NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of radiofrequency ablation 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 may lead 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).

This overview describes the use of this intervention as a standalone procedure and not as an adjunct to vertebroplasty or kyphoplasty.

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Abbreviations

Word or phrase	Abbreviation
Health-related quality of life	HRQoL
Not reported	NR
Oswestry Disability Index	ODI
Radiofrequency ablation	RFA
Randomised controlled trial	RCT
Visual Analog Scale	VAS

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 for palliation of painful spinal metastases

Professional societies

- British Society of Interventional Radiology
- Faculty of Clinical Oncology, Royal College of Radiologists
- Faculty of Clinical Radiologists, 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 always 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 people 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.

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

This is a standalone RFA procedure and not an adjunct to vertebroplasty or kyphoplasty.

Efficacy summary

Pain reduction

In a prospective pilot study of 16 patients with painful spinal metastases treated with RFA alone (n=8) or RFA plus cement augmentation (n=8), pain decreased significantly after treatment (RFA alone group: from mean baseline VAS 7.6 to 5.5, p=0.018; RFA plus cement augmentation group: from mean baseline VAS 7.9 to 5.0, p=0.005) and between 15 and 36 months follow up in both the groups respectively (RFA group: 7.6 to 4.0, p<0.008; RFA plus cement augmentation group: 7.9 to 3.5, p<0.005; Proschek 2009).

In a small prospective study of 10 patients with spinal metastases who had RFA alone (in 4) or RFA plus cement augmentation (in 6), mean VAS score decreased from baseline 4.3 to 1.7 (p=0.0004) in the RFA alone group and from 6.6 to 1.7 (p=0.003) in the RFA plus cement augmentation group at 1 week follow up (Nakatsuka 2009).

In a retrospective analysis of 66 patients with painful vertebral metastases (26 treated with RFA alone and 40 treated with RFA plus vertebroplasty), the mean VAS scores significantly changed at all follow-up periods compared to baseline in both the groups (in the RFA alone group, scores changed from 8.3±1.07 at baseline to 4.8±1.03 at day 1, 3.67±1,07 at 1 month, 4.50±1.57 at 3 months and 4.42±1.08 at 6 months; p<0.001 for all time points; in the RFA plus vertebroplasty group, scores changed from 7.44±1.06 at baseline to 4.38±1.00 at day 1, 2.94±1.04 at 1 month, 2.44±1.61 at 3 months and 2.31±1.42 at 6 months; p<0.001 at all time points). The pain scores decreased at a rate of 59% in the RFA alone group and 83% in the RFA plus vertebroplasty group (Yildizhan 2021).

In a prospective cohort study of 36 patients treated with bipolar RFA alone for palliation of pain in advanced tumours near the spine and adjacent to neurological structures, pain relief was reported in 53% of cases (Gazis 2004).

Progression or recurrence of vertebral metastases

The prospective pilot study of 16 patients reported that none of the patients had a local recurrence after treatment with RFA alone or RFA in combination with vertebroplasty (Proschek 2009).

Health-related quality of life (HRQoL)

In the pilot study of 16 patients, 8 who had RFA alone and 8 who had RFA plus vertebroplasty reported improved quality of life (mean ODI scores improved from 64% at baseline to 33%, p=0.06 at 3 to 6 months follow up in RFA group; and

from 66% at baseline to 35%, p=0.071 at 15 to 36 months follow up in RFA plus vertebroplasty group; Proschek 2009).

In the retrospective analysis of 66 patients with painful vertebral metastasis (26 treated with RFA alone and 40 treated with RFA plus vertebroplasty), mean ODI scores significantly changed at all follow-up periods compared to baseline in both groups (in the RFA alone group, scores changed from 79% at baseline to 66% at day 1, 62% at 1 month, 55% at 3 months and 30% at 6 months; p<0.001 for all time points; in the RFA plus vertebroplasty group, scores changed from 79% at baseline to 56% at day 1, 45% at 1 month, 40% at 3 months and 14% at 6 months; p<0.001 at all time points). Seventy per cent of patients in the RFA alone group and 53% of patients in the RFA plus vertebroplasty group showed significant improvements in quality of life (Yildizhan 2021).

Safety summary

Neural damage

Transient neural damage related to the high temperature rise during RFA treatment was reported in 1 patient in a small study of 10 patients. This resolved 2 days after the procedure with intravenous administration of steroids (Nakatsuka 2009).

Death

Deaths due to systemic problems during the follow-up period (and unrelated to the procedure) were reported in 6 patients in the RFA alone group and another 6 patients in the RFA plus vertebroplasty group (Yildizhan 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: 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 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	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with painful spinal metastases.
Intervention/test	Radiofrequency ablation 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 128 patients from 3 prospective case series and 1 retrospective analysis.

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 for palliation of painful spinal metastases

Study 1 Yildizhan (2021)

Study details

Study type	Retrospective analysis
Country	Turkey (single centre)
Recruitment period	2015-2020
Study population and number	N=66 patients with painful spinal metastases. RFA alone (n=26) compared with RFA +vertebroplasty (n=40) Sites: thoracic in 22, lumbar in 18; multiple metastasis in 20
Age and sex	Mean age 59.5 years, range 52 to 69 years); 100% female
Patient selection criteria	Inclusion criteria: patients above 18 years, with osteolytic vertebral metastasis, spinal involvement and neurologically stable, primary tumour under control, with analgesic-resistant pain, and with more than 3 months of life expectancy were included. Exclusion criteria: Patients with active primary tumours, neurologically unstable and previously received radiotherapy for the spine, and those in need of surgical decompression and instrumentation were excluded.
Technique	Imaging was done in all patients before the procedure. Percutaneous RFA was administered to the vertebrae infiltrated by the neoplastic lesions, under local anaesthesia and conscious sedation at an average temperature of 90°C for 2 to 4 min. In the RFA group, decompression surgery was performed in 10 patients with 50% collapse of the vertebral corpus or fragments in the spinal canal during 6 months. 40 patients with vertebral metastases underwent vertebroplasty with polymethylmethacrylate radio-opaque bone cement injection after RFA.
Follow up	6 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow up was at 1, 3 and 6 months. Loss to follow up not reported.
Study design issues: a single centre retrospective study with some risk of bias.
Radiological images were assessed before and after the procedure. Pain was evaluated

using VAS (on a scale 0-10) before and after the therapy and at follow up. Quality of life was assessed using the Oswestry Disability Questionnaire.

Population issues: 26 patients had middle and posterior element fracture out of the corpus. Most common primary tumour was multiple myeloma and all patients had increased analgesic use before the procedure.

Key efficacy findings

Number of patients analysed: 66

Pain reduction

Mean VAS score (higher scores represented worst pain)

	Baseline	After treatment	1 month	3 months	6 months	p value
RFA alone group (n=26)	8.33 ± 1.07	4.80 ± 1.03	3.67 ± 1.07	4.50 ± 1.57	4.42 ± 1.08	P<0.001
RFA + vertebroplasty (n=40)	7.44 ± 1.06	4.38 ± 1.00	2.94 ± 1.04	2.44 ± 1.61	2.31 ± 1.42	P<0.001

The pain scores decreased at a rate of 59% in the RFA alone group and 83% in the RFA plus vertebroplasty group.
VAS score comparison between the groups showed a significant decrease in pain in all patients from both groups (p<0.001). However, 8 patients in RFA alone group required analgesics at the end of the 3 months follow up.

Health-related quality of life (HRQoL)

Mean ODI score

	Baseline	After treatment	1 month	3 months	6 months	p value
RFA alone group (n=26)	79.33±3.75	66.33 ± 6.26	62.28 ± 6.32	54.67 ± 11.86	29.67 ± 8/77	P<0.001
RFA + vertebroplasty (n=40)	78.50 ± 5.20	56.25 ± 9.66	44.68 ± 10.34	39.75 ± 16.09	14.20 ± 12.32	P<0.001

70% of patients in the RFA alone group and 53% of patients in the RFA plus vertebroplasty group showed significant improvements in quality of life.

ODI score comparison between the groups showed a significant improvement in QoL, with a lower degree of pain interfering with daily activities.

Key safety findings

	RFA alone % (n)	RFA+ vertebroplasty % (n)
Death due to systemic problems (during follow up)	N=6	N=6
Cement leakage from posterior element of the corpus vertebrae of the spinal canal (no further intervention needed)		25% (4/40)

Study 2 Proschek (2009)

Study details

Study type	Prospective pilot study
Country	Germany
Recruitment period	Not reported
Study population and number	N=16 patients with painful spinal metastases of breast cancer. Site: vertebral body of the lumbar and thoracic spine Average tumour size: 1.9 cm (range 1.2 to 3.5 cm) 8 treated with RFA alone and 8 treated with RFA plus bone cement.
Age and sex	mean age 59.5 years, range 52 to 69 years); 100% female
Patient selection criteria	Inclusion criteria: pain (refractory to previous treatment) and imminent fracture or instability of the bone due to rapid tumour growth, absence of neurological deficits and an increase of the pain during movement or excessive stress. Exclusion criteria: any vertebral fractures, radicular neurological symptoms, coagulation disturbances, rheumatic diseases, allergy to local anaesthesia, pregnancy and any infections (e.g. spondylitis, spondylodiscitis).
Technique	Percutaneous RFA of bone tumour with Celon pro surge and Celon power system. This is an outpatient procedure done with CT guidance and under local anaesthesia. A bipolar and impedance-controlled radiofrequency system was used. After RFA, bone cement was injected into the necrosis cavity in half of the patients (n=8).
Follow up	Mean 20.4 months (range 836).
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: follow up was at 1 week and every 6 months after the procedure. Loss to follow up not reported.
Study design issues: a single centre prospective small pilot study with some risk of bias. Radiological images were assessed by an independent radiologist before the procedure. Pain was evaluated by physician and patients themselves using VAS (on a scale 0-10) before, 6 hours after the therapy and at follow up. Quality of life was assessed using the Oswestry Disability Questionnaire.

Key efficacy findings

Number of patients analysed: 16

Pain reduction

Assessed using VAS. Higher scores represented worst pain.

	Baseline	After treatment	15-36 months	Mean reduction of pain%
RFA group (n=8)	Mean 7.6 (range 6- 10 points)	5.5 (range 3-8 points; p=0.018)	4.0 (range 2-6 points; p<0.008)	49.4%
RFA + cement (n=8)	Mean 7.9 (7-10 points)	5.0 (range 3-7 points; p=0.005)	3.5 (range 1-5; p<0.005)	53.9%

Progression or recurrence of vertebral metastases

Imaging showed a complete ablation of the bone tumour in all patients. None of the patients had a local recurrence after treatment with RFA alone or RFA in combination with vertebroplasty at follow up.

Health-related quality of life (HRQoL)

Assessed using Oswestry Disability Questionnaire (ODI)

	Baseline	After treatment	3-6 months	15-36 months
RFA group (n=8)	64% (range 38-84%)	34% (range 28-38; p=0.014)	33%, range 23-38%; p=0.06	-
RFA + vertebroplasty (n=8)	66% points (range 39-86%)	36% (range 31- 39%; p=0.003)	-	35%, range 26-38%; p=0.071

There were no statistically significant differences regarding pain relief (p=0.074) or improvement in quality of life (p=0.917) between both groups,
Patients in both groups (n=16) had a significant reduction of pain (p=0.0065) and an improvement in quality of life (p=0.043).

Key safety findings

All procedures were performed without side-effects and complications.

Study 3 Nakatsuka 2009

Study details

Study type	Prospective case series
Country	Japan
Recruitment period	2005-2007
Study population and number	n=10 patients with painful spinal tumours Lesions were located mainly in lumbar or thoracic area. Metastases origin from breast, lung, and renal cancers. previous treatments (n=4) chemotherapy, radiation therapy, surgery, or a combination. Tumour size: mean 4.9 cm (range 3-8 cm); The distance between tumour and spinal cord mean, 2.4 mm (1-4mm). location of tumour: thoracic (3), lumbar (6), sacral (1). All invaded the posterior cortex of the vertebral body or pedicle and were facing spinal canal.
Age and sex	Mean age 61 years; 60% male.
Patient selection criteria	Inclusion criteria: a painful spinal tumour refractory to previous medical treatment with radiation therapy and/or chemotherapy and a distance of 1 cm or less between the spinal tumour invaded the posterior cortex of the vertebral body or pedicle and spinal cord. Exclusion criteria a Zubrod performance status of 4, the presence of symptomatic spinal cord compression, or a platelet count of less than 50,000/lL or an international normalized ratio greater than 1.5.
Technique	Patients were treated with monopolar RFA and had cement augmentation. RFA was done under conscious sedation and local anaesthesia. Cool-tip RFA ablation system was used. The thermocouple was placed in the spinal canal (epidural space in 6, subarachnoid space in 4) under CT fluoroscopic guidance. On average RFA was applied for 8 minutes. Monitoring of the spinal canal temperature was done during the procedure. Temperature in tumour was mean 77 degrees. When the spinal canal temperature reached 45 degree C, RFA was immediately stopped (in 9). In 1 patient it suddenly rose to 48 degree C. When a tumour was located in the vertebral body and greater than 3 cm, bone cement was injected immediately after RFA to minimize the risk of future fracture in 6 patients.
Follow up	Mean 4.5 months (range 2.7 to 7.1 months)
Conflict of interest/source of funding	Not reported.

Analysis

Follow-up issues: complete follow up.

Study design issues: single centre prospective study with very small sample and high risk of bias; baseline lab tests and imaging was done. One author with experience performed all procedures. Patient medical records were reviewed to assess major complications.

Study population issues: patients had different previous treatments for various primary lesions.

Key efficacy findings

Number of patients analysed: 10

Technical success (procedure done without major complications) 100%

Pain relief (assessed using VAS score at 1 week and every 4 weeks after RFA) Higher scores represented worst pain.

Clinical success (defined as a fall in the VAS score of at least 2 point compared with baseline) 100% within 1 week.

Intervention	Baseline	Post-operative	Mean difference (P value)	Mean pain reduction %
RFA (all patients)	7.5	2.7 (1 week)	4.8 (0.00005)	64
RFA alone (n=4)	4.3	1.7 (1 week)	2.6 (0.0004)	60
RFA + cement augmentation (n=6)	6.6	1.7 (1 week)	4.9 (0.003)	74

Local pain relief was reported in 90% (9/10) during survival period. All patients died at a mean follow up of 4.5 months (range 2.7 to 7.1). One patient reported recurrent pain 2 months after treatment. Two patients reported newly developed pain 2 months after treatment.

Key safety findings

Transient neural damage (grade II) related to high temperature rise (48 degrees C) during RFA was reported in 1 patient. This was resolved 2 days after the procedure with intravenous administration of steroids.

Study 4 Gazis 2004

Study details

Study type	Prospective cohort study
Country	Germany (single centre)

Recruitment period	2006-2009
Study population and number	n=36 patients with advanced tumours with primary or secondary tumour involvement of spine and near neurological structures. location of tumour: lumbar 22, thoracic 16, sacral 2, cervical 1
Age and sex	Mean age 67.8 years (range 40 to 84 years); 60% male.
Patient selection criteria	Inclusion criteria: patients with disease progression despite previous surgery, maximal chemotherapy, maximal radiation and hormone therapy, lack of highly invasive surgical option, severe local tumour pain, insufficiently responsive to opiates and other analgesics, intervertebral tumour spread, risk of paraplegia or fracture because of tumour progression, locomotor disability because of a local tumour process, and osteolytic and mixed metastases with palliative intention. Exclusion criteria: presence of intradural and intramedullary tumours, risk of bleeding (acetylsalicylic acid, anticoagulants), acute general infections, local infections in the target zone, and allergies against one of the periinterventional applied drugs.
Technique	Patients were treated with bipolar RFA (39 lesions) under general anaesthesia by 3 neuroradiologists. CelonLab Power and Celon Aquaflow III ablation systems were used. RFA power was limited to 50 watts. Average power was 27.28 watts (range 9.51 to 36.58 watts). Average energy needed was 33.46 kJ (varied from 9.95 to 85 kJ).
Follow up	Not reported
Conflict of interest/source of funding	None

Analysis

Follow-up issues: loss to follow up not reported.

Study design issues: single centre prospective study with high risk of bias. Retrospective analysis. Primary outcome was reduction of the tumour.

Study population issues: most patients had poor prognosis because of late stage tumours.

Key efficacy findings

Number of patients analysed: 36

Duration of the procedure was mean 22.6 minutes (range 12 to 43 minutes).

The extent of the ablation zones did not cross the planned dorsal and ventral boundaries, avoiding heating of unwanted areas.

Pain

At discharge, pain reduction was observed in 52.8% (19/36) patients. No changes were seen in 36.1% (13/36) cases and worsening of pain was documented in 11% (4/36) of patients. Because of advanced tumours with multiple osseus metastases, pain could not always be attributed to a single lesion and it was not clear if change in pain was due to the RFA procedure.

Key safety findings

None

Validity and generalisability of the studies

- There are no RCTs comparing the effect of RFA alone with other treatments for painful vertebral metastases.
- Limited evidence included was mainly from small prospective and retrospective studies with short to medium term follow up.
- RFA systems with different ablation methods (bipolar or monopolar RF electrodes) and temperatures, protocols were used in studies.
- Outcomes were variable patient reported outcomes and are subject to high risk of bias.
- 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-osseus 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 performed 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 following different tumour treatments (like RFA) in patients with painful vertebrae due to 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 (Apr 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. 4 Professional expert questionnaires for radiofrequency ablation 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 was 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.

References

1. Yildizhan S, Boyaci, MG, Rakip U et al. (2021) Role of radiofrequency ablation and cement injection for pain control in patients with spinal metastasis. BMC musculoskeletal disorders; 22 (1); 91.
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3. Nakatsuka A , Yamakado K , Takaki H et al. 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 (2009) 32:70–75
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6. Tsoumakidou G, Too CW, Koch G et al (2017). CIRSE guidelines on percutaneous vertebral augmentation. Cardiovasc Intervent Radiol; 40:331-342.
7. Coleman R, Hadji P, Body JJ et al. (2020) Bone health in cancer: ESMO Clinical Practice Guidelines. Annals of Oncology. 31 (12), 1650–1663.
8. Swarm RA, Paice JA, Anghelescu DL et al. (2019). NCCN Clinical Practice Guidelines in Oncology. Adult Cancer Pain Version 3.2019 J Natl Compr Canc Netw 2019;17(8):977–1007.

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.

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
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 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 a minimally invasive and safe procedure, and can be repeated multiple times.	Case report
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
Filippiadis D, Kelekis A (2021) Percutaneous bipolar radiofrequency ablation for spine metastatic lesions. European Journal of Orthopaedic Surgery and Traumatology	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	Review

		offered focusing upon clinical and performance status along with life expectancy of the patient as well as upon lesion characteristics.	
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 evidence summary.
Goetz MP, Callstrom MR, Charboneau JW, et al. Percutaneous image-guided radiofrequency ablation of painful metastases involving bone: a multicenter study. J Clin Oncol. 2004 Jan 15;22(2):300-6.	Case series N= 43 patients with painful osteolytic metastases (pelvis, rib, sacrum, other) involving bone were treated with image guided RFA using a multi-tip needle. Median follow-up 16 weeks.	Pain and opioid usage significantly decreased. Transient incontinence in 1, second degree skin burn in 1 and a fracture in 1 were reported.	Tumours located in various sites and not just spinal metastasis. Paper does not explicitly state if cement was used or not.
Gronemeyer DH, Schirp S, Gevargez A. (2002). Image-guided radiofrequency ablation of spinal tumors: preliminary experience with an expandable array electrode. Cancer J 8:33–9.	Case series N=10 (21 vertebral lesions) spine metastases were treated with radiofrequency ablation. Vertebroplasty done in only 4 cases. Follow-up average 5.8 months.	90% of patients reported pain relief, disability reduced by 27%, neurological function preserved in 9, general health stabilised in 6 and improved in 3.	Results not reported separately for RFA alone.
Gevargez A, Groenemeyer DH. Image-guided	Case series 10 patients with unresectable	RFA was successfully performed in all. Needles were placed accurately	Results not presented separately

radiofrequency ablation (RFA) of spinal tumors. Eur J Radiol. 2008 Feb;65(2):246-52.	spine metastases were treated with RFA. Vertebroplasty was performed in 4 patients. Follow-up 5.8 months.	under image guidance, and a controlled lesion was created. Pain and back pain-related disability was clearly reduced, and neurologic function was preserved or stabilized.	for RFA and RFA plus vertebroplasty.
Hillen TJ, Anchala P, Friedman MV 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 tumors) with painful metastatic posterior vertebral body tumors, 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 tumors	Not clear if cement augmentation was used.
Kai G, Chuan L and Fang L (2015). Minimally invasive treatments of spinal metastases: Vertebroplasty, radiofrequency ablation and radiation therapy. Chinese Journal of Tissue Engineering Research. 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. Curr. Treat.		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.

Options in Oncol. 18: 74.			
Kotecha R, Schiro BJ, Sporrer J et al. (2020) Radiation therapy alone compared with 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 compared with radiotherapy) Protocol only
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. Skeletal Radiol; 45:1213-1219.	Retrospective study N=11 RFA procedures done to treat 16 sacral metastases. RFA alone was done in 3 and 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.	Larger studies with longer follow-up included in summary of evidence.
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 (R2 ¼ .66, 95% confidence interval -0.76 to -0.55, I^2 = 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^2 = -.75, 95% confidence interval -0.80 to -0.70, I^2 = 2.66%, fail-safe N	RFA for osseous metastases (not just spinal metastasis … only 4 studies related to spinal metastasis were included).

		= 910). Addition of cementoplasty after RF ablation did not 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 tumors was identified, implying possible increased palliative effects for RF ablation on axial over appendicular lesions.	
Sagoo NS, Haider AS, Chen AL, Vannabouathong C, Larsen K, Sharma R, Palmisciano P, Bin Alamer O, Igbinigie 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 12–24-month follow-up; and 7.29/ 10 (95% CI 6.67–7.91) at a >24-month follow-up (range 24–55 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 wound dehiscence were reported in 4/354 (1.1%) patients. No Grade III-V complications were reported.	Not spinal metastasis.
Saravana-Bawan S, David E, Sahgal A et al. (2019) Palliation of bone metastases—exploring options beyond radiotherapy. Ann Palliat Med;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 vertebral augmentation including RFA.	Review

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. 13 (12), 1137–1145.	Review of epidemiology, pathophysiology, natural history, and traditional management of metastatic bone disease and Spinal Tumor Ablation with Radiofrequency (STAR) System for treatment of osseous metastases.	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.	Review