

Salvage wide resection with intraoperative electron beam therapy or HDR brachytherapy in the management of isolated local recurrences of soft tissue sarcomas of the extremities and the superficial trunk

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ABSTRACT

PURPOSE: To assess the toxicity and efficacy of salvage wide resection (SWR) with intraoperative electron beam radiation therapy (IOERT) or perioperative high-dose-rate brachytherapy (PHDRB) in previously unirradiated patients (PUP) vs. previously irradiated patients (PIP) with isolated local recurrence of soft tissue sarcomas (STS) of the extremities and the superficial trunk.

METHODS AND MATERIALS: PUP received SWR and IOERT/PHDRB with external beam radiation therapy. PIP received SWR and IOERT/PHDRB only.

RESULTS: Fifty patients were analyzed retrospectively. PUP ($n = 24$; 48%) received IOERT ($n = 13$) or PHDRB ($n = 11$). PIP ($n = 26$; 52%) received IOERT ($n = 10$) or PHDRB ($n = 16$). Reintervention because of complications was not required in PUP. Nine of 26 (34%) PIP required re-intervention ($p = 0.01$). After a median followup of 3.7 years (range, 0.2–18.3), the 5-year rates of locoregional control, distant control, and overall survival were 54%, 66%, and 56%, respectively. Five-year locoregional control was higher in PUP than in PIP (81% vs. 26%, $p = 0.01$) and in the extremity locations compared with trunk locations (68% vs. 28%, $p = 0.001$). Five-year overall survival was superior in unifocal vs. multifocal presentations (70% vs. 36%, $p = 0.03$) and for tumor sizes <4 vs. ≥ 4 cm (74% vs. 50%, $p = 0.05$).

CONCLUSIONS: Prior irradiation is the main determinant of locoregional control in patients with isolated local recurrence of STS. The locoregional control rates in PUP were similar to those described in primary STS. In PIP, SWR + IOERT/PHDRB reirradiation yielded modest locoregional control rates and was associated with significant morbidity, especially in PHDRB cases.

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Keywords:

Soft tissue sarcomas; Locally recurrent; Salvage surgery; IOERT; HDR brachytherapy

Introduction

Several randomized studies performed in primary soft tissue sarcomas (STS) have demonstrated that combined modality treatment consisting of conservative surgery (wide resection) followed by adjuvant radiotherapy provides improved local control rates compared with surgery alone. However, 6–15% of patients, who receive combined

modality treatment, are expected to develop isolated locoregional relapses (isolated local recurrence of soft tissue sarcomas [ILRS]) (1–3). Treatment of ILRS remains challenging because of the aggressive biology of most recurrent tumors and the anatomical constraints induced by prior local treatments, in particular if radiotherapy (dosimetric constraints) was previously used. In patients with resectable ILRS, surgical treatment may include radical or salvage wide resection (SWR).

SWR is often preferred to preserve as much functionality as possible because extended radical surgery or amputation does not prevent the uncertainty of additional distant failure or death (4). However, SWR often leaves microscopic residual disease considered as R1 resection with the risk of

Received 14 February 2013; received in revised form 3 September 2014; accepted 9 September 2014.

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a subsequent local failure. The average rate of R1 resections after conservative surgery for primary STS varies from 15% to 30% (1, 3, 5). In ILRS, this rate may be higher than 50% (6–10), especially in previously irradiated patients (PIP).

This complex radiosurgical scenario justifies the use of adjuvant local treatments provided that the rates of severe complications are acceptable. The experience in the management of patients with ILRS (both previously unirradiated patients [PUP] and PIP) includes reports of patient cohorts treated with combined modality therapy. In these publications, 5-year local control rates vary widely between 18% and 100% (7, 8, 10–13). The available data of SWR alone for ILRS are limited, with 5-year local control rates reported ranging from less than 40% in PIP (7, 10) to 80% in PUP (2). Severe complications arise in a substantial number of patients with ILRS treated with combined modality therapy. About half of the patients treated, especially those with prior irradiation, develop associated toxicity (7, 8, 10, 11).

Toxicity rates are highly dependent on radiation lifetime dose and size of reirradiation target volume. For this reason, intraoperative techniques have been introduced, such as intraoperative electrons (intraoperative electron beam radiation therapy [IOERT]) or perioperative high-dose-rate brachytherapy (PHDRB), which may optimize the irradiated volume and potentially minimize long-term complications. In addition, intraoperative techniques also have the ability to partially or completely spare dose-limiting structures present in the surgical bed, such as nerves, bone, and vessels.

The Radiation Oncology Division of our institution established an IOERT program in 1984. It was replaced in 2000 by a PHDRB program that remains active. Fifty patients diagnosed with recurrent STS and treated with SWR followed by either IOERT or PHDRB and treated over a 25-year period comprise the patient population in this report.

Methods and materials

Patient and tumor characteristics

We analyzed patients with ILRS of the extremities and superficial trunk salvage by surgery and intraoperative radiotherapy in our institution between March 1985 and February 2010. Those with metastatic disease or ILRS with histological subtypes of uncertain behavior (i.e., aggressive fibromatosis) were excluded. All patients were treated with SWR and IOERT from 1985 to 1999 or with PHDRB from 2001 to 2010. Previously unirradiated ILRS received IOERT or PHDRB followed by a standard course of external beam radiation therapy (EBRT). PIP received IOERT or PHDRB without further EBRT reirradiation. A detailed description of patient and treatment characteristics is shown in Table 1.

Treatment characteristics

SWRs were classified into R0 resections (no residual microscopic disease with negative margins of at least 10 mm in all directions), R1 resections (residual microscopic

Table 1
Salvage treatment characteristics

Characteristics	Unirradiated (n = 24)	Previously irradiated (n = 26)
SWR margins, n (%)		
Negative margins (≥ 10 mm)	8 (33.3)	2 (7.7)
Close margins (<10 mm)	10 (41.7)	13 (50.0)
Positive margins	6 (25.0)	11 (42.3)
Special radiation technique in salvage treatment, n (%)		
IOERT	13 (54.2) ^a	10 (38.5)
PHDRB	11 (45.8) ^a	16 (61.5)
Nominal median dose		
IOERT	12.5 Gy (range, 10–20)	15.0 Gy (range, 10–20)
PHDRB	24.0 Gy (range, 16–24)	40.0 Gy (range, 32–40)
EBRT	45.5 Gy (range, 27–60)	
EQD2 ($\alpha/\beta = 10$)		
IOERT	23.4 Gy	31.3 Gy
PHDRB	28.0 Gy	46.7 Gy
IOERT + EBRT in unirradiated	69.4 Gy	NA
PHDRB + EBRT in unirradiated	73 Gy	NA
Brachytherapy parameters		
Time surgery to brachytherapy		4 d (range, 0–9)
Median V_{100}		60 cc (range, 8–882)
Median V_{150}		21 cc (range, 2.8–295)
DHI		0.66 (range, 0.59–0.78)

SWR = salvage wide resection; IOERT = intraoperative electron beam radiation therapy; PHDRB = perioperative high-dose-rate brachytherapy; EBRT = external beam radiation therapy; EQD2 = biologically effective doses for tumor control standardized at 2-Gy equivalents; NA = not available; V_{100} = volume encompassed by 100% of prescribed dose in PHDRB; V_{150} = volume encompassed by 150% of prescribed dose in PHDRB; DHI = dose homogeneity index.

^a IOERT or PHDRB plus EBRT in previously unirradiated patients.

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