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Computed tomography-guided argon-helium cryoablation for sacrum chordoma

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Abstract

We examined the therapeutic effects of argon-helium cryoablation guided by computed tomography (CT) in the treatment of sacral chordoma.

This is a retrospective study. CT-guided argon-helium cryoablation was used to treat 9 sacral chordoma patients at our centers between January 2016 and June 2019. We collected data on treatment response and success. Data from long-term follow-up of treatment outcomes were also assessed.

All patients were treated successfully according to the indicated technical parameters. There were no reports of procedure-related complications from any of the patients. Complete response (CR) was also achieved in all patients. Six patients (66.7%) achieved initial CR after 1 treatment session and 3 patients (33.3%) achieved secondary CR after 2 treatment sessions. The chordoma-related symptoms improved significantly in all patients after treatment. The mean visual analogue scale score improved from 7.3 before treatment to 4.2 after treatment ($P<.001$). The mean function score improved from 3.2 before treatment to 1.4 after treatment ($P<.001$). The median length of follow-up for all patients was 33 months (range: 6–46 months). All patients were alive during the follow-up. Two (22.2%) patients experienced local recurrence (LR) at 6 and 9 months after treatment, respectively. These patients had revised treatment with trans-arterial embolism (n=1) or repeat ablation (n=1). The median progression-free survival was 36.8 months.

Treatment of sacral chordoma with CT-guided argon-helium cryoablation is effective and offers a potentially beneficial therapeutic alternative for patients with the condition.

Abbreviations: CR = complete response, CT = computed tomography, LR = local recurrence, MRI = magnetic resonance imaging.

Keywords: argon-helium cryoablation, computed tomography, sacrum chordoma

1. Introduction

While relatively uncommon among primary bone cancers, chordoma tumors originate from notochord remnants anywhere along the length of the spine.[1–3] Sacral chordoma is the most common type of chordoma.[4] At present, surgical management is still the first line treatment for chordoma.[1–3] However, sacral chordoma is difficult to manage with surgery and radiation therapy because of morbidity to collateral structures, such as nerves, and the high radiation doses that are required.[5] The mainstay of treatment for chordomas is maximal debulking by surgery followed by adjuvant radiation or proton radiation treatment. Unfortunately, chordomas have a relatively high recurrence rate, low disease-free survival rate, and high rate of morbidity from conventional treatments. Surgery to debulk the tumor and reduce local pain can also be considered for palliation.[5]

Along with the rapid development of interventional radiology and other minimally invasive techniques, treatment of tumors has also become minimally invasive. Percutaneous argon-helium cryoablation can be performed with the patient under local anesthesia and conscious sedation in the outpatient setting.[6,7] At present, percutaneous argon-helium cryoablation has been widely used for treating solid tumors.[6,7]

At present, there is limited evidence in the literature supporting the use of minimally invasive treatments for chordoma. Here, we outline our findings from treating sacral chordoma patients effectively using argon-helium cryoablation guided by computed tomography (CT).

2. Materials and Methods

The study was carried out at 2 centers and involved retrospective analysis of patient records. All work was reviewed and approved by the Institutional Review Board. As the study was a

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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Table 1

Baseline data of these 9 patients.

No./Sex/Age (yr)	Duration (d)	Size (cm × cm)	Location	Sacral foramen involved
1/Female/35	35	8.6 × 4.8	Sacral vertebrae 1–3	Yes
2/Female/58	30	8.0 × 5.2	Sacrococcygeal region	Yes
3/Female/55	12	12.5 × 9.1	Sacrococcygeal region	Yes
4/Female/60	28	7.8 × 6.3	Sacrococcygeal region	Yes
5/Male/57	19	11.2 × 7.1	Sacrococcygeal region	Yes
6/Female/47	11	8.8 × 4.5	Sacrococcygeal region	Yes
7/Male/65	22	8.5 × 5.3	Sacrococcygeal region	Yes
8/Male/51	28	8.3 × 5.2	Sacrococcygeal region	Yes
9/Female/55	23	8.6 × 5.5	Sacrococcygeal region	Yes

Duration: interval from onset to diagnosis.

retrospective analysis of medical records, informed and written patient consent was not required.

3. Patients

Argon-helium cryoablation was used on 9 sacral chordoma patients between January 2016 and June 2019 at our center. The inclusion criteria were:

(a) definite diagnosis of sacral chordoma; and

Symptomatic cases. The exclusion criteria were:

(a) patients who refused to receive argon-helium cryoablation; and
(b) patients who experienced severe cardiac, renal, lung, or coagulatory dysfunctions.

The indications of CT-guided argon-helium cryoablation included:

(a) the surgeons preoperatively assessed the sacral chordoma and considered that the lesion could not be curative resected; and
(b) patients refused to undergo surgical treatment. Table 1 summarizes the baseline patient characteristics.

4. Diagnosis

Magnetic resonance imaging (MRI), contrast-enhanced pelvic CT, CT-guided biopsy and patient history were used to diagnose sacral chordoma in each patient. Tumor locations were further evaluated by CT and MRI results. CT was used to measure tumor size.

4.1. Argon-helium cryoablation

A PQ6000 Spiral CT Scanner (Philips, Amsterdam, Netherlands) was used by 3 interventional radiologists to treat the sacral chordoma patients while they lay flat on their chests.

In combination, an argon-helium based CryoHit^{TM} cryoablation system (Galil Medical, Tel Aviv, Israel) was used on each patient. First, tumor locations were determined by CT. As shown in Figure 1a, CT also revealed tumor range and size. Next, preoperative CT and MRI were used to confirm whether tumors were proximal to any important nerves and blood vessels. Tumor size determined the number of argon/helium cryoprobes (diameter: 1.47 mm, freezing range: 3.5 × 1.5 cm) required and up to 25 were used. Tumor probing sites were determined by the tumor shape and environment (Fig. 1b). It was important to ensure that the maximum distance between probes was 1.5 cm at any 1 location. Lidocaine (2%, 5 mL) was used as local anesthetic to place the probes. Cancerous cells were killed by temperatures below –40°C which was achieved by ensuring that the freezing area extended 0.5 to 1 cm beyond the edge of the tumors.

Upon positioning all the cryoprobes, duplicate 10-minute freezing followed by 3-minute thawing periods were conducted for each tumor. Quick expansion of argon gas inside an enclosed cryoprobe absorbed heat from the surrounding to cause accelerated tissue freezing. In fact, temperatures at the tip of the cryoprobe descended to as low as −140 ° C in fractions of a minute. Substituting helium for argon caused thawing. Pelvic CT was performed directly afterwards to monitor ice ball scale.

Trophic nerve, anti-inflammatory and hemostatic therapies were used while observing patients over the subsequent 3 to 5 days as they recovered from cryoablation.

4.2. Assessment

The presence of Ice balls covering the entire tumor without any major procedure-related complications was considered technical success. Patient reports together with laboratory and CT results were used to detect treatment side-effects. The Society of Interventional Radiology guidelines was used to classify side-effects as minor or major.[8] Local effectiveness of argon-helium cryoablation was evaluated by comparing the preoperative contrast-enhanced CT and 1-month postoperative contrast-enhanced CT results. Complete response (CR) was defined as uniform hypoattenuation at contrast-enhanced CT without enhancement in the ablation zone. Patients with incomplete response underwent repeat cryoablation to achieve CR. If the location of residual lesion was not suitable for cryoablation, trans-arterial embolism was indicated. The return of a tumor inside or near to the site of cryoablation was termed local recurrence (LR). The visual analogue scale score (10: unbearable pain - 0: no pain) was used to evaluate patient's symptoms. The function score was also assessed before and after treatment. Patients were classified into 5 grades of disability as follows: Grade 0: normal or able to perform normal activity; Grade 1: normal activity with effort, but without assistance; Grade 2: requires occasional assistance, or considerable assistance, and frequent care; Grade 3: disabled or severely disabled; Grade 4: very sick or moribund.[9]

Contrast-enhanced pelvic CT and clinical evaluation were undertaken during regular follow up every 1, 2, and 3 months. Then for the initial 2 years follow-up was every 3 months, over the subsequent 3 years it was conducted every 6 months; until it

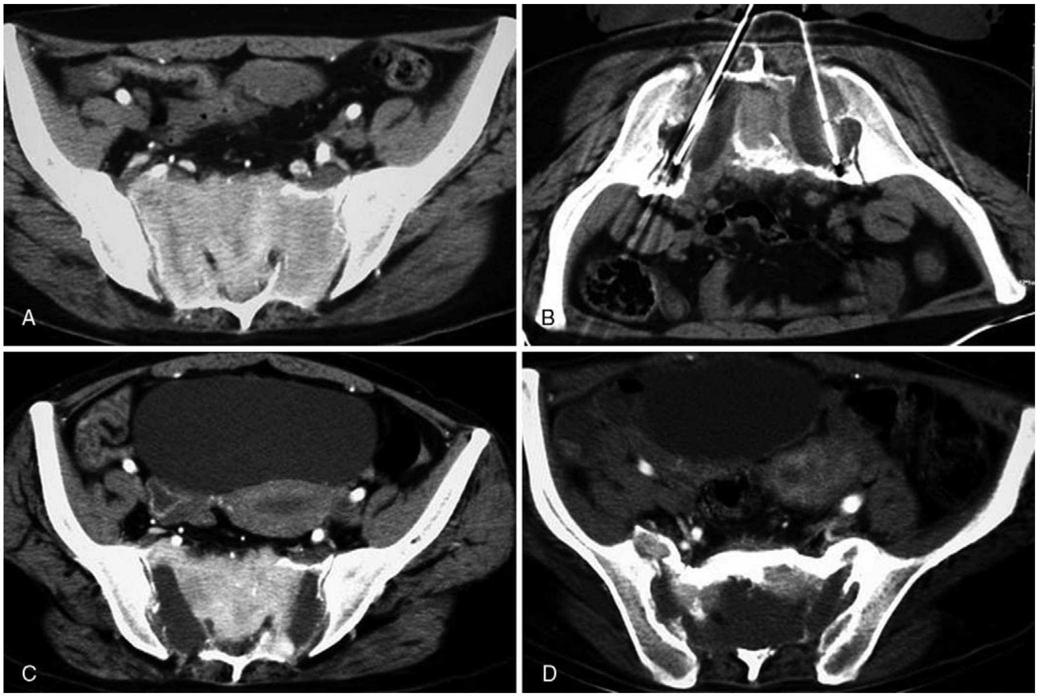

Figure 1. A 35-year-old female underwent computed tomography (CT)-guided argon-helium cryoablation for sacrum chordoma. (a) Preoperative contrast-enhanced CT demonstrated the sacrum chordoma. (b) Procedure of argon-helium cryoablation. (c) One-month postoperative contrast-enhanced CT demonstrated the incomplete response of treatment after the first treatment session. (d) Complete response was obtained after a second time cryoablation.

became once every year following therapy. CT of the brain, neck and abdomen was performed once a year to detect distant metastasis. If patients felt anxious, at any stage they were encouraged to report to hospital. Patient follow-up was intended to continue until death or termination of the study in December 2019.

Statistical analysis

All statistical testing was performed with SPSS v16.0 (SPSS, Inc., Chicago, IL). Continuous variables were analyzed via *t* tests. The duration of patient survival was calculated using the Kaplan–Meier curve. $P < .05$ was maintained as the statistical significance threshold.

5. Results

5.1. Treatment

All patients achieved CR and technical success, with no iatrogenic complications (Table 2). Six patients (66.7%) achieved initial CR after 1 treatment session. The remaining 3 patients (33.3%) achieved incomplete response after the first treatment session (Fig. 1c), they underwent the second treatment session 1 month after the first, and achieved CR (Fig. 1d). The mean visual analogue scale score improved from 7.3 before treatment to 4.2 after treatment ($P < .001$). The mean function score improved from 3.2 before treatment to 1.4 after treatment ($P < .001$).

The chordoma-related symptoms improved significantly in all patients after treatment (Table 3). Lumbosacral pain was found in all patients before treatment, and it was found in 4 patients after treatment. Lower limb pain and dysporia were found in 2 patients before treatment, and no patient had lower limb pain after treatment. Lower limb numb and limp were found in all patients before treatment, and it was found in 2 patients after treatment.

Table 2

Treatment results and outcome.

No.	Treatment sessions	Number of cryoprobes	Visual analogue scale score		Function score		Follow-up (mo)	Local recurrence	Outcome
			Before	After	Before	After			
1	2	6	6	4	3	2	41	Yes	Alive
2	1	6	7	4	4	2	21	No	Alive
3	1	12	9	6	3	1	6	No	Alive
4	1	7	8	5	3	1	46	No	Alive
5	2	10	8	4	3	2	40	No	Alive
6	1	7	7	4	3	1	35	Yes	Alive
7	1	6	6	3	4	2	33	No	Alive
8	2	7	8	4	3	1	20	No	Alive
9	1	7	7	4	3	1	10	No	Alive

Table 3

Symptoms changes before and after treatment.

No.	Symptoms before	Symptoms after
1	LP, LLP, LLN, limp	limp
2	LP, LLN, limp	LLN
3	LP, limp	LP
4	LP, LLP, LLN, limp	None
5	LP, LLN, limp, dysporia	LLN
6	LP, LLN, limp, dysporia	LP
7	LP, LLN, limp	LP
8	LP, LLN, limp	None
9	LP, LLN, limp	LP, limp

LLN = lower limb numb, LLP = lower limb pain, LP = lumbosacral pain.

5.2. Follow-Up

Follow-up for the 3 patients lasted for a median length of 33 months (range: 6–46 months, Table 2). All patients were alive during follow-up. Two (22.2%) patients experienced LR 6 and 9 months after treatment, respectively. The pelvic contrast-enhanced CT revealed residual malignancy at the tumor edge. These patients had revised treatment with trans-arterial embolism (n = 1) or repeat ablation (n = 1). The median progression-free survival was 36.8 months (Fig. 2). No patient experienced distant metastasis during follow-up.

6. Discussion

This brief report demonstrated our clinical results of CT-guided argon-helium cryoablation for treatment of sacrum chordoma. There were strong initial results and all patients attained CR as well as technical success. LR was observed in 1 of 3 (33.3%) patients.

Surgical resection has been widely used for treating sacral chordoma.[1–4] However, the chordoma is usually large and extensive requiring invasive treatment. In addition, the pelvic vasculature is very diffuse. Therefore, the volume of surgical resection-related blood loss is usually large with an approximate mean volume of 800 CC.[1–4] Some researchers performed preoperative temporary aorta balloon occlusion to decrease the intra-operative blood loss when performing sacral chordoma surgery.[1,2] However, this procedure increases operative complexity and cost. Other studies demonstrated that sacrectomy could decrease the long-term recurrence rate of sacral chordoma.[2] However, neurologic impairment after sacrectomy also decreases the quality of life.

Although still a relatively new treatment method argon-helium cryoablation has successfully treated several cancers including prostate cancer, renal carcinoma, hepatocellular carcinoma, etc.[10,11] Many pathways are believed to be involved in cryotherapy-mediated cell-death such as intracellular solution alterations triggering cell hunger and degradation, formation of ice inside cells, growth-limiting anti-tumor immunoreactivity, and hypoxic microvascular destruction.[10,11] Follow-up for extended lengths of time has shown that cryoablation controls tumor growth in up to 95% of cases.[10]

The high technical success (100%) and CR (100%) rate of argon-helium cryoablation in this study could be due to several reasons. To begin with, the puncture sites were confirmed by reviewing the preoperative CT and MRI results, and the puncture was performed under the CT guidance. Secondly, the diameter of

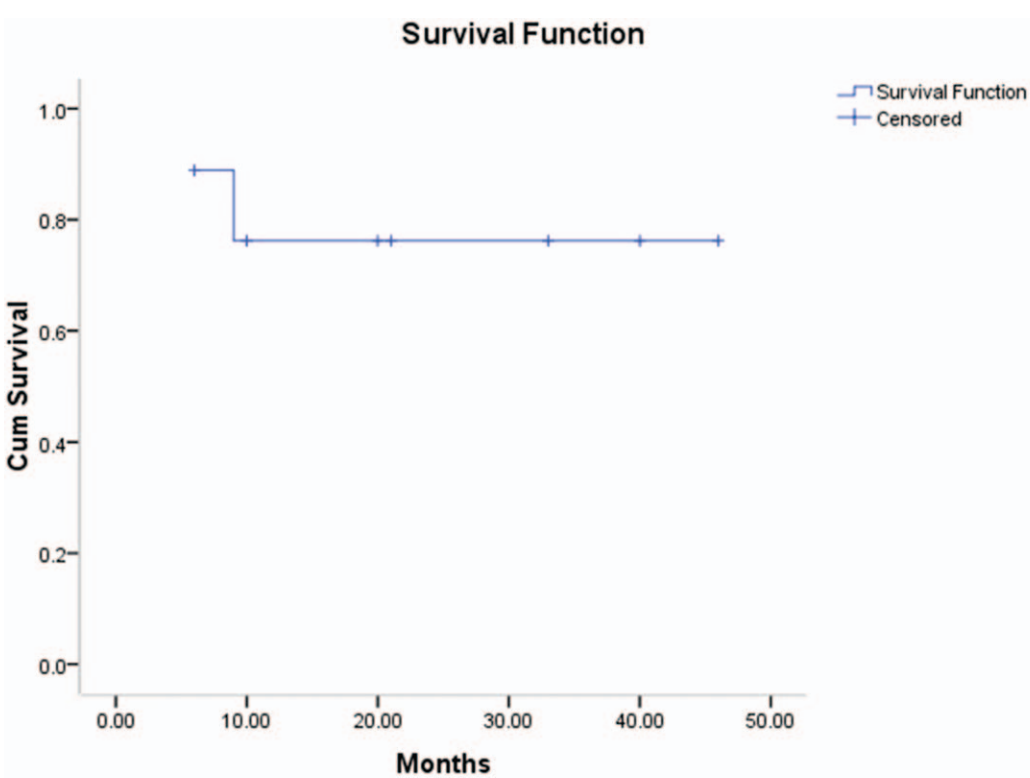

Figure 2. The progression-free survival after treatment.

each cryoprobe is only 1.47 mm, thus, patient wounding was minimal. Thirdly, the well-designed distribution of cryoprobes made the cryoablation area cover the entire tumor.

There are however several shortcomings to this study. The retrospective study design is the most notable weakness. In addition, it is a single-center study with a small sample size of 3. Finally, it lacks the strength of comparison with a well-matched control group of patients.

To conclude, while more clinical investigations are required, the preliminary results we present here suggest that argon-helium cryoablation guided by CT is a plausible treatment alternative for sacral chordoma patients.

Author contributions

Conceptualization: Wei Zhang
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Funding acquisition: Yu-Fei Fu
Investigation: Wei Zhang
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