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Original Article

Stereotactic ablative brachytherapy with or without assistance of 3D-printing templates for inoperable locally recurrent or oligometastatic soft-tissue sarcoma: a multicenter real-world study

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Abstract: The management of inoperable locally recurrent or oligometastatic soft-tissue sarcoma (STS) remains a clinical challenge. This study aimed to explore the long-term outcomes of stereotactic ablative brachytherapy (SABT) for these patients. Patients diagnosed with inoperable locally recurrent or oligometastatic STS from eight hospitals between 2006 and 2021 underwent iodine-125 (I-125) seed SABT, either with or without the assistance of three-dimensional (3D)-printing templates. The analysis concentrated on several key parameters, including objective response rate (ORR), disease control rate (DCR), local control time (LCT), overall survival (OS), adverse events (AEs), pain relief rate, and performance improvement rate. The ORR and DCR reached 78.3% and 95.0%, respectively. The results of multivariate logistic regression analysis indicated that a smaller tumor volume and a higher treatment dose were significantly associated with complete response ($P < 0.001$; $P=0.036$). The 1-, 3-, and 5-year LCT rates were 73.2%, 40.6%, and 37.9%, respectively. The 1-, 3-, and 5-year OS rates reached 83.1%, 50.5%, and 36.1%, respectively. Multivariate analysis revealed that a higher dose, a smaller tumor volume, and utilization of 3D-printing templates were significantly positive prognostic factors of LCT ($P=0.006$; $P=0.007$; $P=0.034$). Moreover, the tumor locations of trunk wall and extremities and lower tumor grade (G1/2) were significantly positive prognostic factors of survival ($P=0.008$; $P=0.002$). Pain relief rate was 88.0%, and the performance improvement rate was 46.7%. The AEs were predominantly of grade ≤ 2 and were well-tolerated. SABT seems to be an efficacious and safe alternative therapy for inoperable locally recurrent or oligometastatic STS.

Keywords: Soft-tissue sarcoma, Iodine-125, stereotactic ablative brachytherapy, interstitial brachytherapy, 3D-printing

Introduction

The soft-tissue sarcoma (STS), a rare and heterogeneous type of tumors that accounts for 1% of all adult malignancies, originates from the connective tissues of head and neck, extremities, trunk wall, retroperitoneum, abdominal cavity, and thoracic cavity [1, 2]. Approximately 86% of STS cases are diagnosed in the localized stage [3]. Surgical resection combined with perioperative radiotherapy is typically the standard treatment for the localized

stage STS. Regrettably, the locoregional recurrent rate and distant metastatic rate reached approximately 27% and 35% within five years, respectively [4, 5].

For patients with locally recurrent or oligometastatic STS after multimodal treatment, clinical management is notably intricate and hinges on various factors, encompassing tumor-related elements (e.g., disease extent, location, and histology), patient-related factors (e.g., patient status, comorbidities, and treatment preference), and treatment-related aspects (previous interventions). Given the limited effectiveness of chemotherapy, local and regional therapies mainly emerge as the preferred approaches when the tumor progression is limited. The salvage surgical resection has been historically regarded as the optimal treatment because complete remission is critical for cure [6, 7]. Whereas, salvage resection is restricted for few patients due to the difficulty of complete resection, high risk of complications, function loss, cosmetic concern, and individual refusal. Regarding inoperable patients, external beam radiotherapy (EBRT) is an alternative option. However, administering sufficiently high and lethal doses of EBRT to the recurrent disease, particularly within previously irradiated areas, is frequently challenging. This challenge is compounded by the intrinsic radioresistance of STS and the constraints imposed by organs at risk (OARs). Moreover, the complexity is risen by the extensive multimodal treatment that the majority of patients undergo, involving multiple surgeries, radiotherapy, chemotherapy, and various combinations of these therapeutic modalities. The majority of these patients are reluctant to salvage surgery, EBRT, and chemotherapy. Therefore, new therapeutic strategies for the inoperable patients with locally recurrent or oligometastatic STS are urgently warranted.

The radioactive iodine-125 (I-125) seed stereotactic ablative brachytherapy (SABT), characterized by delivering the high radiation dose to the tumor and well sparing the adjacent normal tissues, may resolve the above-mentioned challenge. Numerous studies demonstrated that SABT is an effective and safe alternative for diverse recurrent and oligometastatic types of cancer [8-19]. Previous studies have consistently supported these findings in recurrent head and neck STS [11], recurrent cervical cancer [15], recurrent head and neck cancer [10], and rectal cancer [16]. SABT was recommended by the Rectal Cancer National Comprehensive Cancer Network (NCCN) guidelines as a salvage treatment for locally recurrent rectal carcinoma [20], and it was also recommended by the European Society for Medical Oncology (ESMO) clinical guidelines as an ablative treatment for hepatocellular carcinoma [21].

This study aimed to explore the long-term outcomes of I-125 seed SABT for inoperable locally recurrent or oligometastatic STS patients undergoing multimodal treatment, in order to provide additional therapeutic options for STS.

Materials and methods

Patients

Patients diagnosed with inoperable locally recurrent or oligometastatic STS underwent I-125 seed SABT in eight different centers (Peking University Third Hospital, First Affiliated Hospital of the Army Medical University, Qingdao Central Hospital, Tengzhou Central People's Hospital, Affiliated Zhongshan Hospital of Dalian University, The Worker's Hospital of Chengde Iron and Steel Limited Company, The First Hospital of Jilin University, Tongliao City Keerqin District First People's Hospital) from 2006 to 2021.

Ethics committee approval and patient consent

All of the patients have signed the written informed consent form. The study was conducted in accordance with the Declaration of Helsinki, and it was approved by the Institutional Ethics Committee of Peking University Third Hospital (Beijing, China; Approval No. M2021438).

Inclusion and exclusion criteria

The inclusion criteria were as follows: 1) locally recurrent or oligometastatic STS (≤ 3 metastases) confirmed by pathology or imaging; 2) tumor size ≥ 1 cm and ≤ 10 cm; 3) medically inoperable or individual refusal to resection; 4) being inappropriate for EBRT following evaluation by radiation oncologists or due to individual refusal of EBRT; 5) Karnofsky performance status (KPS) score ≥ 60; 6) adequate hemato-

logical reserves, hepatic function, renal function, and cardiac function; 7) expected survival > 3 months. The exclusion criteria were as follows: 1) unconfirmed mass; 2) tumor invading the skin or mucous membrane; 3) patients with severe bleeding; 4) patients with active infectious diseases, trauma, and severe wounds; 5) patients with any mental disorders; 6) patients with other somatic comorbidities of clinical concern; 7) pregnancy and lactation; 8) consent withdrawal.

Treatment

The personalized SABT procedure mainly consisted of individualized preoperative treatment planning, intraoperative radioactive seed implantation, and postoperative dosimetric evaluation (**Figure 1**). All the procedures were performed in accordance with the relevant guidelines and regulations.

Preoperative treatment planning: Following setup and computed tomography (CT) simulation, the delineation of gross tumor volume (GTV) and OARs was performed by radiation oncologists. Then, the pretreatment plans were made by the medical physicists using the brachytherapy treatment planning system (B-TPS; Beijing Feitian Industries Inc. and Beijing University of Aeronautics and Astronautics, Beijing, China). The aim of the pretreatment plan was to maximize the delivery of the prescription dose to 90% of the GTV (GTV D90), while minimizing the dose to the OARs through optimization.

Intraoperative implantation: Two SABT methods were utilized for intraoperative implantation. Method A (SABT guided by CT without the assistance of the three-dimensional (3D)-printing template) was used until 2015, and method B (SABT guided by CT and assisted by 3D-printing template) was employed after 2015 when the 3D printing template was invented by our center (Patent No. ZL2016-20414011.9). Other centers mainly used method A to perform the SABT.

Method A: After re-setup, disposable needles (Mick Radio Nuclear Instruments, Mount Vernon, NY, USA) were inserted into the target volume under CT guidance along the puncture points on the skin, which were designed preoperatively. I-125 seeds (CIAE-6711; Chinese Atomic Energy Science Institution, Beijing, China) were subsequently implanted by the Mick applicator (Mick Radio-Nuclear Instruments Inc., Mount Vernon, NY, USA).

Method B: After the treatment plan was designed in the B-TPS, a personalized 3D template model including the information of needle distribution and the characteristics of the therapeutic area outline (**Figure 1D**, **1E**) was printed by the 3D printer. After re-setup, the 3D-printing template was aligned to the surface of the operative region according to the patient's outline, positioning line on the body, alignment line on the 3D-printing template, and positioning laser. Then, the needles were inserted to the predetermined depth through the guide holes on the template. "Fine-tuning", if necessary, was conducted. After insertion of the needles, the I-125 seeds were implanted into the tumor through these needles the same as method A. Further intra-operative details were previously described [11].

Postoperative evaluation: The CT scan was immediately conducted to validate the postoperative distribution of seeds and calculate the actual dose distribution once the seed implantation was accomplished. Dosimetric parameters, such as the dose to 90% of GTV (D90) were used to evaluate the dosimetry.

Follow-up

The follow-up was performed every 3-6 months for the first 2 years, followed by every 6-12 months from 3 to 5 years, and annually thereafter.

Clinical outcomes

The clinical outcomes included the objective response rate (ORR), disease control rate (DCR), local control time (LCT), overall survival (OS), adverse events (AEs), pain relief, and performance improvement. The clinical responses were evaluated by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, including complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). ORR was calculated from the patient achieving CR and PR, and the DCR was similarly calculated from the patient achieving CR, PR, and SD. LCT was defined as the time from SABT to local progression; OS

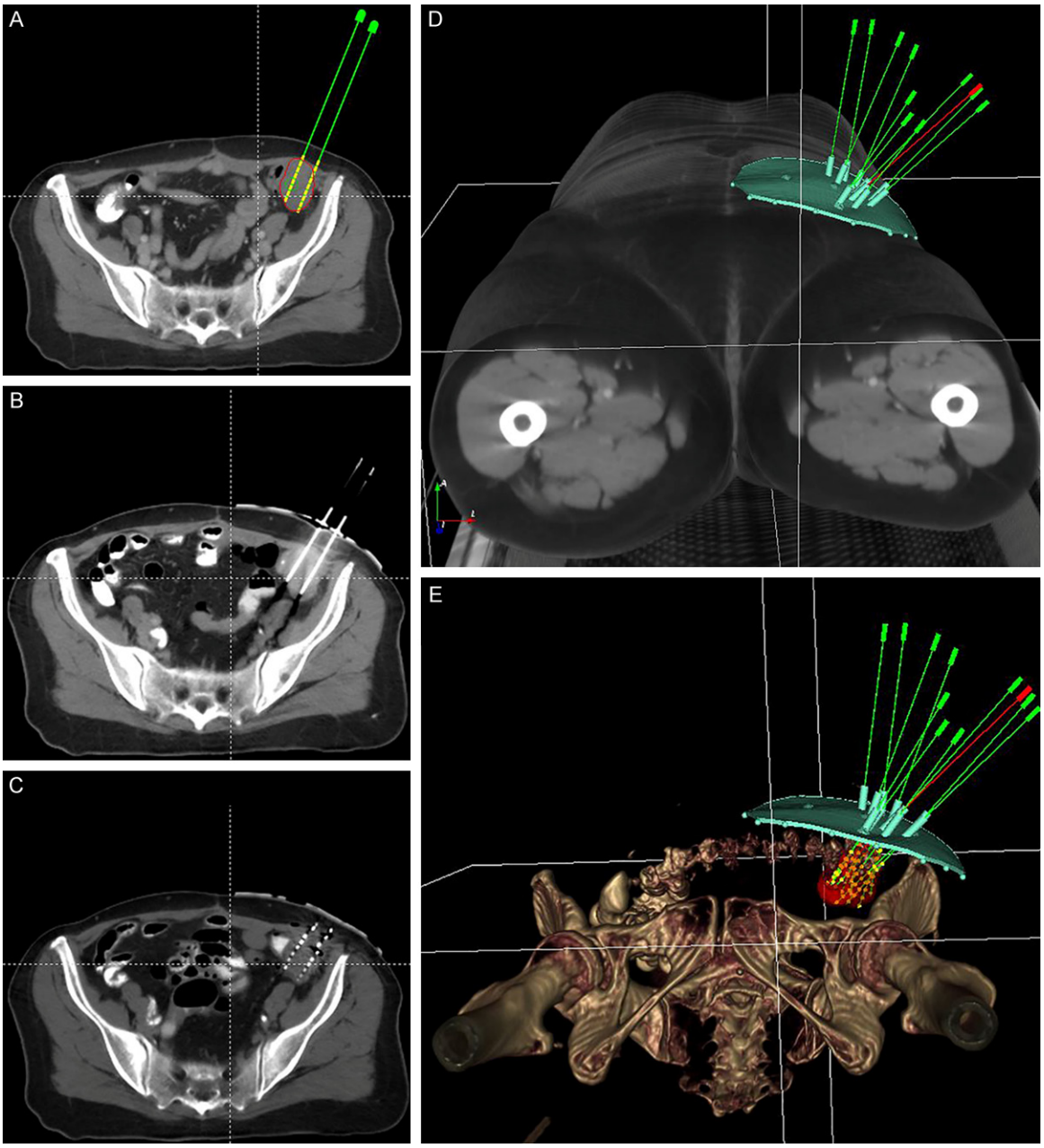

Figure 1. The CT images of pre-, intra-, and post-stereotactic ablative brachytherapy (SABT). (A) shows the preoperative treatment planning including the contouring of gross tumor volume (GTV) and distribution of puncture needles and seeds. The green needles and yellow seeds represent the actual needles and seeds; (B) shows the actual locations of needles during operation; (C) shows the actual distribution of seeds in GTV after operation; (D, E) show the model of personalized three-dimensional (3D)-printing template model in treatment planning system.

was defined as the time from SABT to death from any cause. The AEs were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Numerical rating scale (NRS) was utilized to evaluate the pain level before and after treatment, and the pain relief rate was calculated from the patient achieving pain relief after SABT. KPS was utilized to evaluate the patient's performance status before and after treatment, and the performance improvement rate was calculated from the patient achieving KPS improvement after SABT.

Statistical analysis

The parameters of the patients and SABT were expressed as categorical variables or continu-

ous variables using descriptive statistics analysis. The logistic regression model was used for univariate and multivariate logistic regression analyses of CR. The LCT and OS were described by the Kaplan-Meier method and compared by the log-rank test. The Cox proportional hazard regression model was employed to conduct univariate and multivariate analyses of LCT and OS. The pain and KPS scores before and after SABT were compared by paired T-test, and the pain relief rate and performance improvement rate were described statistically. $P < 0.05$ was considered statistically significant. The statistical analysis was conducted by the SPSS 25.0 software (IBM, Armonk, NY, USA). Nomogram was plotted by R 4.1.3 software.

Results

Patients' characteristics

A total of 132 consecutive patients were initially considered for SABT over a period of 15 years. However, 12 patients were subsequently excluded from the study for the following reasons, 2 patients had active infections, 4 patients presented with tumors that had invaded the skin and resulted in ulceration, 3 patients had a high risk of bleeding, 1 patient had severe diabetes, and 2 patients declined SABT for personal reasons. Ultimately, SABT procedures were conducted for 77 patients with CT guidance and performed with the assistance of a 3D-printing template and CT guidance for additional 43 patients. Patients' characteristics are detailed in **Table 1**.

Treatment response

The CR, PR, SD, and PD were found in 25, 69, 20, and 6 patients, respectively, within 6 months after SABT (**Figure 2A-C**). The ORR and DCR reached 78.3% and 95.0%, respectively.

Univariate and multivariate analyses of CR

Univariate and multivariate logistic regression analyses suggested that the patients with smaller tumor volume (GTV ≤ 60 cm^3) and higher treatment dose (D90 > 135 Gy) were significantly likely to achieve CR (**Figure 3**).

LCT and OS

The median follow-up time was 38.8 (range, 3.0-82.0) months, during which 53 patients experienced local recurrence. The 1-, 3-, and 5-year LCT rates were 73.2%, 40.6%, and 37.9%, respectively, with the median LCT of 29.0 months (**Figure 2D**). Of the 120 patients, 56 patients passed away. There was no treatment-related death. The median OS was 37.0 months, with the 1-, 3-, and 5-year OS rates of 83.1%, 50.5%, and 36.1%, respectively (**Figure 2E**).

Univariate and multivariate analyses of LCT

Univariate analysis by Cox proportional hazard regression model indicated that the tumor grade, tumor location, GTV, D90, and the SABT method were significantly associated with LCT (**Figure 4**). After adjustment for other covariates, multivariate analysis showed that D90, GTV, and SABT method were independent prognostic factors of LCT (**Figures 4**, **5**). The nomogram of LCT (**Figure 6**) was plotted according to the independent prognostic factors (D90, GTV, and SABT method) to predict the local control rate of the cohort.

Univariate and multivariate analyses of OS

Univariate analysis revealed that tumor grade, tumor pathology, and tumor location were significantly correlated with OS (**Figure 7**). Multivariate analysis indicated that the tumor location and tumor grade were independent prognostic factors of OS (**Figures 5**, **7**).

Pain relief and performance improvement

It was revealed that 90.0% (108/120) of patients suffered from different degrees of pain before SABT, which was one of the main reasons indicating patients' admission to our center. After the SABT, 88.0% (95/108) of patients felt complete or partial pain relief (**Figure 8A**). The mean pain score was significantly lower after SABT than that before SABT (2.1 vs. 4.1, $P < 0.001$). Additionally, the KPS score was significantly improved in 36.7% (44/120) of patients with the mean KPS score significantly higher after SABT than that before SABT (84.8 vs. 80.9, $P < 0.001$, **Figure 8B**).

AEs

The puncture-related and radiation-related AEs were followed up, including postoperative hemorrhage, pneumothorax, radiation dermatitis, and mucositis, which were generally graded as

Table 1. The characteristics of the patients

Parameter	Variable	All patients N=120 (%)
Patient variable		
Age	Median (range)	55 (5-87)
Sex	Male	71 (59.2)
	Female	49 (40.8)
KPS	< 90	88 (73.3)
	≥ 90	32 (26.7)
Tumor variable		
Tumor size (cm)	Median (range)	5.1 (1.5-9.2)
Tumor location	Head and neck	32 (26.7)
	Extremity	14 (11.7)
	Trunk wall	26 (21.7)
	Thoracic cavity	17 (14.2)
	Retroperitoneum/Abdominal cavity	31 (25.2)
Tumor pathology	Angiosarcoma	6 (5.0)
	Fibroblastic sarcoma/Fibrosarcoma	20 (16.7)
	Leiomyosarcoma	12 (10.0)
	Liposarcoma	11 (9.2)
	Rhabdomyosarcoma	11 (9.2)
	Spindle cell sarcoma	16 (13.2)
	Soft tissue chondroma	12 (10.0)
	Synovial sarcoma	9 (7.5)
	Other	23 (19.2)
Tumor grade	G1	16 (13.3)
	G2	38 (31.7)
	G3	48 (40.0)
	Gx	18 (15.0)
SABT variable		
SABT target	Local recurrence	93 (77.5)
	Oligometastasis	27 (22.5)
GTV (cm^3)	Median (range)	60 (2-594)
Prescription dose (Gy)	Median (range)	140 (90-200)
No. of needles	Median (range)	15 (1-60)
No. of Seeds	Median (range)	67 (6-311)
Seed activity (mCi)	Median (range)	0.7 (0.4-0.9)
D90 (Gy)	Median (range)	135 (77-219)
SABT method	CT-guided	43 (35.8)
	CT-guided and template-assisted	77 (64.2)
Time of SABT (min)	Median (range)	60 (15-240)
Previous treatment		
Surgery	Yes	113 (94.2)
	No	7 (5.8)
Radiotherapy	Yes	107 (89.2)
	No	13 (10.8)
Systemic treatment	Yes	64 (53.3)
	No	56 (46.7)

Abbreviations: SABT, Stereotactic ablative brachytherapy; KPS, Karnofsky Performance Score; GTV, Gross tumor volume; D90, Dose received by 90% of the GTV; CT, computed tomography.

≤ 2 and well-tolerated (**Table 2**). No patients developed postoperative infection or treatment-related death.

Discussion

In the present study, the majority of patients in the study had previously undergone surgical resection (94.2%, 113/120) and EBRT (89.2%, 107/120) before experiencing recurrence or metastasis. Among them, 26 patients had undergone multiple resections, and 13 patients had received EBRT on two occasions. Treating these patients with local recurrence or oligometastasis after multiple prior treatment failures presented significant challenges. In the current study, these patients were considered inoperable based on consultation with surgeons or their personal preference. Furthermore, re-EBRT was not recommended due to constraints related to normal tissue dose limits and individual choices.

In theory, SABT offers the advantage of delivering a sufficiently high radiation dose to the tumor while effectively sparing adjacent normal tissues. This is attributed to the more rapid dose fall-off and lower dose rate of SABT compared with EBRT [22]. In practice, the efficacy of SABT is well-established, with its inclusion in NCCN guidelines as a standard treatment for prostate carcinoma and in ESMO guidelines for hepatocellular carcinoma, a recommendation that has been in place for several years [21, 23]. Additionally,

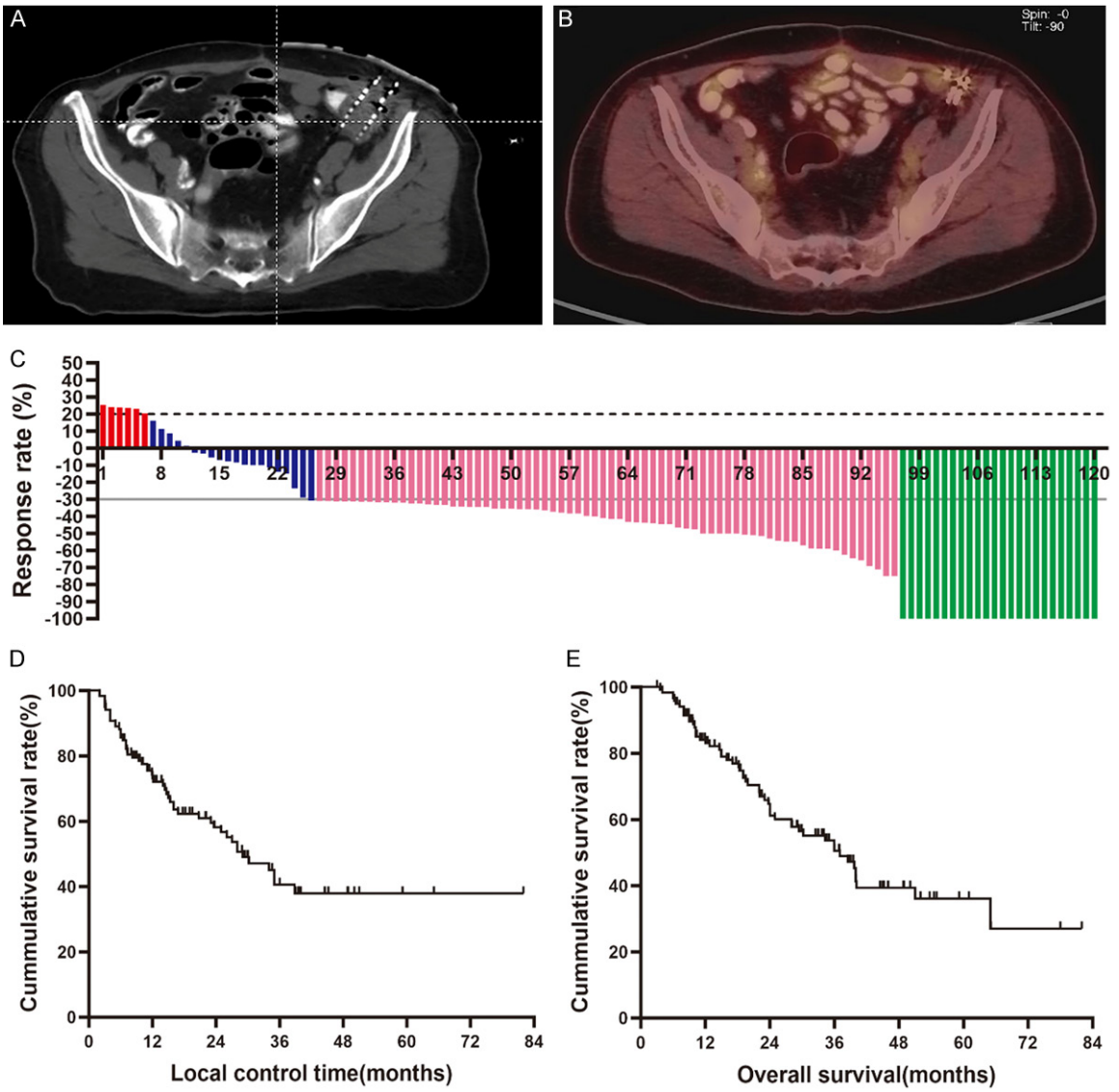

Figure 2. Short- and long-term efficacy of stereotactic ablative brachytherapy (SABT). (A, B) show the complete response of one patient at 6 months after SABT; (C) illustrates the waterfall plot for the responses of the 120 patients; (D, E) show the local control time (LCT) and overall survival (OS) of all patients.

expert consensus supports the use of SABT for various types of cancer, including head and neck cancer, thoracic cancer, abdominal cancer, pelvic cancer, and limb cancer [8, 9, 24]. Over time, the SABT has continued to evolve, particularly with the introduction of the 3D-printing template (Patent No. was not shown here) in our center. This innovation has significantly enhanced the precision, effectiveness, safety, and efficiency of SABT. Consequently, SABT may represent an appropriate alternative for patients with inoperable locoregional recurrent and oligometastatic STS. The current study, with the largest sample size to date, presents long-term outcomes of SABT for inoperable locoregional and metastatic STS. Additionally, to the best of our knowledge, this research may be the first to describe the application of advanced SABT methods, specifically the utilization of 3D-printing templates, for STS treatment.

In the present study, the ORR and DCR, concerning short-term efficacy, were 78.3% and 95.0%, respectively, and the CR rate was 20.0%. The influential factors of CR were fur-

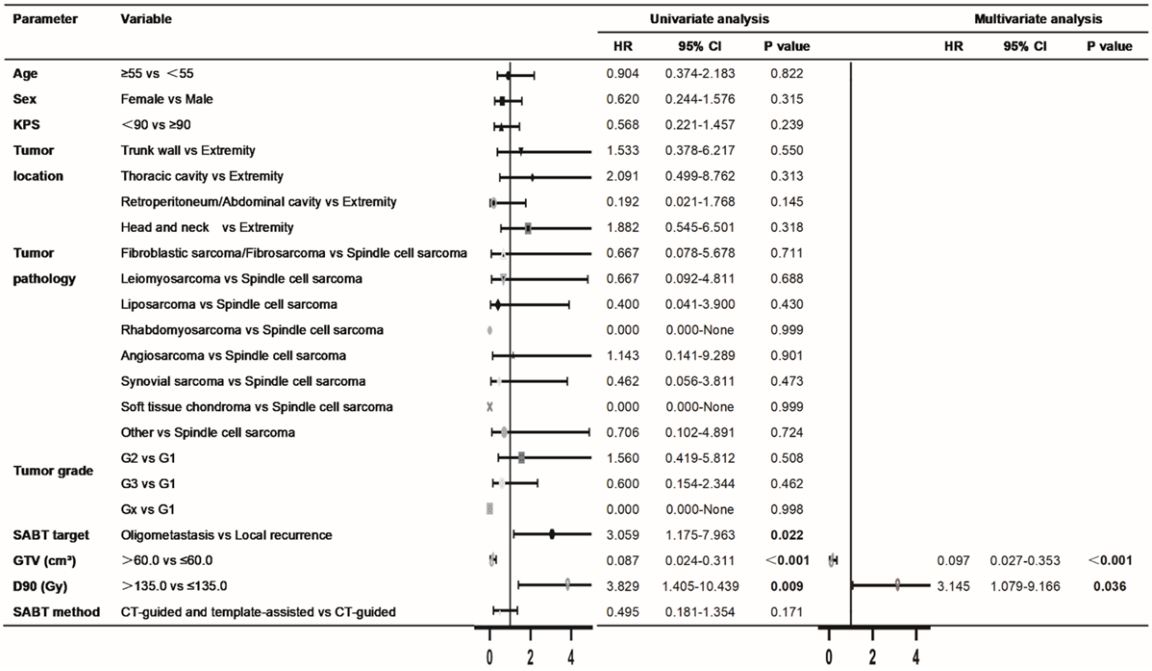

Figure 3. Forest plot of univariate and multivariate logistic regression analyses for complete response (CR).

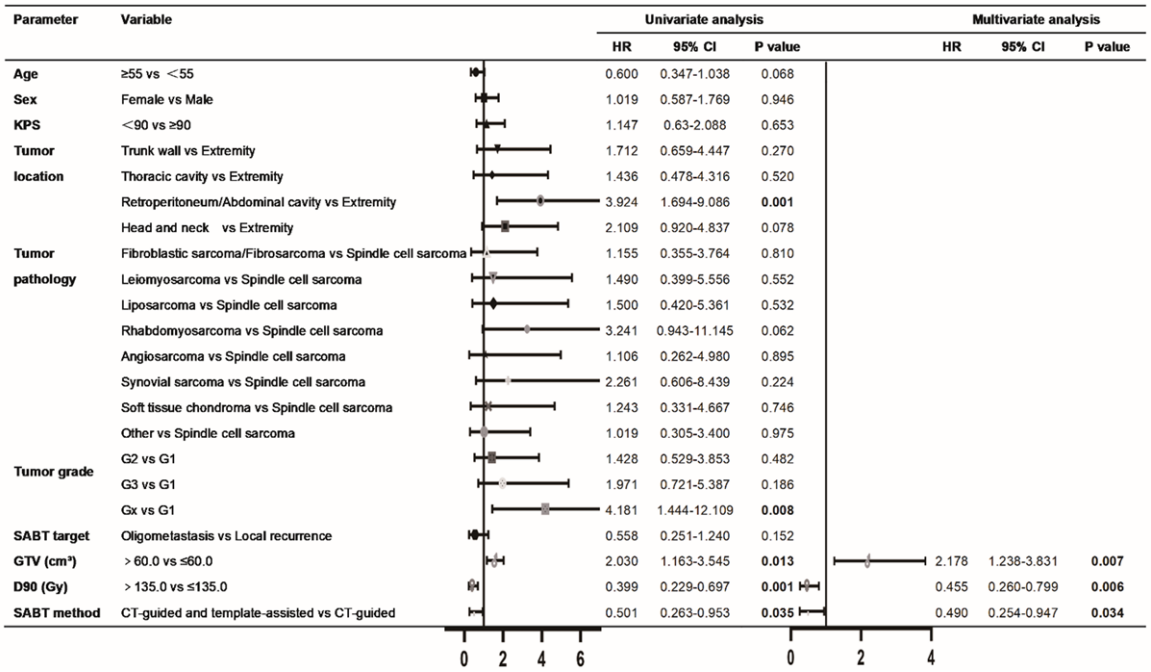

Figure 4. Forest plot of univariate and multivariate analyses for local control time (LCT).

ther analyzed, and it was revealed that smaller tumor volume (GTV ≤ 60 cm^3) and higher treatment dose (D90 > 135 Gy) were significantly associated with CR. Chen et al. [11] reported similar results that the lower T stage and smaller tumor volume were independent positive predictors for CR. Taken together, these studies indicated that increasing the dose and/or treating smaller tumors were more likely to achieve CR for SABT.

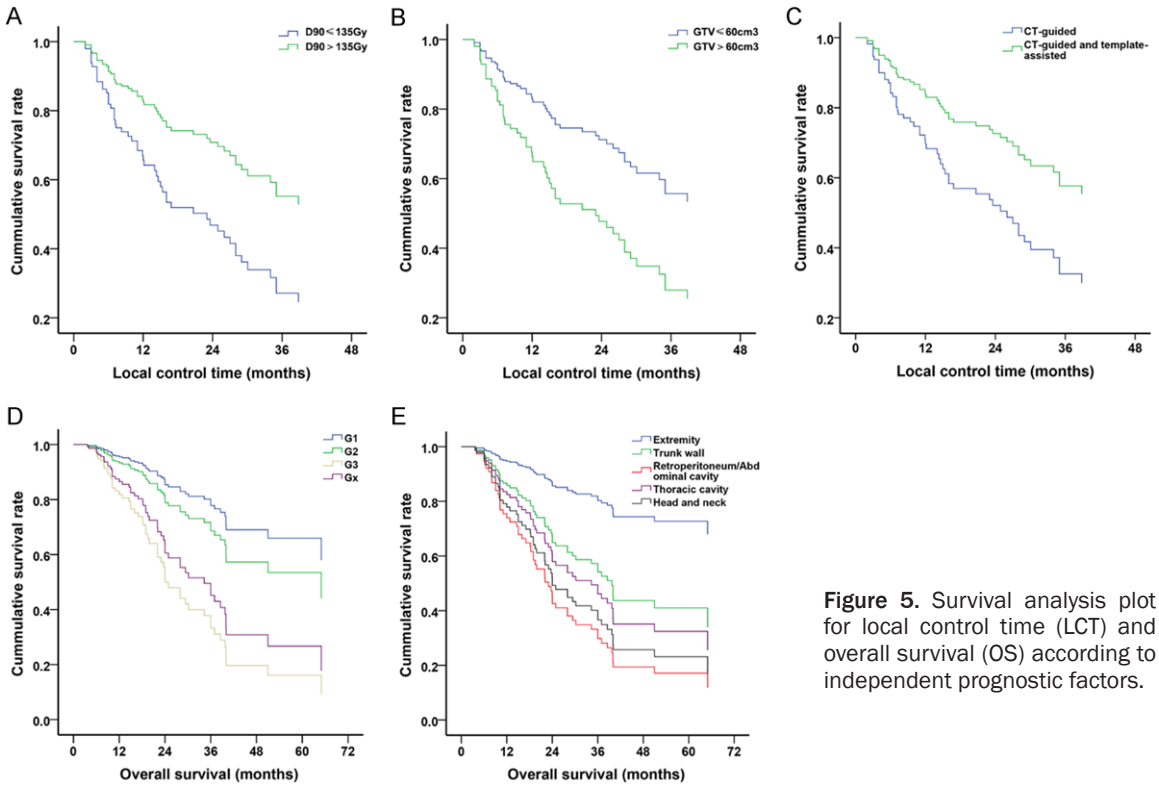

Figure 5. Survival analysis plot for local control time (LCT) and overall survival (OS) according to independent prognostic factors.

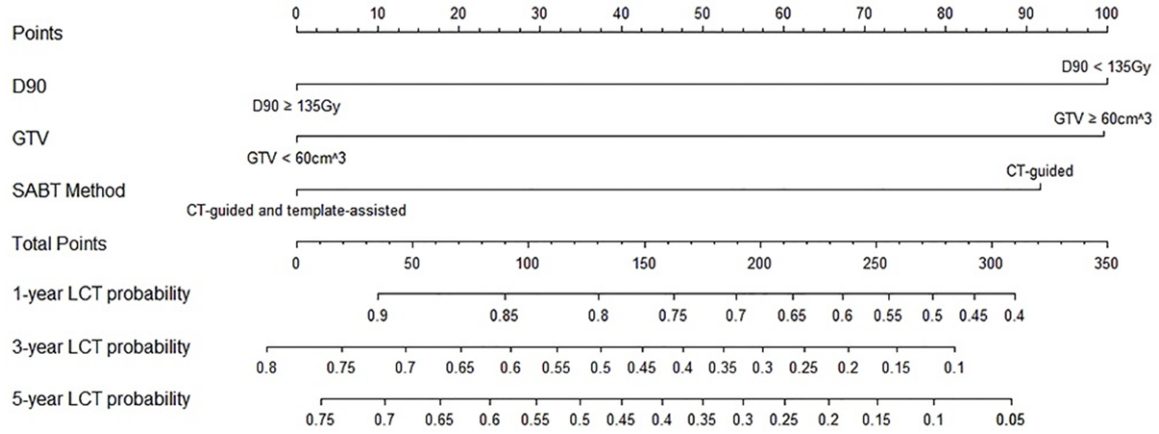

Figure 6. The nomogram of the local control of stereotactic ablative brachytherapy (SABT).

Regarding patients' long-term survival, the present study showed that the median LCT reached 29.0 months with the 1-, 3-, and 5-year LCT rates of 73.2%, 40.6%, and 37.9%, respectively, and the median OS was 37.0 months with the 1-, 3-, and 5-year OS rates of 83.1%, 50.5%, and 36.1%, respectively, which indicated promising local control and survival of SABT for the inoperable locoregional recurrent or oligometastatic STS patients. These noticeable results are consistent with those of previous studies. Li et al. [25] assessed local efficacy of CT-guided SABT for locally recurrent STS, in which the median local control was 41 months with the 1-, 3-, and 5-year local control rates of 78.8%, 78.8%, and 0%, respectively, and the 1-, 3-, and 5-year OS rates were 76.6%, 39.4%, and 39.4%, respectively. Yao et al. [26] explored the feasibility of SABT for pediatric recurrent and metastatic STS, and they demonstrated that local control rates after 1 and 2 years were 70.1% and 62.3%, respectively, and survival

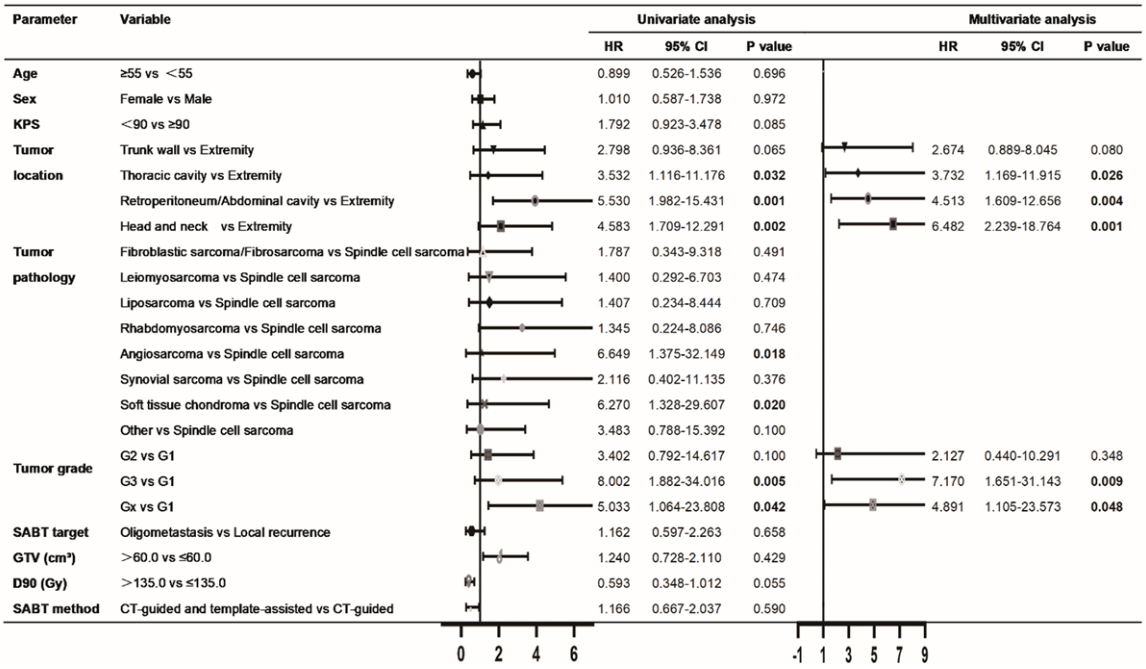

Figure 7. Forest plot of univariate and multivariate analyses for OS.

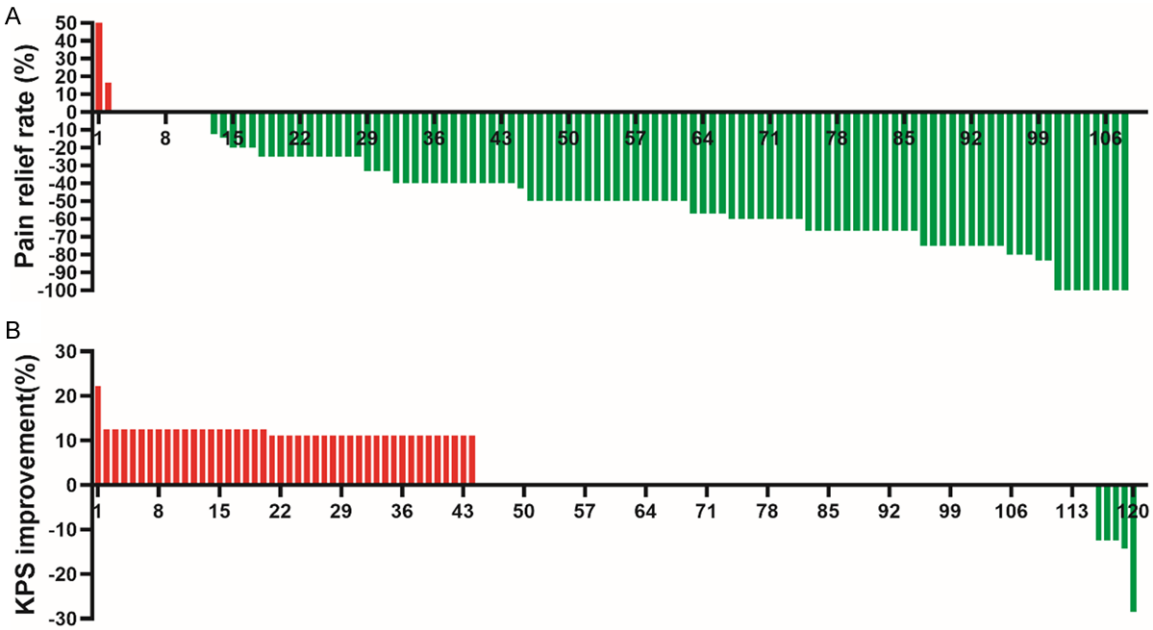

Figure 8. Waterfall plot for pain relief and Karnofsky performance score (KPS) improvement after treatment. (A) presents the waterfall plot for the pain relief after treatment; (B) shows the waterfall plot for the KPS improvement after treatment.

rates after 1 and 2 years were 68.6% and 57.1%, respectively. Chen et al. [11] reconfirmed a satisfactory efficacy for locally recurrent head and neck STS. Moreover, Mo et al. [27] evaluated the feasibility and usefulness of CT-guided SABT for patients with metastatic STS by a retrospective study, and they found that SABT combined with second-line chemotherapy significantly improved the local control compared with chemotherapy alone (1-, 2-, and

Table 2. Adverse events (AEs)

AEs	Category	Level	Frequency (%)
Puncture-related AEs	Postoperative hemorrhage	I	6 (5%)
		II	0 (0%)
		III	0 (0%)
		IV	0 (0%)
	Pneumothorax	I	3 (2.5%)
		II	2 (1.7%)
		III	0 (0%)
		IV	0 (0%)
Radiation-related AEs	Skin reaction	I	16 (13.3%)
		II	4 (3.3%)
		III	0 (0%)
		IV	0 (0%)
	Mucositis	I	3 (2.5%)
		II	1 (0.8%)
		III	0 (0%)
		IV	0 (0%)

Abbreviation: AE, Adverse event.

3-year LCT rates: 46.7%, 28.9%, and 11.1% vs. 18.8%, 6.3%, and 0%, respectively). Previous studies demonstrated that the probability of toxicities ≥ grade 3 was from 0% to 5.5%. Collectively, the present study, conducted with the largest sample size to date (in comparison to previous studies with sample sizes smaller than 49), aligns with earlier research, reinforcing the notion that SABT is marked by its not only effective outcomes but also its low and tolerable toxicity in cases of locally recurrent and oligometastatic STS.

To our knowledge, there is a notable absence of outcomes related to re-irradiation using photon or electron EBRT as a monotherapy for the management of inoperable locoregional recurrent STS within previously irradiated fields. Consequently, the comparison between SABT and EBRT remains pending. For operable recurrences or metastases of STS, the standard of care typically involves surgical resection with or without perioperative radiotherapy. Studies have reported varying outcomes for this approach. Indelicato et al. [28] reported a 5-year local control rate of 18% and a high incidence of serious complications necessitating reoperation or resulting in permanent functional impairment. Lehnert et al. [29] demonstrated that the 5-year LCT rate and OS rate were 26% and 25%, respectively, with a severe grade 3/4 toxicity rate of 10% for STS treatment with surgery and intraoperative radiotherapy with/without (neo)adjuvant EBRT. Calvo et al. [30] achieved more promising results, with a 5-year local control rate and an OS rate of 60% and 52%, respectively, for surgery with or without irradiation in locally recurrent STS. However, this approach was associated with grade ≥ 3 toxicity in 29% of cases. A study performed by Memorial Sloan Kettering Cancer Center reported that 803 recurrent and oligometastatic STS patients underwent pulmonary metastasectomy with a 5-year survival of 34% [31]. A European review of 255 patients undergoing pulmonary metastasectomy showed a 5-year OS rate of 38% [32]. Several single-institution studies investigating pulmonary metastasectomy have reported 5-year survival rates ranging from 15% to 50.9% [33]. It is noteworthy that the efficacy of SABT for inoperable recurrence or oligometastases in our study is comparable to surgery-based combined therapy for operable recurrence or oligometastases. Moreover, SABT is associated with significantly lower adverse events. These findings suggest that SABT may serve as a prospective alternative for carefully selected patients with operable recurrent or oligometastatic STS.

Multivariate logistic regression analysis of LCT showed that the patients with smaller tumor volume, higher dose, and more advanced SABT method were significantly associated with a lower probability of local failure and a longer LCT. Ji et al. [10] demonstrated that a higher dose and a smaller tumor volume were significantly correlated with a better local control in recurrent head and neck cancer. Qu et al. [15] achieved similar results in recurrent cervical carcinoma. These results are also consistent with our routine clinical experience. Enhancing local control can be achieved through dose escalation and careful selection of smaller tumor volumes. Consequently, the investigation of appropriate SABT doses and the selection of appropriate tumor volumes bear vital

clinical significance for recurrent and metastatic STS. Differing from previous studies where SABT was conducted with CT guidance, the present study involved 43 cases of SABT performed with the assistance of 3D-printing templates and CT guidance. Multivariate logistic regression analysis revealed that the local control was significantly improved in the 3D-template group compared with the free-hand group. This improvement can be attributed to the higher accuracy, superior quality control, and better dose distribution achieved through the application of 3D-printing templates. Wang et al. reported similar findings, emphasizing that template assistance significantly enhances the precision and effectiveness of SABT for recurrent rectal cancer [34]. In the present study, the nomogram of LCT was plotted with 3 independent prognostic factors, including D90, GTV, and SABT method, in order to predict and evaluate local control of SABT. The nomogram exhibited that patients with 0-1 risk factor had favorable local control.

Additionally, the multivariate logistic regression analysis of OS revealed that a higher tumor grade and the tumor location were significantly associated with a worse OS. Possible causes for these outcomes may include the following factors: 1) Tumor grade, as higher-grade tumors tend to exhibit more malignant behavior; 2) Tumor location, specifically tumors in challenging areas, such as the head/neck and retroperitoneum/abdomen, which are more resistant to radical SABT treatment. The results of the present study are consistent with those of previous studies. For instance, Qu et al. [15] reported independent prognostic factors of OS, including tumor grade and pathological type for cervical cancer. Chen et al. [11] demonstrated that tumor grade was an independent predictor of OS in head and neck STS. Moreover, a German study on the locally recurrent STS also found that the tumor grade and tumor site were significant prognostic factors of OS [35]. A European study indicated that tumor grade was an independent prognostic factor of OS for oligometastatic STS patients [32]. However, it is noteworthy that D90, GTV, and SABT method are not independent factors of OS. This may be attributed to the primarily palliative nature of SABT in the majority of cases, which has limited effects on systemic tumor burden.

The majority of patients in the present study experienced relief from pain, particularly cancer-related pain, after undergoing SABT. These findings are consistent with those of previous studies [26, 27, 36, 37], indicating that SABT is effective not only in terms of local tumor control but also in providing pain relief. Moreover, 44 patients demonstrated improved performance, which may be attributed to symptom relief and reduced tumor burden following SABT.

However, it is important to acknowledge the limitations of this study, including its retrospective design, affecting the level of evidence. Potential selection bias and confounding variables may also impact the study's outcomes. Nonetheless, this study provides valuable evidence regarding the role of SABT in the treatment of locally inoperable recurrent and oligometastatic STS. Prospective studies are required to further validate the efficacy of SABT in these patients.

Conclusions

In conclusion, for patients with inoperable locally recurrent and oligometastatic STS, SABT exhibited a satisfactory symptom relief along with a promising performance improvement, a high response rate, favorable local control and survival, and a great safety, suggesting that SABT can be a prospective effective and safe alternative option.

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Disclosure of conflict of interest

None.

Abbreviations

AEs, adverse events; B-TPS, brachytherapy treatment planning system; CT, computed tomography; CR, complete response; CTCAE, the Common Terminology Criteria for Adverse Events; DCR, disease control rate; D90, the dose to 90% of GTV; ESMO, European Society

for Medical Oncology; EBRT, external beam radiotherapy; GTV, gross tumor volume; I-125, iodine-125; KPS, Karnofsky performance status; LCT, local control time; NRS, Numerical rating scale; NCCN, National Comprehensive Cancer Network; ORR, objective response rate; OS, overall survival; OARs, organs at risk; PR, partial response; PD, progression disease; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; STS, soft-tissue sarcoma; SABT, stereotactic ablative brachytherapy; 3D, three-dimensional.

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