treating advanced malignant vertebral compression fractures. AJNR Am J Neuroradiology 2007; 28:700-705.	Prospective series N=15 patients with metastatic lesions epidural extension and/or cortical disruption had radiofrequency ablation and cement augmentation.	Extrasosseous extension of cement was observed in 4 cases but was clinically inconsequential. No thermal or neuronal insult was observed. 87% (13/15) of patients reported decreased pain.	Larger studies with longer follow up included in table 2.
Georgy BA. Bone cement deposition patterns with plasma-mediated radiofrequency ablation and cement augmentation for advanced metastatic spine lesions. AJNR Am J Neuroradiology 2009; 30:1197-1202.	Retrospective study N=37 patients with advanced metastatic lesions (at 44 levels) had plasma mediated RFA and cement augmentation. Cavity SpineWand was used. Follow up 2-4 weeks	Procedure allowed greater cement-deposition control, successfully stabilising the anterior two thirds of the vertebral body. This combined technique was useful in cases with posteriorly located lesions. The incidence of cement extravasation was high but clinically insignificant.	Study included in systematic review added to table 2.
Gronemeyer DH, Schirp S, Gevargez A. (2002). Image-guided	Case series N=10 (21 vertebral lesions) spine	90% of patients reported pain relief, disability reduced by	Study included in systematic

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radiofrequency ablation of spinal tumors: preliminary experience with an expandable array electrode. Cancer J 8:33–9.	metastases were treated with radiofrequency ablation. Vertebroplasty done in 4 cases. Follow up average 5.8 months.	27%, neurological function preserved in 9, general health stabilised in 6 and improved in 3.	review added to table 2.
Greenwood TJ, Wallace A, Friedman MV et al. (2005). Combined ablation and radiation therapy of spinal metastases: a novel multimodality treatment approach. Pain Physician; 18:573-581	Retrospective study N= 21 patients with 36 spine metastases were treated with radiotherapy and either RFA or cryoablation.	Mean worst pain score (8.0) significantly decreased at both one week (4.3, p<.02) and 4 weeks (2.9, p<.0003). Radicular pain occurred in 1 patient. Post-procedural imaging at 6 months showed stable disease in 12/13 treatments at 3 months and 10/10 at 6 months.	Combined treatment (RFA plus radiotherapy)
Halpin RJ, Bendok BR, Sato K et al. (2005). Combination treatment of vertebral metastases using image-guided percutaneous radiofrequency ablation and vertebroplasty: a case report. Surgical neurology. 63 (5), 469-474.	Case report n-1 case of vertebral metastases treated with a combination of percutaneous radiofrequency ablation (RFA) and vertebroplasty.	No complications. pain relief was immediate.	Larger studies with longer follow up included in table 2.
Hillen, Jennings et al., Radiology 2015			
<a href="#">Hillen TJ</a> , <a href="#">Anchala P</a> , <a href="#">Friedman MV</a> et al. (2014) Treatment of metastatic posterior vertebral body osseous tumors by using a targeted bipolar radiofrequency ablation device: technical note. Radiology;273(1):261-7.	Retrospective study N=26 patients (47 tumours) with painful metastatic posterior vertebral body tumours some radiation therapy resistant had RFA Follow up 1 month.	Targeted RFA with a newly developed articulating device is both feasible and safe for the treatment of painful posterior vertebral body metastatic tumours	Larger studies with longer follow-up included in table 2.
Holbert JA, Nguyen DA (2018). Percutaneous	Case report	This case showed that epidural disease can be	Larger studies with

Radiofrequency Ablation for painful spinal metastases resulting in resolution of epidural disease: a case report. <i>Cureus</i> 10(5): e2579.	N=1 case of metastatic prostate cancer with epidural extension treated with percutaneous image-guided radiofrequency ablation and vertebral augmentation	treated with radiofrequency ablation and vertebral augmentation.	longer follow up included in table 2.
Kai G, Chuan L and Fang L (2015). Minimally invasive treatments of spinal metastases: Vertebroplasty, radiofrequency ablation and radiation therapy. <i>Chinese Journal of Tissue Engineering Research</i> . DOI: 10.3969/j.issn.2095-4344.2015.16.029	Review of 3 kinds of minimally invasive treatments for spinal metastases.	Vertebral cement augmentation efficiency is 80-90%. Radiofrequency ablation and radiation can kill the tumour but cannot rebuild the vertebral stability. Therefore, the combination of different technologies can improve the therapeutic effect on spinal tumours. Above all, there is not a perfect minimally invasive treatment for spinal metastases	Review
Kam NM, Maingard JM, Kok HK et al. (2017). Combined vertebral augmentation and radiofrequency ablation in the management of spinal metastases: an update. <i>Curr. Treat. Options in Oncol.</i> 18: 74.		Radiofrequency ablation have shown success in reducing pain and improving function in patients with symptomatic spinal metastases. Both vertebral augmentation and RFA are recognised as excellent alternative in patients with spinal metastases.	Opinion statement.
Kastler A, Barbe D-A; Alemann G et al. (2021) Bipolar Radiofrequency Ablation of Painful Spinal Bone Metastases Performed under Local	N=25 patients with refractory painful vertebral metastases had 29 bipolar RFA procedures (16 combined with	Procedure tolerance was graded as either not painful or tolerable in 97% of cases. Follow up post-procedure mean VAS score decrease was 74% at	Results not reported separately for RFA alone and RFA combined

Anesthesia: Feasibility Regarding Patient's Experience and Pain Outcome. Medicina (Kaunas, Lithuania); 57 (9)	vertebroplasty) under local anaesthesia.	day 1: 6.6 (p < 0.001), 79% at 1 month: 6.6 (p < 0.001), 79% at 3 months: 6.5 (p < 0.001), 77% at 6 months, and 79% at 12 months: 6.6 (p < 0.001).	with vertebroplasty.
Kotecha R, Schiro BJ, Sporrer J et al. (2020) Radiation therapy alone versus radiation therapy plus radiofrequency ablation/vertebral augmentation for spine metastasis: study protocol for a randomized controlled trial. Trials; 21 (1); 964 NCT04375891	RCT protocol Patients with spine metastasis from T5-L5, randomized in a 2:1 ratio to either radiofrequency ablation/percutaneous vertebral augmentation (RFA/PVA) and EBRT or EBRT alone.	Primary objective is whether RFA/PVA in addition to EBRT improves pain control compared to palliative EBRT alone, defined as complete or partial pain relief (measured using the Numerical Rating Pain Scale [NRPS]) at 3 months. Secondary objectives are whether combined modality treatment improves the rapidity of pain response, duration of pain response, patient reported pain impact, health utility, and overall QOL.	Combined treatment (radiotherapy plus RFA/PVA versus radiotherapy) Protocol only
Krajnovic, B.; Sadat, S.; Cirovic, D.; Radiofrequency ablation and vertebral kyphoplasty for palliation of painful spinal metastatic lesions. European Spine Journal; 2019; vol. 28; 2726	Retrospective review N=60 patients (75 painful spinal metastases: 46 in the lumbar spine and 29 in the thoracic region) treated with combined RFA and PKP for painful neoplastic bone lesions using OsteoCool™ RF Ablation System. Follow up: postoperative	The mean pre-procedure and post-procedure VAS was 7.2/10 and 2.7/10 respectively. Patients reported clinically significant decreased pain (p value of 0.0001). No neurological complication occurred related to RFA and no cement extravasation into spinal canal was observed. In 2 patients an asymptomatic leak into the needle track, in 2 patients into draining veins and in one patient	Studies with longer follow up included in the summary of evidence.

		into the disc space was detected.	
Kurth A, Muller-Broich JD (2019) STAR RF-ablation for the management of painful vertebral bone metastases. <i>Osteologie</i> ; 28 (1); 46	Retrospective case series N=52 patients with painful vertebral bone metastases (from a wide variety of metastatic lesions). RFA followed by vertebral augmentation. Follow up 6 months	RFA procedures were successfully performed in all. All patients reported pain relief. Average VAS improved from 7.8 pre to 4.4 one week post RFA ( $p < 0.05$ ). and 3.0 after 6 months of the procedure ( $p < 0.05$ ). No device related adverse events were reported.	Larger studies included in summary of evidence.
Li M, Zhang N and Zhang X et al. (2020). Effects of surgery and radiofrequency ablation in the treatment of spinal metastases and analysis of the influencing factors of prognosis. <i>Experimental and Therapeutic Medicine</i> 19: 1072-1078.	Retrospective comparative study N= 132 patients with spinal metastases (65 had surgery alone and 65 had RFA assisted surgery). Follow up 36 months	Operation time and blood loss, rate of complications and 3-year recurrence rate in the RFA assisted surgery group was significantly lower than in surgery alone group ( $p < 0.05$ ). The VAS and KPS scores significantly improved in RFA surgery group compared with those in the control group ( $p < 0.05$ ). The 3-year survival rate was significantly higher than that in the surgery group ( $p < 0.05$ ).	Combined treatment Surgery plus RFA
Madaelil TP, Wallace AN, Jennings JW (2016). Radiofrequency ablation alone or in combination with cementoplasty for local control and pain palliation of sacral metastases: preliminary results in 11 patients. <i>Skeletal Radiol</i> ; 45:1213-1219.	Retrospective study N=11 RFA procedures done to treat 16 sacral metastases. Cementoplasty was done in 63% (7/11) cases. Follow up 4.7 months.	The median pain score decreased from 8 at baseline to 3 at 1 month following RFA ( $p = 0.004$ ). No acute or long-term complications were noted.	Study included in systematic review added to table 2.
Masala S, Roselli M, Massari M et al. (2004).	Case series	Procedure success 100%. swift pain relief	Larger studies with

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Radiofrequency heat ablation and vertebroplasty in the treatment of neoplastic vertebral body fractures. Anticancer Research 24: 3129-3134	N=3 patients with metastatic vertebral collapse.	and reduction in symptoms, associated with an evident augmentation in the weight-bearing resistance.	longer follow up included in table 2.
Mayer T, Cazzato RL, Marini P De et al. (2020). Spinal metastases treated with bipolar radiofrequency ablation with increased (> 70 °C) target temperature: Pain management and local tumor control. Diagnostic and Interventional Imaging 102, 27–34	Retrospective study N=31 patients with 37 metastases who were treated with b-RFA with mean temperature 88 C and vertebroplasty.	Technical success was 100% (37/37). One major complication unrelated to b-RFA was reported. Pain management in 80% (16/20) at a mean follow up of 3.4 months or 100% (6/6) with oligometastatic/oligo-progressive disease at a mean follow up of 5 months. In patients receiving b-RFA to prevent complications, 60% (6/10) had favourable outcome at a mean follow up of 3 months.	Larger studies included in table 2.
Mehta TI, Heiberger C, Kazi S, et al. (2020). Effectiveness of Radiofrequency Ablation in the Treatment of Painful Osseous Metastases: A Correlation Meta-Analysis with Machine Learning Cluster Identification. J Vasc Interv Radiol; 31:1753-62.	Systematic review and meta-analysis N=14 studies (426 patients with recalcitrant pain).	Median pain reduction after RF ablation was 67% over median follow up of 24 weeks (R <sup>2</sup> ¼.66, 95% confidence interval -0.76 to -0.55, I <sup>2</sup> = 71.24%, fail-safe N = 875) with 44% pain reduction within 1 week. A low-heterogeneity subgroup was identified with median pain reduction after RF ablation of 70% over 12 weeks (R <sup>2</sup> = -.75, 95% confidence interval -0.80 to -0.70, I <sup>2</sup> = 2.66%, fail-safe N = 910). Addition of cementoplasty after RF ablation did not	RFA for osseous metastases (not just spinal metastasis ... only 4 studies related to spinal metastasis were included).

		significantly affect pain scores. Primary tumour type and tumour size did not significantly affect pain scores. A particular, positive association between pain after RF ablation and axial tumours was identified, implying possible increased palliative effects for RF ablation on axial over appendicular lesions.	
Mehta T, Heiberger C, Kazi S et al. (2020) Radiofrequency ablation versus stereotactic body radiotherapy for painful osseous metastases: A comparative correlation metaanalysis of pain relief. Journal of Clinical Oncology; 38 (15)	Systematic review Patients with painful osseous-metastases.  SBRT (n=1100) versus RFA (n=557). Median follow up was 24 weeks for SBRT and 18 weeks for <b>RFA</b>	No studies directly compared SBRT to RFA. Median pain reduction of 59% (SBRT R =0.83, 95%CI:0.80-0.87, I =58.63%) and 64% (RFA R =0.52, 95%CI:0.41-0.62, I =48.16%) was reported respectively. Pain reduction and durability post-SBRT or post- <b>RFA</b> are comparable.	RFA for osseous metastases (not just spinal metastasis ... only 4 studies related to spinal metastasis were included).
Nakatsuka A, Yamakado K, Takaki H et al. (2009). Percutaneous radiofrequency ablation of painful spinal tumors adjacent to the spinal cord with real-time monitoring of spinal canal temperature: A prospective study. Cardiovasc Intervent Radiol; 32:70-75.	Prospective study N=10 patients with spinal tumours treated with cool-tip RF ablation system. Follow up 4.5 months	Procedure success was 100%. Clinical success was achieved within 1 week in all patients (100).	Study included in systematic review added to table 2.
Neufeld N, Davis J, Elshihabi S. (2021) Radiofrequency Ablation and Vertebroplasty of Cervical Metastatic	Case report N=1 patient with lymphoma and an anterior C7 metastatic lesion	pain was completely resolved and rated as 0/10. complete resolution of the lesion was seen on CT scan.	Larger studies included in evidence summary.

<p>Lesion: A Novel Anterior Approach Neuromodulation; 24 (4); e219-e220</p>	<p>RFA and cement vertebroplasty through an anterior approach.</p>		
<p>Proschek D, Kurth A, Proschek P, et al. (2009). Prospective pilot study of combined bipolar radiofrequency ablation and application of bone cement in bone metastases. <i>Anticancer Res</i> 29:2787–92.</p>	<p>Prospective study N=16 patients with painful spinal bone metastases treated with RFA alone (n=8) or RFA with bone cement (n=8). Celon prosurge &amp; celon power RFA system was used Follow up 20.4 months</p>	<p>In both groups (RFA alone and RFA with bone cement), pain was reduced significantly (mean reduction of pain 51.7%, p=0.0065). Quality of life was improved up to 61%. No side-effects and complications. Complete ablation of the bone tumour in all. No local tumour progression was seen.</p>	<p>Study included in systematic review added to table 2.</p>
<p>Pusceddu C, De Francesco D, Melis L et al. (2021) The Role of a navigational Radiofrequency Ablation Device and Concurrent Vertebral Augmentation for Treatment of Difficult-to-Reach Spinal Metastases. <i>Current oncology</i>. 28 (5); 4004-4015</p>	<p>Case series N=35 patients with 41 vertebral spinal metastases had CT guided percutaneous targeted RFA, associated with vertebral augmentation. Median follow up of 19 months (4-46 months).</p>	<p>mean VAS score dropped from 5.7 (95% CI 4.9-6.5) before targeted RFA and to 0.9 (95% CI 0.4-1.3) after RFA (p &lt; 0.001). The mean decrease in VAS score between baseline and 1 week follow up was 4.8 (95% CI 4.2-5.4). VAS decrease over time between 1 week and 1 year was similar. No patients showed signs of local progression or recurrence.</p>	<p>Similar studies included in the summary of evidence.</p>
<p>Nakatsuka A, Yamakado K, Maeda M, et al. Radiofrequency ablation combined with bone cement injection for the treatment of bone malignancies. <i>J Vasc Interv Radiol</i> 2004; 15 : 707 – 12.</p>	<p>Case series N=17 (23 bone tumours: spine (n = 17), iliac bone (n = 3), sacrum (n = 2), and ischial bone (n = 1). RFA followed by cement augmentation.</p>	<p>Combined therapy feasible. Technical success 96%. Pain relief within 1 week 100%, significant decrease in the VAS score from 8.4 to 1.1 (P &lt;.001). Neural damage occurred in 4 patients in whom the tumour had invaded the posterior</p>	<p>Included in systematic review added to overview.</p>

		cortex of the vertebral body and pedicle.	
Ragheb A, Vanood A, Fahim DK (2022) The Addition of Radiofrequency Tumor Ablation to Kyphoplasty May Reduce the Rate of Local Recurrence in Spinal Metastases Secondary to Breast Cancer. <i>World neurosurgery</i> ; 161; e500-e507.	Retrospective medical chart analysis N=23 breast cancer patients with metastatic spinal fractures (n = 50 vertebral levels) who underwent RFA and kyphoplasty 6 months follow up.	Significant reductions in pain levels were observed postoperatively, at discharge (3.5; P < 0.05), at 1-month follow up (2.8; P < 0.05), at 3-month follow up (1.1; P < 0.05), and at 6-month follow up (0.7 P < 0.05),	Larger studies included in summary of evidence.
Sandri A, Carbognin G, Regis D et al. (2010). Combined radiofrequency and kyphoplasty in painful osteolytic metastases to vertebral bodies. <i>Radiol med</i> ; 115:261–271	Case series N=11 patients with painful osteolytic vertebral body metastases unresponsive to conservative treatments had combined radiofrequency ablation and kyphoplasty.	No complication occurred but an asymptomatic cement leakage noted in 1. Pain significantly decreased: the mean VAS pain score before treatment was 8 vs. 1.8 and 1.9 at 72 h and 6 weeks. Analgesic reduction was achieved in all.	Larger studies with longer follow up added to table 2.
Schafer O, Lohrmann C, Markmiller M et al. (2003). Combined treatment of a spinal metastasis with radiofrequency heat ablation and vertebroplasty. <i>Technical Innovation. AJR</i> ; 180:1075–1077	Case report N=1 case of spinal metastases treated with radiofrequency ablation and vertebroplasty. Follow up 3 months	A stable vertebral body with no further tumour growth reported. The patient was pain-free and had no limitations in his activity.	Larger studies with longer follow up added to table 2.
Saravana-Bawan S, David E, Sahgal A et al. (2019) Palliation of bone metastases—exploring options beyond radiotherapy. <i>Ann Palliat Med</i> ;8(2):168-177.	Review	This educational review discusses safety, technique and indications for emerging technology in the area of locoregional treatment of bone metastases in conjunction with	Review

		vertebral augmentation including RFA.	
Sayed D, Jacobs D, Sowder T et al. (2019). Spinal Radiofrequency Ablation Combined with Cement Augmentation for Painful Spinal Vertebral Metastasis: A Single-Center Prospective Study. Pain Physician; 22:E441-E449	Prospective study N=30 patients undergoing RFA with cement vertebral augmentation for a painful thoracic or lumbar vertebral metastases.	Average NRS-11 scores decreased from a baseline of 5.77 to 4.65 (3 days; p = 0.16), 3.33 (one week; p<0.01), 2.64 (one month; p<0.01), and 2.61 (3 months; p<0.01). FACT-G7 increased from a baseline average of 13.0 to 14.7 (3 days; p=0.13), 14.69 (one week; p=0.15), 14.04 (one month; p=0.35), and 15.11 (3 months; p=0.07). No major adverse events were reported.	Larger studies included in table 2.
Sagoo NS, Haider AS, Chen AL, Vannabouathong C, Larsen K, Sharma R, Palmisciano P, Bin Alamer O, Igbini M, Wells DB, Aoun SG, Passias PG, and Vira S. Radiofrequency ablation for spinal osteoid osteoma: A systematic review of safety and treatment outcomes. Surgical Oncology. 2022;42:101747	Systematic review on radiofrequency ablation (RFA) for painful spinal osteoid osteoma (OO). 14 studies (354 patients)	The estimated pain reduction on the numerical rating scale was 6.85/10 (95% confidence intervals [95%CI] 4.67–9.04) at a 12 to 24-month follow up; and 7.29/ 10 (95% CI 6.67–7.91) at a >24-month follow up (range 24 to 55 months). Protective measures (e.g., epidural air insufflation or neuroprotective sterile water infusion) were used in 43/354 (12.1%) patients. Local tumour progression was seen in 23/354 (6.5%) patients who were then successfully re-treated with RFA or open surgical resection. Grade I-II complications such as temporary limb paraesthesia and	Not spinal metastasis.

		wound dehiscence were reported in 4/354 (1.1%) patients. No Grade III-V complications were reported.	
Senol N, Oguzoglu AS, Goksel HM. (2022) Radiofrequency Ablation and Augmentation in the Management of Spinal Metastases: Clinical Experience in 41 Patients. World neurosurgery; 163; e420-e425	Retrospective case series N=41 combined radiofrequency ablation and vertebral augmentation in patients with metastatic spinal tumours. Follow up 6 months.	No serious complications were seen. 2 patients had transient neurological motor deficits without cement leakage, and 1 patient had a pulmonary embolism with transient mild symptoms. Significant pain control and good functional state were reported at 6 months follow up.	Larger studies were included in the summary of evidence.
Shawky A, Ahmed EA, Krajnovic B et al. (2021) Radiofrequency ablation and balloon kyphoplasty for palliation of painful spinal metastases. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society; 30 (10); 2874-2880	Retrospective case series N=60 patients with 77 spinal metastases had RFA and Balloon kyphoplasty.	Mean pre-procedure and post-procedure VAS for back pain was 7.2/10 and 2.7/10, respectively (p value = 0.0001). No neurological complications related to RFA were found and no cement extravasation into the spinal canal was observed. In two patients, asymptomatic leaks into the needle track, in two patients into draining veins and in one patient into the disk space were detected.	Similar studies included in the summary of evidence.
Tomasian A, Hillen TJ, Chang RO et al. (2018). Simultaneous bipedicular radiofrequency ablation combined with vertebral augmentation for local tumor control of spinal metastases. AJNR Am	Retrospective study N=27 patients (33 tumours) with vertebral metastases treated with simultaneous bipedicular radiofrequency	Local tumour control was achieved in 96% (25/26) of tumours median follow up of 16 weeks. No complications were reported, and no patients had clinical evidence of metastatic	Larger studies included in table 2.

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J Neuroradiology 39:1768 –73	ablation combined with vertebral augmentation. Posterior vertebral body or pedicle involvement or both present in 94% (31/33) of cases.	spinal cord compression at the treated levels.	
Wallace AN, Greenwood TJ, Jennings JW (2015). Radiofrequency ablation and vertebral augmentation for palliation of painful spinal metastases. J Neurooncol; 124:111-118.	Retrospective study N=72 patient with 110 spinal metastases. RFA and vertebral augmentation in 95% (105/110) ablations. Star tumour ablation system was used. Follow up 1 month	Patients reported clinically significant decreased pain scores at both 1-week (mean, $3.9 \pm 3.0$ ; $p < 0.0001$ ) and 4-week (mean, $2.9 \pm 3.0$ ; $p < 0.0001$ ) follow-up. No major complications related to RFA and no cement extravasation reported.	Study included in systematic review added to table 2.
Wallace AN, Tomasian A, Vaswani D et al. (2016). Radiographic local control of spinal metastases with percutaneous radiofrequency ablation and vertebral augmentation. AJNR Am J Neuroradiology; 37:759-765.	Retrospective review (sub-group analysis) N=55 tumours reporting rate of radiographic local control in patients with spinal metastases treated with RFA and vertebral augmentation. Star tumour ablation system was used. Follow up 1 year in 93% (51/55) patients. (median 34 weeks)	Radiographic local tumour control rates were 89% (41/46) at 3 months, 74% (26/35) at 6 months, and 70% (21/30) at 1 year. No complications were reported, and no patients had metastatic spinal cord compression at treated levels.	Subgroup analysis of above study (included in systematic review added to table 2).
Wang, F., Gu, J., Xu, C. <i>et al.</i> (2022) The combination of radiofrequency ablation and vertebroplasty	Retrospective comparative case series	VAS scores in group A decreased rapidly after 1 week and remained stable at 6 months than in group B ( $P < 0.05$ ).	Similar studies included in

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<p>shows advantages over single vertebroplasty in treating vertebral neoplastic lesions. Skeletal Radiol 51, 565–571  <a href="https://doi.org/10.1007/s00256-021-03788-7">https://doi.org/10.1007/s00256-021-03788-7</a></p>	<p>N=35 patients with vertebral neoplastic lesions who had RFA combined with vertebroplasty (group A, 15 patients with 17 lesions) or single vertebroplasty (group B, 20 patients with 24 lesions)</p>	<p>The cement injected in group A (<math>5.95 \pm 1.45</math> mL) was significantly more than that in group B (<math>4.09 \pm 0.55</math> mL) (<math>P &lt; 0.05</math>). The ratio of vascular cement leakage in group A was significantly lower than that in group B (<math>P &lt; 0.05</math>), while no statistical difference was found in the non-vascular cement leakage (<math>P &gt; 0.05</math>).</p>	<p>summary of evidence.</p>
<p>Yang PL, He XJ, Li HP, et al. (2017). Image-guided minimally invasive percutaneous treatment of spinal metastasis. Exp Ther Med 13:705–9.</p>	<p>Retrospective case series  N=25 (32 vertebral lesions)  RFA plus cement augmentation  Follow up mean 7.8 months.</p>	<p>Biomechanical stability of the spine increased, pain within 6 weeks reduced, while the daily activities and quality of life improved. Mean progression-free survival of tumours was <math>330 \pm 54</math> days, and no complications occurred.</p>	<p>Study included in systematic review added to table 2.</p>
<p>Yuntong M, Wallace AN, Madaelil TP et al. (2016). Treatment of osseous metastases using the Spinal Tumor Ablation with Radiofrequency (STAR) system. e: Expert review of medical devices. VOL. 13, NO. 12, 1137–1145</p>	<p>Review of epidemiology, pathophysiology, natural history, and traditional management of metastatic bone disease and Spinal Tumour Ablation with Radiofrequency (STAR) System for treatment of osseous metastases.</p>	<p>Although evidence supporting the efficacy of RFA for the treatment of bone metastases is limited to case series, it is a reasonable therapy when other options have been exhausted, especially given the safety and minimal morbidity of the procedure. The STAR Tumor Ablation System has expanded the anatomic scope of bone metastases that can be safely and effectively treated with percutaneous ablation.</p>	<p>Review</p>
<p>Yevich S, Chen S, Metwalli Z (2021)</p>	<p>Review</p>	<p>Article reviews the indications, clinical</p>	<p>Review</p>

Radiofrequency ablation of spine metastases: A clinical and technical approach. Seminars in musculoskeletal radiology; 25 (6); 795-804		work-up, and technical approach for RFA of spine metastases.	
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