Prospective Evaluation

Spinal Radiofrequency Ablation Combined with Cement Augmentation for Painful Spinal Vertebral Metastasis: A Single-Center Prospective Study

Dawood Sayed, MD, Daniel Jacobs, DO, Timothy Sowder, MD, Daniel Haines, MD, and Walter Orr, MPH

From: Department of Anesthesiology, University of Kansas Medical Center, Kansas City, KS

Address Correspondence:
Dawood Sayed, MD
Department of Anesthesiology
University of Kansas Medical Center
3901 Rainbow Blvd., MS 1034
Kansas City, KS 66160
E-mail: dsayed@kumc.edu

Disclaimer: Funding for this study was provided by DFINE Inc. and Merit Medical Systems Inc.
Conflict of interest: Dawood Sayed served as a consultant for DFINE Inc. and Merit Medical Systems Inc.

Manuscript received: 10-16-2018
Revised manuscript received: 01-11-2019
Accepted for publication: 03-26-2019

Free full manuscript:
www.painphysicianjournal.com

Background: The spine is the most common site of skeletal metastatic disease. Vertebral body metastases (VBM) can cause crippling pain, fractures, and spinal cord compression. Radiofrequency ablation (RFA) is a minimally invasive technique that has proven to be a safe method of targeted tissue destruction. Studies have shown that RFA combined with cement vertebral augmentation is safe and effective and has been associated with significant improvements in pain and quality of life.

Objectives: The purpose of this study was continued evaluation of the safety and efficacy of this technique.

Study Design: Prospective cohort.

Setting: A single academic medical center.

Methods: Patients undergoing RFA with cement vertebral augmentation for a painful thoracic or lumbar VBM were eligible for inclusion. Additional inclusion criteria included pain concordant with a metastatic lesion on cross-sectional imaging, aged 18 years or older, and considered candidates for spinal tumor ablation by the operating physician. Patients with vertebral metastatic disease in the cervical spine or patients with spinal cord compression from posterior tumor extension were excluded. Ablation within each VBM was performed using a bipolar radiofrequency probe with an extensible electrode and available articulation, permitting vertebral body navigation percutaneously. Patients were evaluated at baseline, 3 days, one week, one month, and 3 months using the Numeric Rating Scale (NRS-11) and Functional Assessment of Cancer Therapy-General 7 (FACT-G7) to assess pain and quality-of-life, respectively. A one-sample t test was performed, and 95% confidence intervals were calculated to assess changes in average NRS-11 and FACT-G7 scores.

Results: A total of 30 patients met inclusion criteria and underwent RFA of one or more VBM. Patients with 13 different primary cancers types underwent treatment. Patients received RFA to either one (n = 26; 87%) or 2 vertebral body levels (n = 4; 13%). Of the 34 levels, 13 were thoracic vertebra (38%) and 21 were lumbar vertebra (62%). 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.

Limitations: A heterogeneous patient population, small sample size, and potential confounders of concurrent variable adjuvant therapies were limitations. Additionally, most patients received both cement augmentation and targeted RFA, making it difficult to distinguish independent analgesic benefits of the therapies.

Conclusions: This study demonstrates that minimally invasive targeted RFA with cement augmentation of spinal metastatic lesions is an effective treatment for patients with VBM.
Key words: Cancer, cancer pain, spinal metastasis, radiofrequency ablation, tumor ablation, cement augmentation

Pain Physician 2019: 22:E441-E449

The spine is the most common site of skeletal metastatic disease. This is thought to be because of its high vascularity, with antegrade arterial spread and retrograde seeding through the valveless extradural Batson's venous plexus (1). Up to 30% of all new cancers diagnosed in the United States displayed symptomatic vertebral metastases at presentation (2), with an incidence of vertebral metastases of 30% to 70% in patients with known metastatic disease (3-5). Vertebral body metastases (VBM) are predominantly found in thoracic vertebrae (70%), followed by lumbosacral vertebrae (22%), and cervical vertebrae (8%) (6). These VBM often cause crippling pain, fractures, and spinal cord compression, further debilitating this patient population (7-9). With a median survival time of less than one year, treatment is focused on pain reduction, improving function and quality of life, and maintaining mechanical stability all while minimizing recovery time. However, because of advances in chemotherapy and hormonal therapy, increasing life expectancy of patients with metastatic spine disease warrants more attention to addressing debilitating painful spinal metastatic lesions. Depending on an array of factors including intensity of symptoms, vertebral stability, presence and/or degree of epidural extension, life expectancy, performance status, and prior radiation, management of VBM now involves a patient-centered, multidisciplinary integrated approach involving bisphosphonates, steroids, chemotherapy, radiation therapy, surgical management, and interventional augmentation and ablative therapies (10-14).

Radiofrequency ablation (RFA) is a minimally invasive thermal technique in which a high-frequency alternating current is applied to tissue causing local ionic agitation and frictional heat, resulting in localized coagulative necrosis with minimal impact on the surrounding healthy tissue. RFA has proven to be a safe method of targeted tissue destruction (15,16). RFA is well-established as a treatment of metastases to the liver, kidneys, and bone (17-21), and more recently has been applied to vertebral metastatic tumors (14,15). In conjunction with the destruction of the vertebral metastases, cement filling of the pathologic lytic lesion and the resultant defect in the vertebrae restores the integrity and support of the vertebral body.

Our institution contributed (n = 14) to a 50 patient multicenter retrospective study by Bagla et al (22) in 2016, evaluating the safety and efficacy of RFA combined with cement vertebral augmentation using an articulating tumor ablation system that permits navigation within bone. Cement augmentation was delivered via the same cannula in cases of known compression fractures or pathologic lytic lesions with suspected structural instability. That study revealed statistically significant improvements in Numeric Rating Scale (NRS-11), Functional Assessment of Cancer Therapy-General 7 (FACT-G7), and Oswestry Disability Index (ODI) with no complications related to the procedure reported. The purpose of this single-center prospective study was continued evaluation of the safety and efficacy of this technique in cancer patients with metastatic spine disease.

Methods

Patients

In addition to the 14 patients who were contributed to the Bagla et al (22) study, we prospectively enrolled an additional 16 patients in which this procedure was performed at our institution for a total cohort of 30 patients. This study was approved by our medical center's institutional review board and data were collected between August 2013 and September 2017. Written informed consent was obtained from all study patients, and the study was conducted in compliance with federal HIPAA regulations. Inclusion criteria included at least one painful thoracic or lumbar VBM with pain concordant with a metastatic lesion on cross-sectional imaging, aged at least 18 years or older, and considered candidates for spinal tumor ablation by the operating physician. Exclusion criteria were defined as vertebral metastatic disease in the cervical spine or patients with spinal cord compression from posterior tumor extension.

Measurement

Patients were evaluated at baseline (preprocedure) and at 3 days, one week, one month, and 3 months postprocedure using the NRS-11 and FACT-G7 to assess pain and quality-of-life, respectively, both of which have been validated (23,24). NRS-11 is a numeric version of the visual analog scale (VAS) in which a patient selects a whole number to represent the severity of their pain with 0 being no pain and 10 being the most severe. FACT-G7 is a shortened validated version of the Functional Assessment of Cancer Therapy-General using a subset of 7 questions from the original 27 questions within the survey to assess the patients' quality of life, with higher overall scores indicating greater quality of life.

Procedure

Patients underwent an initial evaluation by an interventional pain physician including a physical examination, review of available imaging, and verification of concordant pain with a VBM via cross-sectional imaging. Ablation within each VBM was performed using an articulating bipolar radiofrequency probe, permitting percutaneous navigation within the vertebral body (STAR Tumor Ablation System, Merit Medical Systems, South Jordan, UT). Multiple thermocouples embedded along the length of the RFA probe provided a real-time thermal profile of the ablation zone and were used to intraoperatively monitor the size of the ablation (Figs. 1, 2, and 3). The procedure was considered successful if

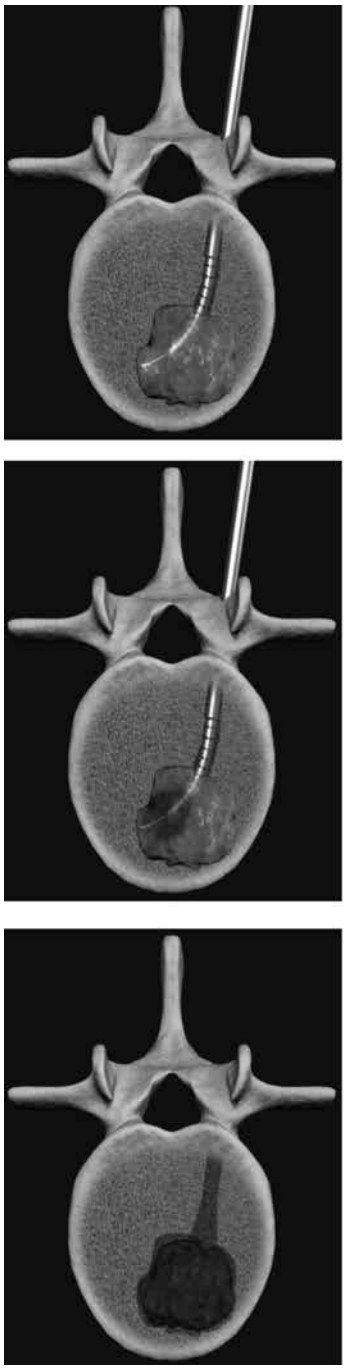

Fig. 1. *Illustration of transpedicular approach to vertebral body tumor ablation and cement augmentation.*

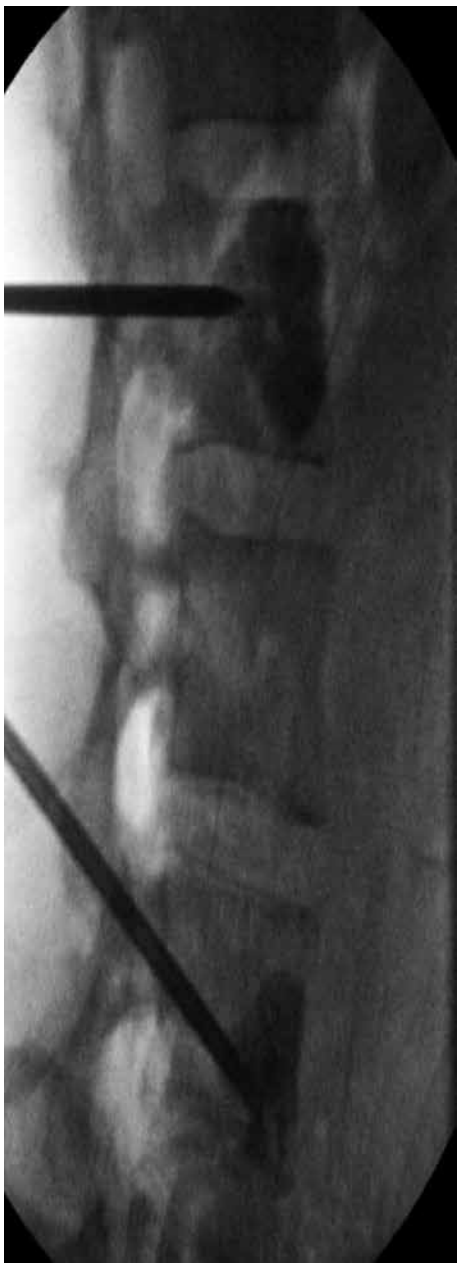

Fig. 2. *Lateral view of L3 and L5 cement augmentation after tumor ablation.*

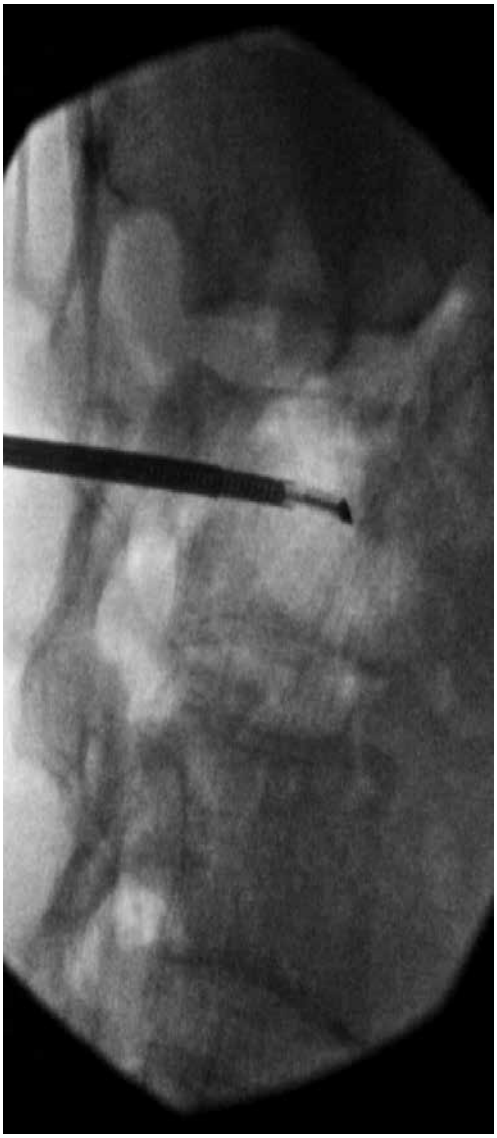

Fig. 3. *Lateral view of vertebral body tumor ablation.*

adequate overlapping ablation zones encompassing the metastatic lesion were achieved within the vertebra per the preoperative plan.

Patients were sedated via intravenous conscious sedation for the procedure to enable them to provide biofeedback during the ablation, with the goal of preventing neurologic injury. Using a transpedicular or parapedicular approach under fluoroscopic guidance, a 10-gauge coaxial cannula was used to obtain either bipedicular or unipedicular access to the vertebra (Fig. 1). The decision on whether to access bipedicular versus unipedicular was based on preoperative imaging of the vertebral body tumor. A bipedicular approach was employed if the bony metastasis was noted to cross the midline. A unipedicular, ipsilateral approach was employed if the tumor did not cross the midline. Cross-sectional preoperative imaging was used to determine the location and size of the desired ablation zone. The radiofrequency probe was inserted into the vertebra through the coaxial cannula and articulated to access the metastatic lesions. RFA thermal energy was applied to achieve the desired ablation zones using the thermocouples located on the electrode shaft to confirm and quantify the ablation zone. Repositioning was performed as necessary to create overlapping zones and attempt complete tumor ablation. In 28 of the 30 patients, cement augmentation was performed following the RFA via the same access cannula. Only 2 small posterior lesions were not augmented, as they were considered to be of little risk of impending vertebral body fracture.

Statistical Analysis

A one-sample t test was performed, and 95% confidence intervals were calculated to assess changes in average NRS-11 and FACT-G7 scores across timepoints.

Results

A total of 30 patients met inclusion criteria and underwent RFA of one or more VBM. Patient demographics and baseline characteristics are presented in Table 1. Patients with 13 different primary cancers types underwent treatment. Primary cancer types included 7 patients with metastatic renal cancer, 6 breast, 5 lung, 2 bladder, 2 melanoma, 2 hepatic, one adenocarcinoma, one multiple myeloma, one maxillary sinus, one prostate, one thyroid, and one patient with metastatic colon cancer. Patients received RFA to either one (n = 26; 87%) or 2 vertebral body levels (n = 4; 13%). Of the 34 levels, 13 were thoracic vertebra (38%) and 21 were lumbar vertebra (62%). Unipedicular access was performed in 19 levels (56%). There was a 100% technical success rate among the procedures with a mean total ablation time of 9.56 minutes per level (standard deviation 4.58). 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; $P < 0.01$) (Table 2). 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; $P = 0.07$). Additionally, no major adverse events were reported. In the 2 patients in which we were able to obtain a postprocedure magnetic resonance imaging scan, local tumor control was observed, and pain control was documented (Figs. 4 and 5).

Discussion

It is estimated that symptomatic spinal metastasis is present in 10% of patients with cancer (25). Over 50% of these patients have multiple spinal levels involved with metastatic cancer (26). In many cases, the etiology of this pain can be related to a combination of vertebral instability and/or fracture, periosteal stretching, neurostimulating cytokines, and canal and/or neuroforaminal involvement as a result of the metastatic lesions (27). Current standard radiation therapy treatment modalities have variable results, and patients frequently suffer from inadequate pain relief, despite the best effort of their physicians (28). Surgical intervention is associated with a higher degree of morbidity and can be high risk in these patients owing to decreased performance status, postsurgical healing challenged by poor bone quality, and decreased life expectancy (29).

Table 1. *Patient demographics.*

Characteristics	Value
Patients (n)	30
Gender Male, n (%) Female, n (%)	 19 (63%) 11 (37%)
Mean age (years ± SD)	62.9 ± 13.45
Race White, n (%)	 27 (90%)
Primary cancers, n (%) Renal Breast Lung Liver Bladder Melanoma Adenocarcinoma Multiple myeloma Maxillary sinus Prostate Thyroid Colon	 7 (23%) 6 (20%) 5 (17%) 2 (7%) 2 (7%) 2 (7%) 1 (3%) 1 (3%) 1 (3%) 1 (3%) 1 (3%) 1 (3%)

Abbreviation: SD, standard deviation

Table 2. *Changes in pain (NRS-11) and quality of life (FACT-G7) measure scores over study timepoints*

		Baseline	3 days	One week	One month	3 months
NRS-11	n	30	23	26	25	18
	mean ± SD	5.77 ± 2.81	4.65 ± 2.82	3.33 ± 2.59	2.64 ± 2.41	2.61 ± 2.28
	P value		0.1571	0.0014*	0.0001*	0.0002*
FACT-G7	n	30	23	26	25	18
	mean ± SD	13.0 ± 3.64	14.7 ± 4.49	14.69 ± 4.92	14.04 ± 4.49	15.11 ± 3.97
	P value		0.1341	0.1464	0.347	0.0711

Abbreviation: SD, standard deviation

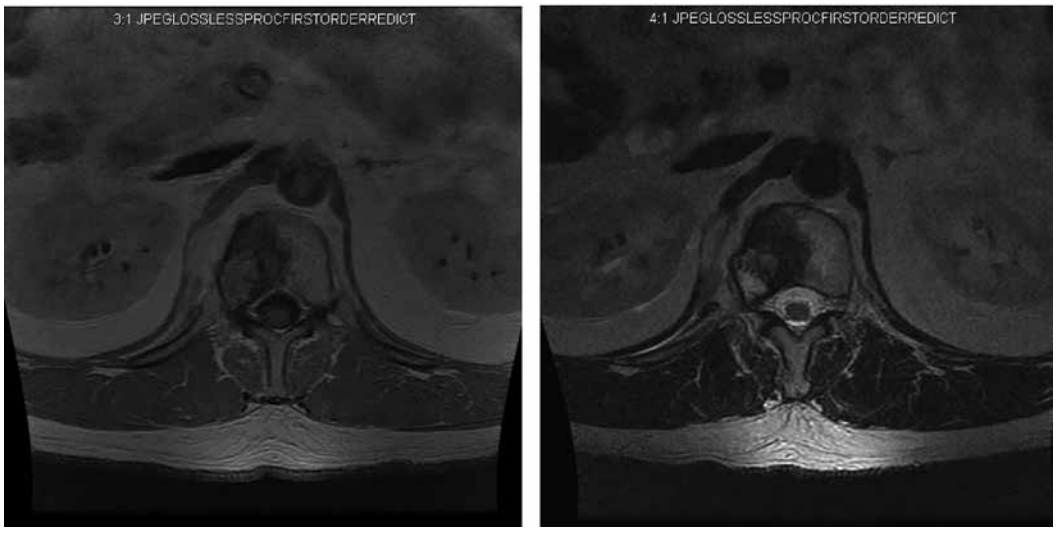

Fig. 4. *A. Preprocedure magnetic resonance imaging scan of T12 vertebral metastasis from lung cancer. T2- and T1-weighted images. B. Postprocedure magnetic resonance imaging scan of T12 vertebral metastasis from lung cancer. T2- and T1-weighted images. Note local tumor control and decrease in size of posterior body lytic mass. Magnetic resonance imaging scan was taken at 90 days postprocedure.*

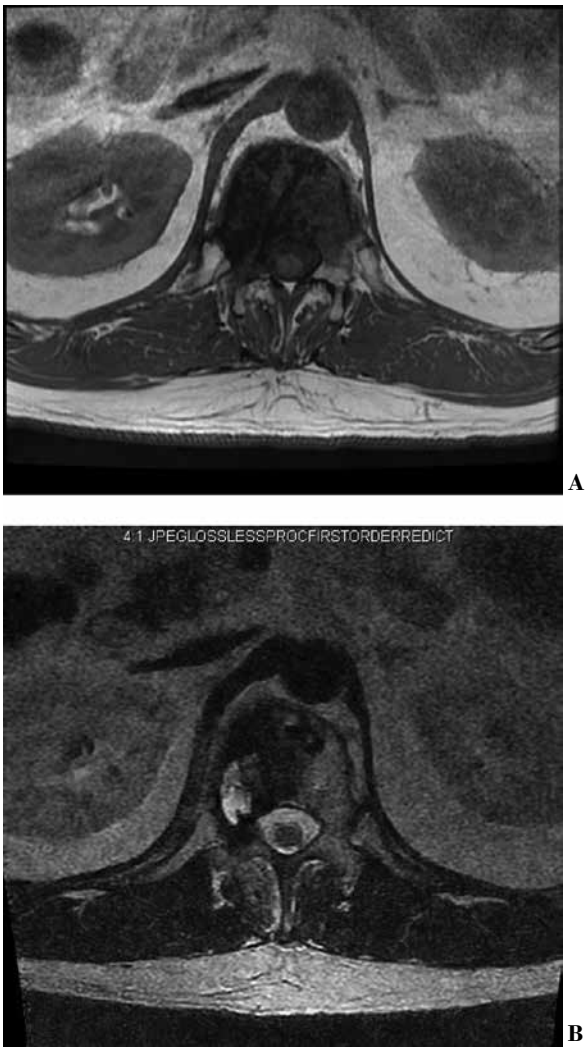

Fig. 5. A. Preprocedure magnetic resonance imaging scan of T12 pedicle tumor secondary to metastatic renal cancer. Fig. 5. B. Postprocedure magnetic resonance imaging scan of T12 pedicle tumor secondary to metastatic renal cancer. Note local tumor control. Magnetic resonance imaging scan was taken at 90 days postprocedure.

As described earlier, RFA is a targeted therapy that has been proven to be safe and effective following decades of use in the ablation of liver and lung tumors. The use of RFA in osseous lesions was first described by Rosenthal et al (30) in 1992, and has since been increasingly used in the management of bony metastases (19,20). However, this treatment method is only one of many being applied to this patient population, as many already undergo traditional treatment methods of radiation and chemotherapy. The results of several studies outlining the application of RFA therapy, with and without vertebral augmentation, have shown positive impacts on VAS scores in this patient population. This treatment is also used in concert with current adjuvant therapies in many cases when pain control is not optimal after treatments such as radiation.

In 2010, Sandri et al (31) published the retrospective results of 11 patients who received RFA with cement augmentation, reporting significantly decreased VAS pain scores from 8 (range, 7-10) before treatment to 1.8 (range, 0-3) at 72 hours, and 1.9 (range, 1-3) at 6 weeks after the treatment with no reported complications. In 2014, Anchala et al (32) published data from a multicenter retrospective study examining 128 lesions in 92 patients who underwent RFA with or without vertebral cement augmentation and showed significant ($P < 0.01$) decreases in VAS scores at one week, one month, and 6 months postoperatively. The reported preoperative average VAS score was 7.51, which improved over a range of 1.73 to 2.25 throughout follow-up. Another multicenter study by Wallace et al (33) evaluated 72 RFA treatments of 110 spinal metastases with vertebral augmentation performed after 95% (105 of 110) of ablations. Patients reported clinically significant decreased pain scores at both one-week ($P < 0.0001$) and 4-week ($P < 0.0001$) follow-ups with pre- and posttreatment VAS scores of 8.0 and 1.9, respectively. No major complications occurred related to RFA, and there were no instances of symptomatic cement extravasation. In 2018, Zhao et al (34) reported their results of RFA treatment of spinal metastatic lesions in conjunction with cement augmentation in 16 patients. They reported significant ($P < 0.05$) improvements in pain from a VAS score of 8.1 reduced to 5.5 at 24 hours, 2.8 at one week, and 1.4 at 6 months. In addition to these outcomes, no intraprocedural complications occurred. Our results affirm these findings, as we found similar significant decreases in pain at one week, one month, and 3 months.

In 2011, Berenson et al (35) published their results on the efficacy of balloon kyphoplasty compared with conservative management for patients with malignant compression fractures (CAFE study). In this study, a statistically significant improvement in Roland Morris Disability score at one month was found compared with the control arm. Because the CAFE study did not measure pain as a primary endpoint, it is difficult to compare the efficacy of a com-

bined vertebral augmentation + RFA technique versus vertebral augmentation (kyphoplasty) alone. One can infer a similar, very low adverse effect rate in both our prospective series and the patients in the CAFE study, suggesting that spinal RFA does not add any additional risk when performing 2 very similar procedures in terms of invasiveness.

As mentioned previously, 14 of the patients reported in this current cohort were included in a previous multicenter study by Bagla et al (22) in 2016. That study revealed, at 90 days postprocedure, NRS-11 improved from 5.9 to 2.1 ($P < 0.0001$), ODI improved from 52.9 to 37.0 ($P < 0.01$), and FACT-G7 improved from 10.9 to 16.2 ($P = 0.0001$). No complications related to the procedure were reported. We found that our baseline NRS-11 scores were similar to the Bagla et al (22) study; however, baseline scores for the FACT-G7 were elevated. Although we saw similar decreases in pain via the NRS-11, we did not see statistically significant differences in FACT-G7 quality of life scores.

The listed studies reported pain scores ranging from 7.51 to 8.1 pretreatment to a range of 1.4 to 1.8 posttreatment. Pain scores of 5.77 pretreatment and, at their lowest, 2.61 posttreatment in this study were consistent with those reported in the multicenter study of which our data were used. Although our *P* values at one week ($P = 0.0014$), one month ($P = 0.0001$), and 3 months ($P = 0.0002$) were statistically significant, the initial 3-day follow-up was not statistically significant ($P = 0.1571$). Most authors in the previously cited studies reported significant pain improvement within days of their interventions, whereas our results were not statistically significant until one week postprocedure. Given the downward trend in pain score, we suspect this is due to fewer patients available for follow-up (23 of 30) at 3 days posttreatment. Most relevant is that the rate at which significant pain relief occurred following RFA and cement augmentation is significantly more rapid than the 4 to 6 weeks reported to achieve full palliative relief following conventional fractionated external beam radiotherapy, a standard of care for spinal metastatic disease (36). FACT-G7 showed improvement from 13 at baseline to 15.11 at 3 months, but this was not statistically significant. It is important to note that this could be because of an elevated baseline (13 vs. 10.9) and smaller sample size (30 vs. 50) when compared with Bagla et al (22). Additionally, statistically significant improvements in quality of life can be difficult to achieve in metastatic cancer patients with multifactorial pain.

The important clinical implications of documented reduced pain and increased quality of life noted in this and other studies following RFA are highlighted in the National Comprehensive Cancer Network (37) guidelines version 1.2018 for adult cancer pain. This guideline states that survival is linked to symptom control, and pain management contributes to broad quality of life improvements and prevention of expected analgesic side effects (37). Clinicians who care for patients with debilitating pain from terminal disease, family members who witness it, and patients who experience it are frequently frustrated at the variable response of the disease to available treatment modalities. Having one more promising method of treatment available in the armamentarium, especially one that can couple well with existing therapies, may offer reassurance to all involved as these patients seek comfort in their final days.

Limitations of this study include the heterogeneous patient population as well as a small sample size. There were also potentially confounding variables of concurrent adjuvant therapies that varied between patients. The authors, however, believe that the best pain control is achieved in this patient population by adjuvant administration of both therapies because of the unique pain generating features of spinal vertebral metastasis (mechanical and biological).

Conclusions

This single-center study demonstrates that minimally invasive targeted RFA with cement augmentation is an effective palliative treatment for patients with painful spinal metastatic lesions. Specifically, we found significant decreases in pain at one week, one month, and 3 months postprocedure, but no significant differences in quality of life scores. An increasing number of prospective studies continue to affirm the safety and efficacy of this treatment. Prospective randomized trials are needed to determine the efficacy of this combined therapy relative to or in conjunction with current conventional treatments.

References

1. Batson OV. The role of the vertebral veins in metastatic processes. *Ann Intern Med* 1942; 16:38-45.
2. Tatsui H, Onomura T, Morishita S, Oketa M, Inoue T. Survival rates of patients with metastatic spinal cancer after scintigraphic detection of abnormal radioactive accumulation. *Spine (Phila Pa 1976)* 1996; 21:2143-2148.
3. Boland PJ, Lane JM, Sundaresan N. Metastatic disease of the spine. *Clin Orthop Relat Res* 1982:95-102.
4. Harrington KD. Metastatic disease of the spine. *J Bone Joint Surg Am* 1986; 68:1110-1115.
5. Wong DA, Fornasier VL, MacNab I. Spinal metastases: The obvious, the occult, and the impostors. *Spine (Phila Pa 1976)* 1990; 15:1-4.
6. Brihaye J, Ectors P, Lemort M, Van Houtte P. The management of spinal epidural metastases. *Adv Tech Stand Neurosurg* 1988; 16:121-176.
7. Nielsen OS, Munro AJ, Tannock IF. Bone metastases: Pathophysiology and management policy. *J Clin Oncol* 1991; 9:509-524.
8. Loblaw DA, Perry J, Chambers A, Laperriere NJ. Systematic review of the diagnosis and management of malignant extradural spinal cord compression: The Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. *J Clin Oncol* 2005; 23:2028-2037.
9. Leone A, Cianfoni A, Zecchi V, Cortese MC, Rumi N, Colosimo C. Instability and impending instability in patients with vertebral metastatic disease. *Skeletal Radiol* 2019; 48:195-207.
10. Harel R, Angelov L. Spine metastases: Current treatments and future directions. *Eur J Cancer* 2010; 46:2696-2707.
11. Filippiadis DK, Papagelopoulos P, Kitsou M, Oikonomopoulos N, Brountzos E, Kelekis N, Kelekis A. Percutaneous vertebroplasty in adult degenerative scoliosis for spine support: Study for pain evaluation and mobility improvement. *Biomed Res Int* 2013; 2013:626502.
12. Joaquim AF, Powers A, Laufer I, Bilsky MH. An update in the management of spinal metastases. *Arq Neuropsiquiatr* 2015; 73:795-802.
13. Filippiadis DK, Marcia S, Masala S, Deschamps F, Kelekis A. Percutaneous vertebroplasty and kyphoplasty: Current status, new developments and old controversies. *Cardiovasc Intervent Radiol* 2017; 40:1815-1823.
14. Theologis A, Jennings JW, Buchowski JM. Percutaneous thermal ablation of spine metastasis. In: Marco RAW (ed). *Metastatic Spine Disease: A Guide to Diagnosis and Management*. 1st ed. New York, Springer, 2018: pp. 281-291.
15. Hoffmann RT, Jakobs TF, Trumm C, Helmberger TK, Reiser MF. RFA of renal cell carcinoma in a solitary kidney. *Abdom Imaging* 2008; 33:230-236.
16. Vaswani D, Wallace AN, Eiswirth PS, Madaelil TP, Chang RO, Tomasian A, Jennings JW. Radiographic local tumor control and pain palliation of sarcoma metastases within the musculoskeletal system with percutaneous thermal ablation. *Cardiovasc Intervent Radiol* 2018; 41:1223-1232.
17. Jakobs TF, Hoffmann RT, Trumm C, Reiser MF, Helmberger TK. Radiofrequency ablation of colorectal liver metastases: Mid-term results in 68 patients. *Anticancer Res* 2006; 26:671-680.
18. Lencioni R, Della Pina C, Bartolozzi C. Percutaneous image-guided radiofrequency ablation in the therapeutic management of hepatocellular carcinoma. *Abdom Imaging* 2005; 30:401-408.
19. Dupuy DE, Liu D, Hartfeil D, Hanna L, Blume JD, Ahrar K, Lopez R, Safran H, DiPetrillo T. Percutaneous radiofrequency ablation of painful osseous metastases: A multicenter American College of Radiology imaging network trial. *Cancer* 2010; 116:989-997.
20. Goetz MP, Callstrom MR, Charboneau JW, Farrell MA, Maus TP, Welch TJ, Wong GY, Sloan JA, Novotny PJ, Petersen IA, Beres RA, Regge D, Capanna R, Saker MB, Gronemeyer DHW, Gevargez A, Ahrar K, Choti MA, de Baere TJ, Rubin J. Percutaneous image-guided radiofrequency ablation of painful metastases involving bone: A multicenter study. *J Clin Oncol* 2004; 22:300-306.
21. Kurup AN, Schmit GD, Morris JM, Atwell TD, Schmitz JJ, Weisbrod AJ, Woodrum DA, Eiken PW, Callstrom MR. Avoiding complications in bone and soft tissue ablation. *Cardiovasc Intervent Radiol* 2017; 40:166-176.
22. Bagla S, Sayed D, Smirniotopoulos J, Brower J, Neal Rutledge J, Dick B, Carlisle J, Lekht I, Georgy B. Multicenter prospective clinical series evaluating radiofrequency ablation in the treatment of painful spine metastases. *Cardiovasc Intervent Radiol* 2016; 39:1289-1297.
23. Ornetti P, Dougados M, Paternotte S, Logeart I, Gossec L. Validation of a numerical rating scale to assess functional impairment in hip and knee osteoarthritis: Comparison with the WOMAC function scale. *Ann Rheum Dis* 2011; 70:740-746.
24. Yanez B, Pearman T, Lis CG, Beaumont JL, Cella D. The FACT-G7: A rapid version of the functional assessment of cancer therapy-general (FACT-G) for monitoring symptoms and concerns in oncology practice and research. *Ann Oncol* 2013; 24:1073-1078.
25. Maccauro G, Silvia Spinelli M, Mauro S, Perisano C, Graci C, Attilio Rosa M. Physiopathology of spine metastasis. *Int J Surg Oncol* 2011:107969.
26. Bilsky MH, Lis E, Raizer J, Lee H, Boland P. The diagnosis and treatment of metastatic spinal tumor. *Oncologist* 1999; 4:459-469.
27. Sutcliffe P, Connock M, Shyangdan D, Court R, Kandala NB, Clarke A. A systematic review of evidence on malignant spinal metastases: Natural history and technologies for identifying patients at high risk of vertebral fracture and spinal cord compression. *Health Technol Assess* 2013; 17:1-274.
28. Valesin Filho ES, de Abreu LC, Lima GHV, de Cubero DIG, Ueno FH, Figueiredo GSL, Valenti VE, de Mello Monteiro CB, Wajnsztejn R, Fujiki EN, Neto MR, Rodrigues LM. Pain and quality of life in patients undergoing radiotherapy for spinal metastatic disease treatment. *Int Arch Med* 2013; 6:6.
29. Health Quality Ontario. Vertebral augmentation involving vertebroplasty or kyphoplasty for cancer-related vertebral compression fractures: A systematic review. *Ont Health Technol Assess Ser* 2016; 16:1-202.
30. Rosenthal DI, Alexander A, Rosenberg AE, Springfield D. Ablation of osteoid osteomas with a percutaneously placed electrode: A new procedure. *Radiology* 1992; 183:29-33.
31. Sandri A, Carbognin G, Regis D, Gaspari D, Calciolari C, Girardi V, Mansueto G, Bartolozzi P. Combined radiofrequency and kyphoplasty in painful osteolytic metastases to vertebral bodies. *Radiol Med* 2010; 115:261-271.
32. Anchala PR, Irving WD, Hillen TJ, Friedman MV, Georgy BA, Coldwell DM, Tran

ND, Vrionis FD, Brook A, Jennings JW. Treatment of metastatic spinal lesions with a navigational bipolar radiofrequency ablation device: A multicenter retrospective study. *Pain Physician* 2014; 17:317-327.

33. Wallace AN, Greenwood TJ, Jennings JW. Radiofrequency ablation and vertebral augmentation for palliation of painful spinal metastases. *J Neurooncol* 2015; 124:111-118.
34. Zhao W, Wang H, Hu JH, Peng ZH, Chen JZ, Huang JQ, Jiang YN, Luo G, Yi GF, Shen J, Gao BL. Palliative pain relief and safety of percutaneous radiofrequency ablation combined with cement injection for bone metastasis. *Jpn J Clin Oncol* 2018; 48:753-759.
35. Berenson J, Pflugmacher R, Jarzem P, Zonder J, Schechtman K, Tillman JB, Bastian L, Ashraf T, Vrionis F; Cancer Patient Fracture Evaluation (CAFE) Investigators. Balloon kyphoplasty versus nonsurgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: A multicentre, randomised controlled trial. *Lancet Oncol* 2011; 12:225-235.
36. Johnstone C, Lutz ST. External beam radiotherapy and bone metastases. *Ann Palliat Med* 2014; 3:114-122.
37. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Adult Cancer Pain. Version 1.2018. Plymouth Meeting, PA, National Comprehensive Cancer Network, 2018.