

# High-Intensity Focused Ultrasound (HIFU) for the Treatment of Pediatric Ewing Sarcoma: A Single-Center Retrospective Study

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**Abstract:** Purpose: To evaluate the safety, clinical outcomes, and advantages of HIFU as a non-invasive local therapy for Ewing sarcoma in children and adolescents, especially for limb-salvage in patients with extensive bone destruction or unresectable lesions. Methods: A retrospective review was conducted of all pediatric patients with pathologically confirmed Ewing sarcoma treated with HIFU at a single tertiary children's hospital between January 2010 and June 2023. Clinical data, imaging features, treatment protocols, complications, and survival outcomes were analyzed. Results: Seven patients were enrolled, including 3 males and 4 females, with a median age of 7.4 years (range 3.7–17.0 years). Four patients had localized disease, and three had widespread metastatic lesions at initial diagnosis. All four localized patients had extensive bone invasion that precluded limb-salvage resection. HIFU combined with chemotherapy achieved complete local tumor ablation in 2 patients, and all four localized patients remained alive at the final follow-up. Among the three metastatic patients, HIFU significantly reduced tumor burden, relieved pain, and improved quality of life, although all eventually died of systemic progression. Conclusion: HIFU is a safe, effective, and non-invasive local treatment for pediatric Ewing sarcoma. It serves as a valuable limb-salvage modality for localized patients with extensive bone destruction. For metastatic patients, HIFU provides effective palliation with minimal trauma and may be used as part of multidisciplinary comprehensive therapy. **Keywords:** pediatric Ewing sarcoma; HIFU; high-intensity focused ultrasound; limb-salvage; non-invasive ablation; pediatric bone tumor

## 1. Introduction

Ewing sarcoma family tumor (ESFT) is a highly malignant group of small-round-cell tumors that mainly occur in children and adolescents. It is the second most common malignant bone tumor in the pediatric population, characterized by high invasiveness, osteolytic destruction, and a strong tendency for early metastasis[1][2]. Before the 1970s, amputation was the main surgical treatment for Ewing sarcoma in the extremities. With the development of multidisciplinary therapy including chemotherapy, radiotherapy, and advanced surgical techniques, limb-salvage treatment has become the mainstream strategy. However, a small proportion of patients present with massive tumor infiltration, extensive neurovascular involvement, or severe bone destruction, making curative resection impossible[3].

High-intensity focused ultrasound (HIFU) is a non-invasive thermal ablation technique that focuses ultrasonic energy externally to induce irreversible coagulative necrosis in targeted solid tumors[4]. It has been widely used in the treatment of bone and soft-tissue tumors. This study aimed to evaluate the clinical value of HIFU in pediatric Ewing sarcoma, especially for limb-salvage in unresectable cases and palliation in metastatic patients.

## 2. Materials and Methods

### 2.1 Study Population

A retrospective review was conducted of consecutive pediatric patients with pathologically confirmed Ewing sarcoma treated with HIFU at the Children's Hospital of Chongqing Medical University from January 2010 to June 2023.

Inclusion criteria:

- (1) Age < 18 years;
- (2) Pathologically proven Ewing sarcoma;
- (3) Received HIFU as part of multidisciplinary treatment;
- (4) Complete clinical, imaging, and follow-up data available.

Exclusion criteria:

- (1) Loss to follow-up;
- (2) Incomplete medical records.

## 2.2 HIFU Treatment Protocol

All procedures were performed under general anesthesia or epidural anesthesia. The treatment range included the entire bone lesion, 1–2 cm of adjacent normal soft tissue, and 3–5 mm of normal bone tissue. The acoustic power was 60 W. Treatment parameters were determined by three senior HIFU specialists.

## 2.3 Data Collection

Clinical data including age, gender, disease stage, tumor location, tumor size, treatment process, complications, and follow-up outcomes were collected.

## 2.4 Follow-Up

Patients were followed up at 3, 6, and 12 months after HIFU treatment using MRI and CT. Local tumor control, limb function, survival status, and complications were evaluated.

# 3. Results

## 3.1 Baseline Characteristics

Seven patients were enrolled, including 3 males and 4 females, with a median age of 7.4 years (range 3.7–17.0 years). Median disease course was 59 months (range 20–98 months). Localized disease: 4 patients; metastatic disease: 3 patients.

## 3.2 Local Control and Survival Outcomes

Localized group (n=4): Among them, 4 children had localized disease, including 2 males and 2 females, with a median age at diagnosis of 5.9 years (range 3.7–10.0 years) and a median disease course of 89 months (range 34–98 months). three patients underwent HIFU combined with chemotherapy (VAC/IE regimen: alternating vincristine, doxorubicin, and cyclophosphamide with ifosfamide and etoposide) because of extensive tumor infiltration and severe bone destruction, and their parents refused amputation. patient 4 had a pelvic tumor measuring 15 cm in diameter. After chemotherapy and HIFU treatment, the tumor shrank to approximately 3 cm and was then completely resected surgically. Patient 3 eventually underwent amputation due to tumor recurrence.

Metastatic group (n=3): Three children had metastatic disease, including 2 males and 1 female, with a median age at diagnosis of 10.7 years (range 7.0–17.0 years) and a median disease course of 33 months (range 29–50 months). All patients received comprehensive treatment including chemotherapy and radiotherapy. Preoperative CT and MRI showed that the lesions could not be completely resected surgically, and the patients were in poor general condition, so surgical trauma might be fatal to them. patients 1 and 2 had large masses with multiple bone involvements such as the ilium. They received HIFU treatment after 6 cycles of chemotherapy. Postoperative color Doppler ultrasound and CT showed that most of the lesions were necrotic tumor tissue. patient 3 underwent complete resection of the back mass but developed 7 liver metastases, and received HIFU treatment for liver metastases. Postoperative CT and ultrasound showed no obvious blood supply in the liver masses. all patients underwent complete preoperative CT and MRI for evaluation and localization, and were treated by specialized physicians. Imaging follow-up was performed at 3, 6, and 12 months after surgery.

## 3.3 Complications

Second-degree skin burn: 1 case; common peroneal nerve injury: 1 case; transient mild fever: observed in some patients and resolved spontaneously within 3 days.

# 4. Discussion

HIFU Ewing sarcoma accounts for approximately 3% of all pediatric malignant tumors, with a male-to-female ratio of 1.30–1.51:1[5]. The tumor commonly arises in the femur, pelvis, and long bone diaphyses, with rare soft tissue involvement[6]. The main clinical manifestations include local pain, swelling, and palpable masses, with occasional pathological fractures[7][8]. Typical computed tomography and X-ray features include “onion-skin” periosteal reaction and osteolytic lesions.

Current treatment consists of systemic chemotherapy combined with local radiotherapy or surgical resection. However, a subset of patients remains ineligible for conventional surgery or refuses amputation[9]. HIFU provides a novel noninvasive treatment modality for these patients.

In this study, 3 localized patients with large tumors and unclear boundaries refused amputation and received HIFU. Complete ablation of malignant bone tumors was achieved in 2 patients, with preserved limb function. One patient experienced transient common peroneal nerve injury and recovered after rehabilitation. One patient with a large retroperitoneal tumor achieved significant tumor shrinkage after HIFU and underwent subsequent complete surgical resection.

For 3 patients with widespread metastases, HIFU achieved local tumor necrosis, reduced tumor burden, relieved local pain, and preserved limb function, significantly improving quality of life.

HIFU is characterized by good directivity, strong focusing ability, and high tissue penetration[10]. It induces tumor cell death via mechanical effects, thermal coagulation, and cavitation effects. With technological advancement, HIFU has been widely used in the treatment of solid tumors such breast cancer, liver cancer, pancreatic cancer, and uterine fibroids[11]. Later, with technological maturity, HIFU was gradually applied to the treatment of bone tumors. It is generally used for pain relief and local control in patients with bone metastases, while its application in primary bone tumors is relatively rare. It is mostly used as a local treatment for unresectable lesions, limb salvage, or recurrent osteosarcoma that cannot be surgically removed.

Wang et al. treated 80 cases of primary bone tumors with HIFU, achieving complete ablation in 69 cases, with a recurrence rate of only 7%. Among these, 3 children had Ewing's sarcoma and showed favorable prognosis. The 5-year survival rate of patients with stage III disease was 15.8%, which was similar to the 15.7% reported in a control group treated with incomplete surgical resection [12]. Another study used HIFU in 27 children with locally recurrent osteosarcoma who were ineligible for surgical resection, achieving a local control rate of 85.2% [13].

In our center, among 4 children with localized disease, 1 underwent amputation after recurrence, and the remaining 3 showed no recurrence by the last follow-up. This result is consistent with the above literature.

In the study by Wang et al., among 60 patients with stage IIb disease, the 5-year survival rate was 35.9% in 30 patients who did not complete the full treatment protocol for various reasons, whereas the rate was significantly higher (86.4%) in the remaining 30 who completed the full protocol. By comparison, completion of the full treatment regimen is critical for survival in this disease.

In our center, 1 of 4 children with localized disease underwent amputation after recurrence, and the remaining 3 showed no recurrence by the last follow-up. However, due to the small sample size, whether the overall 5 year survival rate is improved still needs to be verified by large sample data.

The main complications of HIFU include local pain, edema, and mild fever, which resolve spontaneously within a short period. Early complications include mild skin burn, which has become rare with improved clinical experience. Neural injury is also a common complication, which is mostly mild and recovers spontaneously. The main side effects of HIFU treatment include local pain and edema, which usually resolve within a short period. Fever occurs in 12% of patients, mostly below 38.5°C, and generally resolves spontaneously within 3 days without antipyretic treatment. In the early stage, the most common complication of this treatment was mild skin burns, mainly due to the lack of experience of clinicians in performing high-intensity focused ultrasound ablation. This complication was mainly reported in the 1990s [14].

In addition, neurological injury is also a relatively common complication. The reasons for this complication are analyzed as follows: first, the current ultrasound imaging equipment cannot directly display nerve tissue during HIFU ablation; if the anatomical position of certain nerves is altered, nerve injury may occur during treatment. Nerves are sensitive to ultrasound energy, and inevitable injury may occur when tumors are adjacent to nerves. The recovery degree of nerve injury is critically dependent on rehabilitation and whether the nerve remains intact during treatment.

In this study, among the 7 patients, 1 had second-degree skin burn, 1 had common peroneal nerve injury, and the others developed fever after treatment, which resolved spontaneously. These findings are consistent with the literature.

The prognosis of most patients treated with HIFU is similar to that of patients undergoing amputation, but their quality of life is significantly better. This article describes the application of HIFU in children with localized and metastatic Ewing's sarcoma, analyzes its advantages and disadvantages, and provides additional treatment options for children and families who strongly desire limb salvage.

## 5. Conclusion

HIFU is a safe, effective, and non-invasive local treatment for pediatric Ewing sarcoma. For localized patients with extensive bone destruction who cannot undergo conventional resection, HIFU can be used as a primary local therapy to achieve limb-salvage. For metastatic patients, HIFU can serve as an effective palliative treatment to reduce tumor burden, relieve pain, and improve quality of life as part of multidisciplinary comprehensive therapy.

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