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The Efficacy of Radiofrequency Ablation Therapy in the Treatment of Musculoskeletal Tumors

*Junsung Koo and So Hak Chung**

Department of Orthopedic Surgery, Kosin University Gospel Hospital, Korea

Abstract

Background: Some musculoskeletal tumors cause severe pain and reduce the quality of life of patients. Radiofrequency Ablation (RFA) is thought to be a promising minimally invasive treatment option for painful musculoskeletal lesions. RFA may be beneficial to patients who are unable to undergo surgery, chemotherapy, or radiotherapy or who exhibit ineffective treatment results. The purpose of this study was to evaluate the efficacy of RFA in the treatment of musculoskeletal tumors.

Methods: Between April 2007 and October 2017, 43 patients with musculoskeletal tumors underwent percutaneous RFA. The median age of the patients was 59 years (range: 31 to 75 years) and the median follow-up duration was 67.2 months (range: 10.2 to 130.5 months). Of the 43 patients, 26 were male and 17 were female. Overall, 34 of the patients had metastatic bone tumors, 5 had chordomas, 3 had osteosarcoma, and 1 had a giant cell tumor. The pain levels and functional ability of the patients were evaluated using a Visual Analogue Scale (VAS) and the Musculoskeletal Tumor Society (MSTS) functional scoring system, respectively. Scores were recorded preoperatively and 1 and 4 weeks postoperatively. The Kaplan-Meier method was used to analyze the outcomes over time and calculate the 1-year, 2-year, and 5-year survival rates.

Results: The mean VAS scores of all patients; Pre-OP, 1 week, and 4 weeks were 8.21, 3.91, and 3.67, respectively. The mean preoperative MSTS score was 64.0% (range: 32% to 87%). The mean postoperative MSTS score was 71.0% (range: 40% to 90%). The median survival time was 20 months. The Kaplan-Meier analysis showed that the survival rates at 1, 2, and 5 years were 95.3%, 69.8%, and 30.2%, respectively.

Conclusion: In this study, RFA was shown to be effective in decreasing the pain levels and increasing the functional ability of patients with musculoskeletal tumors.

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Correspondence:

So Hak Chung, Department of Orthopedic Surgery, Kosin University Gospel Hospital, 262 Gamcheon-ro, Seo-gu, Busan 49267, Korea, Tel: 82-51-990-6467; Fax: 82-51-243-0181; E-mail: shchung@kosin.ac.kr

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Introduction

Recently, palliative treatment of primary or metastatic musculoskeletal tumors using minimally invasive techniques has become a challenge for physicians [1].

Some musculoskeletal tumors cause severe pain and reduce the quality of life of patients. Radiofrequency Ablation (RFA) is thought to be a promising minimally invasive technique for the treatment of painful musculoskeletal lesions and beneficial to patients who are unable to undergo surgery, chemotherapy, or radiotherapy or who exhibit ineffective treatment results. When targeted tissue receives a lethal dose of heat during RFA therapy, it becomes necrotic through the process of tissue coagulation [1].

CT-guided RFA provides the ability to locate musculoskeletal lesions accurately and has shown great promise in the treatment of musculoskeletal tumors. This procedure is relatively safe and alleviates pain for the patient. Furthermore, patients can undergo this procedure on an outpatient basis [1].

RFA has been used in the treatment of liver metastases, hepatocellular carcinoma, and renal and lung tumors and is regarded as the treatment of choice for osteoid osteoma [2-4]. For the treatment of painful musculoskeletal tumors, RFA is a relatively new technique, so that indication of RFA for musculoskeletal tumors is not established academically.

The purpose of this study was to evaluate the efficacy of RFA in the treatment of overall musculoskeletal tumors such as metastatic bone tumors, osteosarcoma, chordomas, and giant cell tumors.

Materials and Methods

The design and protocol of this retrospective study were approved by the Institutional Review Board of authors. Between April 2007 and October 2017, 56 patients with musculoskeletal tumors underwent percutaneous RFA. 13 patients who stopped receiving treatment, who moved to other hospitals during the treatment process, or who lost of follow up before 3 months were excepted and 43 patients were included. The median age of the patients was 59 years (range: 31 to 75 years) and the median follow-up duration was 67.2 months (range: 10.2 to 130.5 months). Of the 43 patients, 26 were male and 17 were female. We retrospectively reviewed the medical and radiologic records of each patient. All patients had musculoskeletal tumors that were treated with RFA under CT guidance. Overall, 34 patients had metastatic bone tumors (Group 1), 5 had chordomas (Group 2), 3 had osteosarcoma with multiple metastatic lesions (Group 3), and 1 had a giant cell tumor (Group 4). Group 1 comprised 19 male and 15 female patients. The median age was 61 years (range: 44 to 75 years) and the median follow-up duration was 65.8 months (range: 55 to 130.5 months). Group 2 comprised five male patients. The median age was 58 years (range: 48 to 65 years) and the median follow-up duration was 100.8 months (range: 84 to 110 months). Group 3 comprised two male patients and one female patient. The median age was 40 years (range: 31 to 45 years) and the median follow-up duration was 60.2 months (range: 10.2 to 85 months). Group 3 comprised the patients who were treated with adequate cycles of chemotherapy; nevertheless, the cancer was not reduced when 6 months after the chemotherapy. Group 4 comprised one female patient who was aged 31 years and was followed-up for 42 months. The distribution of the musculoskeletal tumors and the corresponding primary malignancies in Group 1 are presented in Table 1. Before ablation, the size of the target was measured using multiplanar cross-sectional imaging. Three categories were used to classify the radiographic pattern: Lytic, blastic, and mixed. Previously obtained imaging examinations were analyzed to evaluate lesion characteristics and the feasibility of electrode positioning and ablation.

RFA is performed under conscious sedation with general anesthesia. CT is conducted to determine the exact location and depth of the lesion in relation to the skin. The skin is prepared with povidone iodine solution, and the electrode is then inserted into the affected tissue of the musculoskeletal tumor. In some cases, a guide needle is necessary for coaxial placement of the electrode. Insulated guide needles are now available and can prevent skin burns at the needle insertion site should the active tip of the electrode remain in contact with the guide needle during the ablation. Depending on the size of the lesion, one or more ablations are performed with an emphasis on treating the tumor-bone interface [5].

In this study, 17-G internally cooled adjustable-length electrodes (Proteus RF Electrode; STARmed, Gyeonggi-do, Republic of Korea) and a 200-W RF generator (VIVA RF System; STARmed) were used. The type of electrodes and the length of the active tip were chosen based on the size, location, and geometry of the tumor and the preference of the surgeon. The electrode tip was inserted approximately 1 cm from the center of the target. The electrodes were then deployed slowly, taking into account the need to ablate the lesion-bone interface. Each ablation had duration of 30 sec and an energy level of 100 W. The number of electrode placements, individual (per electrode) and total ablation times, total energy delivered to the target, and lesion

Table 1: The distribution of the musculoskeletal tumors and the corresponding primary malignancies for 34 patients in Group 1.

Site of primary neoplasm		Site of metastasis	
Kidney	5	L-Spine	17
Lung	5	Sacrum	5
Liver	4	C-Spine	3
Prostate	4	Scapula	3
Colon/rectum	4	T-Spine	2
Thyroid	4	Ilium	2
Bladder	4	Humerus	1
Stomach	3	Acetabulum	1
Uterus	1		
Total	34	Total	34

Table 2: Patient demographics and characteristics.

Variable	Number	%
Sex		
Male	26	61
Female	17	40
Site of primary tumor		
Kidney	5	12
Lung	5	12
Sacrum	5	12
Other	28	65
Site of metastasis		
L-Spine	17	40
Sacrum	10	23
Other	16	37
Size		
<3 cm	28	65
≥ 3 cm	15	35
Radiographic pattern		
Lytic	31	72
Blastic	9	21
Mixed	3	7
Cortical bone disruption		
No	22	51
Yes	12	28
Previous surgery		
No	27	63
Yes	16	37
Previous Radiation Therapy		
No	30	70
Yes	13	30
Concomitant chemotherapy		
No	24	56
Yes	19	44
Imaging modality used for follow-up		
CT	7	16
PET-Scan	5	12
MRI	21	49

temperatures achieved were recorded.

The follow-up imaging was done using MRI between 3 to 6 months. The pain levels and functional ability of the patients were evaluated using a Visual Analogue Scale (VAS) and the Musculoskeletal Tumor Society (MSTS) functional scoring system. The MSTS system assigns numerical values (0-5) to six categories: Pain, and function and emotional acceptance in the upper and lower extremities; use of supports, and walking and gait in the lower extremity; and hand positioning, and dexterity and lifting ability in the upper extremity [6]. Each category is scored from 0 to 5, and the maximum total score is 30. The Kaplan-Meier method was used to analyze the outcomes over time and calculate 1-year, 2-year, and 5-year survival probabilities. The survival rates at 1, 2, and 5 years were evaluated for the patients who were followed-up for 5 years.

Results

For lesions smaller than 3 cm (28 of the 43 cases), one electrode placement was adequate, while larger than 3 cm (15 of the 43 cases), two or more electrode placements were required (Table 2).

The effect of RFA on the pain levels of the patients was evaluated using a VAS. Pain reduction was fast and occurred during the first week after the procedure in the majority of the patients. In Group 1, the VAS scores for a day before the operation, 1 week, 4 weeks, 12 weeks, and 24 weeks were 8.32, 4.00 (51.92% reduction), 3.71, 3.52, and 3.42 respectively. In Group 2, the VAS scores for a day before the operation and 1 week, 4 weeks, 12 weeks, and 24 weeks after the operation were 7.20, 3.80 (47.22% reduction), 3.60, 3.42, and 3.26 respectively. In Group 3, the VAS scores for a day before the operation and 1 week, 4 weeks, 12 weeks, and 24 weeks after the operation were 7.00, 3.33 (52.43% reduction), 3.00, 2.75, and 2.54 respectively. In Group 4, the VAS scores for a day before the operation and 1 week, 4 weeks, 12 weeks, and 24 weeks after the operation were 7, 3 (57.14% reduction), 2, 1.81, and 1.64, respectively. When all patients were considered together, the VAS scores for a day before the operation and 1 week, 4 weeks, 12 weeks, and 24 weeks after the operation were 8.21, 3.91 (52.38% reduction), 3.67, 3.31, and 3.12 respectively (p-value <0.5) (Figure 1 and 2).

The mean preoperative scores in the six domains of the MSTS scoring system were as follows: pain - 3.1, function - 3.0, emotional acceptance - 3.2, use of supports/hand positioning- 3.9, walking ability/dexterity - 3.5, and gait/lifting ability - 2.5. The mean total score was 19.2. The mean preoperative MSTS score was 64.0% (range: 32% to 87%). The mean postoperative scores in the six domains of the MSTS scoring system were as follows: pain - 4.0, function - 3.1, emotional acceptance - 3.5, use of supports/hand positioning- 4.0, walking ability/dexterity - 3.9, and gait/lifting ability - 2.8. The mean total score was 21.3. Therefore, the mean postoperative MSTS score was 71.0% (range: 40% to 90%). The median survival time was 20 months. These results revealed a marked decrease in pain with subsequent improvement in the life quality for all participants since the first week post-treatment that lasted throughout the 4-week follow-up period.

Local control was defined as a tumor volume equal to or less than the tumor volume at start of radiotherapy. The effect of RFA on local progression was evaluated using size and local control rate. In Group 1, the size before the operation, after the operation and the local control rate were 2.6 cm, 2.2 cm, and 0.85 respectively. In Group 2, the size before the operation, after the operation and the local control

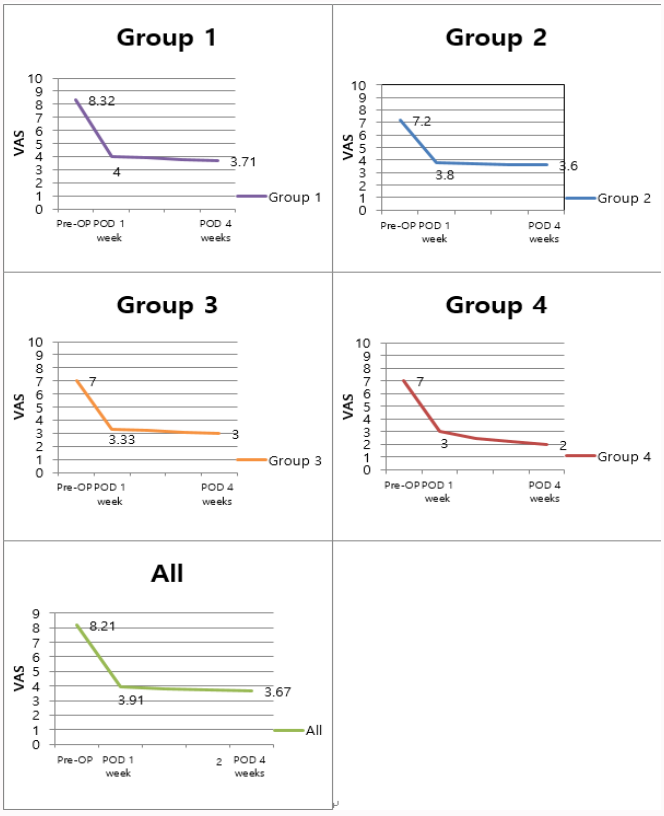

Figure 1: Pre- and postoperative visual analogue scale scores of patients treated with radiofrequency ablation (Group 1: metastatic bone tumor, Group 2: chordoma, Group 3: osteosarcoma, and Group 4: giant cell tumor).

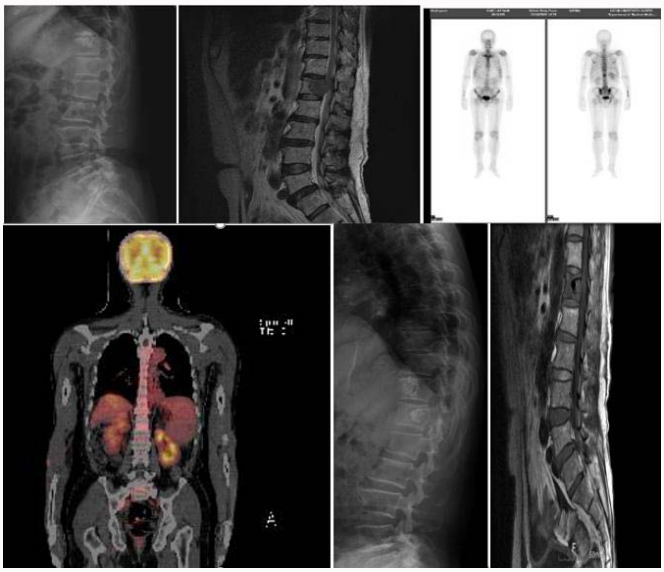

Figure 2: A 75-year-old male patient with an L1 tumor as a result of metastatic hepatocellular carcinoma. The patient was treated with radiofrequency ablation. A. X-ray, B. MRI, C. Bone scan, D. PET-CT, E. X-ray after RFA, F. MRI after RFA.

Table 3: Lesion characteristics and treatment.

Number of lesions	Lesion size (cm)	Number of electrode placements	Duration of radiofrequency energy deposition (min)
28	<3	1	3
9	3	1	4
2	4	4	8
3	5	4	10
1	7	8	15
Total 43			

Table 4.1: The effect of radiofrequency ablation on the pain levels of the patients, evaluated using a visual analogue scale.

	Pre-OP	POD 1 week	POD4 weeks	POD 12 weeks	POD 24 weeks	p-value
Group 1	8.32	4	3.71	3.52	3.41	<0.002
Group 2	7.2	3.8	3.6	3.42	3.26	<0.005
Group 3	7	3.33	3	2.75	2.54	<0.004
Group 4	7	3	2	1	1	-
All	8.21	3.91	3.67	3.31	3.12	<0.003

*Pre-OP: a day before the operation
*POD: Post-Operative Day

Table 4.2: Effect of radiofrequency ablation on the functional ability of the patients, evaluated using the MSTS functional scoring system.

MSTS scoring system domain	Pre OP score	Post OP score
Pain	3.1	4
Function	3	3.1
Emotional acceptance	3.2	3.5
Use of supports/hand-positioning	3.9	4
Walking ability/dexterity	3.5	3.9
Gait/lifting ability	2.5	2.8
Total	19.2	21.3
Percentage (%)	64	71

MSTS: Musculoskeletal Tumor Society

rate were 2.8 cm, 2.6 cm, and 0.93 respectively. In Group 3, the size before the operation, after the operation and the local control rate were 1.7 cm, 1.4 cm, 0.82 respectively. In Group 4, the size before the operation, after the operation and the local control rate were 1.0 cm, 0.8 cm, 0.80 respectively. When all patients were considered together, the size before the operation, after the operation and the local control rate were 2.6 cm, 2.2 cm, 0.85 respectively (Table 3 and 4).

Table 4.3: The effect of radiofrequency ablation on local progression, evaluated by the size and local control rate.

	Pre-OP (cm)	Post-OP (cm)	Local control rate
Group 1	2.6	2.2	0.85
Group 2	2.8	2.6	0.93
Group 3	1.7	1.4	0.82
Group 4	1	0.8	0.8
All	2.6	2.2	0.85

The Kaplan-Meier analysis showed that the survival rates at 1, 2, and 5 years were 95.3%, 69.8%, and 30.2%, respectively.

There are several side effects of RFA, such as infection,

hemorrhage, neurological complications, or skin burns. However, no adverse effect was noted in this report.

Discussion

The development of RFA technology can be traced back to neurosurgeon Harvey Cushing, who teamed up with physicist Bovie in 1928 to develop a device that used focused heat to perform surgical coagulation and cutting; this device was the precursor to the Bovie electrocautery device [7]. RFA has since been used to treat trigeminal neuralgia and to perform dorsal rhizotomy, among other applications. Tillotson et al. [8] conducted a pioneering study into the effects of RFA in dog femurs. In their study, radiofrequency treatments at a temperature of 80°C induced marrow fat necrosis and reactive fibrosis, creating lesions between 0.9 and 1.3 cm in size. The use of RFA to treat osteoid osteoma was first reported in 1992 [9]. RFA has since been used in the management of other musculoskeletal lesions, most commonly metastatic bone disease [1].

RFA works in the same way as standard surgical electrocautery. An electric current is delivered into the body *via* an electrode and exits through ground pads that are usually placed on the legs. Lesion size after RFA is dependent on many factors, namely the type of tissue, duration of current, and temperature. Ionic agitation causes tissue heating, resulting in near-instantaneous cell death when tissue temperatures reach 60°C. Temperatures between 46 and 60°C are also associated with cell death, but longer exposure durations are required [10].

However, caution must be exercised when higher temperatures are used, as temperatures >100°C have been found to cause boiling and vaporization of the surrounding tissue. This result in the formation of a coagulum and increased impedance to further current, thereby limiting the effective zone of treatment [1].

Resistive heating occurs in the surrounding tissue, inducing immediate cell death. The tissue adjacent to the electrode is heated to the highest temperature, and as the distance from the electrode increases, the heat decreases exponentially in a single electrode device. More distant tissues are instead heated by thermal conduction, thus limiting the size of the lesion generated by this technique. Due to its inherent cauterizing effect, RFA is minimally invasive and can be safely conducted percutaneously [11-14].

Image-guided RFA is widely used in clinical practice to treat various types of tumors with satisfactory outcomes. In their preliminary study, Dupuy et al. [15] reported that RFA provided palliative treatment to patients with painful osseous metastases. Furthermore, Callstrom et al. [16] reported that RFA provided substantial pain relief to 12 patients with painful osteolytic metastases.

A multicenter study involving 43 patients with painful osseous metastases was conducted by Goetz et al. [17], in which RFA provided significant pain relief and decreased opioid usage, and was associated with only minor complications. Neeman et al. [18] used percutaneous RFA to treat a patient whose chordoma had metastasized to the pararectal region and was causing local and sciatic pain.

The mechanisms by which RFA decreases pain may involve: Pain transmission inhibition via the destruction of sensory nerve fibers in the periosteum and bone cortex; decreased stimulation of sensory nerve fibers via the reduction of lesion volume; the destruction of tumor cells that produce nerve-stimulating cytokines such as tumor necrosis factor-alpha and interleukins, and the inhibition of osteoclast activity [19,20].

There were several limitations of our study. First, it was not a randomized prospective study, so the efficacy of RFA was not compared with that of other treatment modalities. Second, the present study included heterogeneous patients with different disease entities and tumors in different anatomical locations. Third, the sample size of our study was relatively small compared to that of other studies. Fourth, strict protocols for the administration of RFA have yet to be defined. Further studies are therefore required to define protocols for this technique and to evaluate the safety and long-term efficacy of RFA in the treatment of other neoplasm's [21].

Nevertheless, we believe that the results derived from this study will help to identify patients with musculoskeletal tumors who would benefit from RFA. In this study, RFA reduced the pain levels and increased the functional ability of patients with musculoskeletal tumors, assessed using a VAS and the MSTS functional scoring system, respectively since the first week post-treatment that lasted throughout the 4-week follow-up period. In some patients who underwent RFA, recurrence of the tumor was not noted during the follow-up period. Also, patients treated with RFA show low 5-year survival rate. Therefore, RFA could potentially serve as both a palliative and curative treatment. Furthermore, RFA may be a therapeutic option for patients who are unsuitable for radiotherapy, chemotherapy, and surgery, or who exhibit insufficient therapy results.

In conclusion, imaged-guided RFA is a promising technique for the treatment of painful musculoskeletal tumors, and appears to be effective, safe, and well-tolerated by patients. In this study, RFA decreased the pain levels and increased the functional ability of patients with musculoskeletal tumors.

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