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Scientific Article

Optical Surface-guided Radiation Therapy for Upper and Lower Limb Sarcomas: An Analysis of Setup Errors and Clinical Target Volume-To-Planning Target Volume Margins

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Purpose: To assess the clinical benefits of surface-guided radiation therapy (SGRT) in terms of setup error, positioning time, and clinical target volume-to-planning target volume (CTV-PTV) margin in extremity soft tissue sarcoma (STS).
Methods and Materials: Fifty consecutive patients treated with radiation therapy were selected retrospectively. Treatment setup was performed with either laser-based imaging only (control group), or with laser-based and daily optical surface-based imaging (SGRT group). Pretreatment cone beam computed tomography images were acquired daily for the first 3 to 5 fractions and weekly thereafter, with the frequency adjusted as necessary. Translational and rotational errors were collected. CTV-PTV margin was calculated using the formula, $2.5\Sigma + 0.7\sigma$.
Results: Each group consisted of 10 and 15 upper and lower limb STSs, respectively. For patients with upper limb sarcomas, the translation errors were 1.64 ± 1.34 mm, 1.10 ± 1.50 mm, and 1.24 ± 1.45 mm in the SGRT group, and 1.48 ± 3.16 mm, 2.84 ± 2.85 mm, and 3.14 ± 3.29 mm in control group in the left-right, supero-inferior, and antero-posterior directions, respectively. Correspondingly, for patients with lower limb sarcomas, the translation errors were 1.21 ± 1.65 mm, 1.39 ± 1.71 mm, and 1.48 ± 2.10 mm in the SGRT group, and 1.81 ± 2.60 mm, 2.93 ± 3.28 mm, and 3.53 ± 3.75 mm in control group, respectively. The calculated CTV-PTV margins of the SGRT group and control group were 5.0, 3.8, 4.1 versus 5.9, 9.1, 10.1 mm for upper limb sarcomas; and 4.2, 4.7, 5.2 mm versus 6.3, 9.6, and 11.4 mm for lower limb sarcomas in the left-right, supero-inferior, and antero-posterior directions, respectively.
Conclusions: Daily optical surface guidance can effectively improve the setup accuracy of extremity STS patients, and safely reduce the required CTV-PTV margins.

Introduction

Wide resection combined with radiation therapy for extremity soft tissue sarcoma has been shown to be conducive for the preservation of limb function and the reduction of local recurrence rates.[1,2] However, due to many multiaxial joints, the accurate and firm positioning of

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the limbs represents a well-recognized challenge during radiation therapy.[3,4] Immobilization of the limb on an individual patient basis with customized immobilization devices to provide reproducible daily setup is strongly recommended[5]; however, regardless of immobilization strategy, large interfractional errors, especially in the rotational axes for upper extremity sarcomas,[6] were observed.

Optical surface imaging is a noninvasive and nonradiation image guidance technology, which has allowed for real-time monitoring of body positioning and has been proved can minimize setup errors during radiation therapy.[7-11] It works by providing surface anatomic information, which can be aligned with images derived from treatment planning. With the help of optical surface imaging, the clinical target volume (CTV) to planning target volume (PTV) margins could be reduced from 1 cm to 5 mm for lower limb sarcomas.[12] Nevertheless, the data are still sparse with small cohorts especially for patients with upper extremity sarcomas. The recommended CTV-to-PTV margins also differ depending on different CBCT frequency adopted by different research.[11,13,14] Hence, our study aimed to analyze the effect of surface-guided radiation therapy (SGRT) retrospectively among patients with extremity soft tissue sarcoma by comparing the setup displacements associated with conventional laser-based imaging only and those with surface-based imaging guidance. We further investigated the effects of SGRT in terms of CTV-PTV margin.

Methods and Materials

Patient selection

Fifty patients with histopathologically confirmed primary extremity soft tissue sarcoma treated with radiation therapy between September 2020 and January 2023 were retrospectively enrolled. The inclusion criteria included: 1) Patients older than 12 years; 2) histopathologically proved soft tissue sarcoma originating from the limbs; and 3) able to tolerate preoperative or postoperative radiation therapy and sign the informed consent form for radiation therapy. The exclusion criteria included patients refusing or withdrawing from radiation therapy.

Among all patients, 25 were classified into the SGRT and control groups, respectively. There were 10 and 15 patients with upper and lower limb sarcomas in each group, respectively.

Patient positioning and CT simulation

All patients were immobilized with a Klarity vacuum cushion (Klarity Medical & Equipment). The supine or prone position was selected based on maximal exposure of the tumor area and sparing of adjacent organs at risk. Three surface crosslines were drawn where possible for laser localization. In cases whereby the target area was sheltered by the body, only 2 crosslines were drawn. Details of patient positioning are shown in Table 1.

All patients were subjected to treatment planning using cone beam computed tomography (CBCT) with either Brilliance Big Bore (Phillips Healthcare) or Somatom Definition AS 40 (Siemens Healthcare). CBCT images were acquired at slice thickness of 5 mm and were subsequently transmitted to the Pinnacle planning system (version 9.10) using the MOSAIQ network system (Elekta).

Image registration and radiation therapy

Radiation therapy was administered using either the intensity modulated radiation therapy or volume

Table 1 Patient positioning in both treatment groups

	Group	SGRT (n = 25)	Control (n = 25)
Tumor site	Forearm	3	2
	Upper arm	7	8
	Lower leg	3	2
	Thigh	12	13
Body position	Supine	24	24
	Prone	1	1
Limb position	Upper limb abduction	6	7
	Upper limb lift	4	3
	Natural leg position	5	6
	Healthy limb abduction	10	9
No. of surface crosslines	2	19	20
	3	6	5

Abbreviation: SGRT = surface-guided radiation therapy.

modulated arc therapy approach. For all patients, the initial treatment setup involved the alignment of skin markings with the laser (Fig. 1). The AlignRT system (Vision RT) was further used in the SGRT group to facilitate with position correction.

Setup errors were assessed in terms of translational and rotational errors, with CBCT images as the reference. Translational errors in the left-right (LR), superior-inferior (SI), and anterior-posterior (AP) directions were recorded as *X, Y,* and *Z,* and rotational errors in the sagittal, transverse, and coronal planes were recorded as *Rx, Ry,* and *Rz.* Positive values were reflective of translational errors in the positive direction of the Cartesian coordinate system, and of rotational errors in the clockwise direction. In addition, systematic errors ($\sum$) were calculated as the standard deviation of the mean setup error, and random errors (σ) were calculated as the root mean square of the standard deviation.[15,16] The formula, $M_{PTV} = 2.5 \sum + 0.7\sigma$,[17,18] was used to calculate the required CTV-PTV margin, to ensure that the 90% of CTV volume can receive at least 95% of the prescribed dose.

As per the Basic Guidelines for Quality Control of Radiation therapy in China,[19] CBCT images were acquired daily for the first 3 to 5 fractions and weekly thereafter. The frequency of CBCT imaging may be increased, when necessary, depending on preceding registration performance. The registration frame was defined as PTV plus a 2 cm margin, with inclusion of long bones and joints when adjacent to the target volume.[20] CBCT images were automatically registered in 6° of freedom based on bony structures and were adjusted manually afterward with surface outlines taken into consideration. For all patients, any translational and rotational deviations of <10 mm and <3 °, respectively, were corrected as per the CBCT images; otherwise, the patients were repositioned. Translational errors of <1 mm and rotational errors of <1° were permitted, as shown in Fig. 2. For patients in SGRT group, we did initial setup with the CT

Figure 1 The standard positioning of a patient with lower limb sarcoma, with surface laser markings and immobilization using a vacuum cushion.

Figure 2 The main interface of the optical surface imaging system used in our study (AlignRT). The size of the region of interest is shown on the right, and real-time setup error monitoring is displayed on the left.

simulation-based surface for every fraction and adopted CBCT images for registration, and 2 consecutive deviations of >5 mm or >2 ° warranted patient repositioning until deviations <5 mm translation and 2 ° rotation were met. Only in such cases, the patient's body surface after CBCT shifts will be recaptured as a reference body surface for subsequent treatment fractions. Otherwise, no new treatment reference surface would be captured to avoid more random errors.

Regarding the delineation of region of interest, we try to use all 3 cameras and keep the range of region of interest consistent with the projection of the PTV on the body surface, including large joints such as knees or elbows as much as possible, to prevent problems with a cylindrical uniform surface, as mentioned in AAPM task group report 302.[21] Inevitably, sometimes the patient's treatment center happens to be in the long bone area of the lower limbs and thighs, and then we can only refer to the positioning marking line on the patient's body supero-inferiorly.

Patient positioning time was also compared between the groups. Positioning time was defined as the time interval between the first fraction of the previous patient's last treatment field and that of the next patient's first treatment field. The data were considered invalid in cases of absentees, delayed presentation, or machine malfunction resulting in an extended time interval of >20 minutes.

Statistical methods

All statistical analyses were performed using the SPSS 22.0 software. All setup errors were assessed using the Shapiro-Wilk test to ensure normality in distribution. The independent sample *t* test was used, with $P < .05$ considered statistical significance.

Results

The median age was 54 years (range, 13-84 years). The median body mass index was 25.8 kg/m^2 (range, 19.9-34.7 kg/m^2). CBCT images were acquired at a median fraction number of 14 (range, 9-30) and 11 (range, 9-26) in the SGRT and control groups, respectively.

Setup errors in upper limb sarcoma patients

Upper limb sarcomas were observed in 10 patients from the SGRT and control groups, respectively. A total of 140 and 166 CBCT images were collected, respectively. The translational and rotational errors of such patients are shown in Table 2. Significant differences in translational error in the LR (*X*) direction, as well as in rotational error in the sagittal (*Rx*) and transverse (*Ry*) planes were demonstrated ($P < .05$).

Table 2 Comparison of upper limb setup errors between the groups

Group		Translational error (mm)			Rotational error (°)		
		X	*Y*	*Z*	*Rx*	*Ry*	*Rz*
SGRT	∑	1.64	1.10	1.24	0.6	0.9	0.7
	σ	1.34	1.50	1.45	0.7	0.9	0.7
Control	∑	1.48	2.84	3.14	1.4	0.8	0.8
	σ	3.16	2.85	3.29	1.8	1.3	1.9
t		3.313	−0.996	0.319	−3.558	6.477	0.275
P		.001	.320	.750	<.001	<.001	.783

Abbreviation: SGRT = surface-guided radiation therapy.

In general, favorable setup results were observed in the SGRT group, as shown in Fig. 3. Significantly lower systematic and random setup errors were observed in the SGRT group compared with the control group, although slightly higher systematic error in the LR (*X*) direction was seen with SGRT. The proportion of translational errors of ≤3 mm in the SGRT group was significantly higher than that in the control group (*X*, 85.0% vs 64.5%; *Y*, 83.6% vs 54.8%; and *Z*, 88.6% vs 50.6%). The proportion of rotational errors of ≤1.5 ° was significantly higher as well (*Rx*, 84.3% vs 53.0%; *Ry*, 67.9% vs 66.3%; and *Rz*, 87.1% vs 61.5%).

Setup errors of lower limb sarcoma

Lower limb sarcomas were observed in 15 patients of the SGRT and control groups, respectively. A total of 253 and 222 CBCT images were collected, respectively. The translational and rotational errors of such patients are shown in Table 3. Significantly lower setup errors were observed in all directions in the SGRT group compared with the control group ($P < .05$).

Superiority in terms of both translational and rotational errors was similarly observed in the SGRT group, as shown in Fig. 3. The proportion of translational errors of ≤3 mm in the SGRT group was significantly higher than that in the control group (*X*, 85.0% vs 72.1%; *Y*, 83.4% vs 59.9%; and *Z*, 77.9% vs 45.5%). The proportion of rotational errors of ≤1.5° was significantly higher as well (*Rx*, 89.3% vs 79.9%; *Ry*, 64.0% vs 49.1%; and *Rz*, 85.4% vs 77.0%).

CTV-PTV margins and positioning time

For upper limb sarcomas, the recommended CTV-PTV margins were as follows: X = 5.0 mm, Y = 3.8 mm, and Z = 4.1 mm in the SGRT group; and X = 5.9 mm, Y = 9.1 mm, and Z = 10.1 mm in the control group. For lower limb sarcomas, the margins were as follows: X = 4.2 mm, Y = 4.7 mm, and Z = 5.2 mm in the SGRT group; and X = 6.3 mm, Y = 9.6 mm, and Z = 11.4 mm in the control group. For any primary site, the required CTV-PTV margins were as follows: X = 4.4 mm, Y = 4.4 mm, and Z = 4.7 mm in the SGRT group; and X = 6.6 mm, Y = 9.4 mm, and Z = 10.9 mm in the control group. In general, SGRT associated with lower CTV-PTV margins in both upper and lower limb sarcomas. Differences of approximately 1 mm in CTV-PTV margins were observed between the upper and lower limbs, suggesting that similar target margin strategies can be employed in all extremity soft tissue sarcomas in clinical practice.

The analysis of positioning time was feasible among 19 and 21 patients from the SGRT and control groups, respectively. Slightly longer positioning time was reported in the control group (average, 10.5 vs 9.3 min), and was consistent with the need for repeated CBCT imaging and repositioning due to excessive setup errors.

Discussion

To our knowledge, our study represents the largest cohort study investigating the clinical benefits of optical surface imaging in terms of reducing setup deviation during radiation therapy for extremity soft tissue sarcoma. SGRT was found to significantly mitigate majority of the translational and rotational setup errors and allowed for a CTV-PTV margin of 5 mm without prolongation of positioning time. We further found that similar target margin strategies can be adopted for all extremity sarcomas, given that differences in the calculated CTV-PTV margins between upper and lower limb diseases were of approximately 1 mm only.

Unlike tumors of other primary sites, the delivery of radiation therapy to those of the extremities is often challenged by the lack of effective and uniform fixation devices. Vacuum bags, Styrofoam, and various customized devices have been used for immobilization of the lower

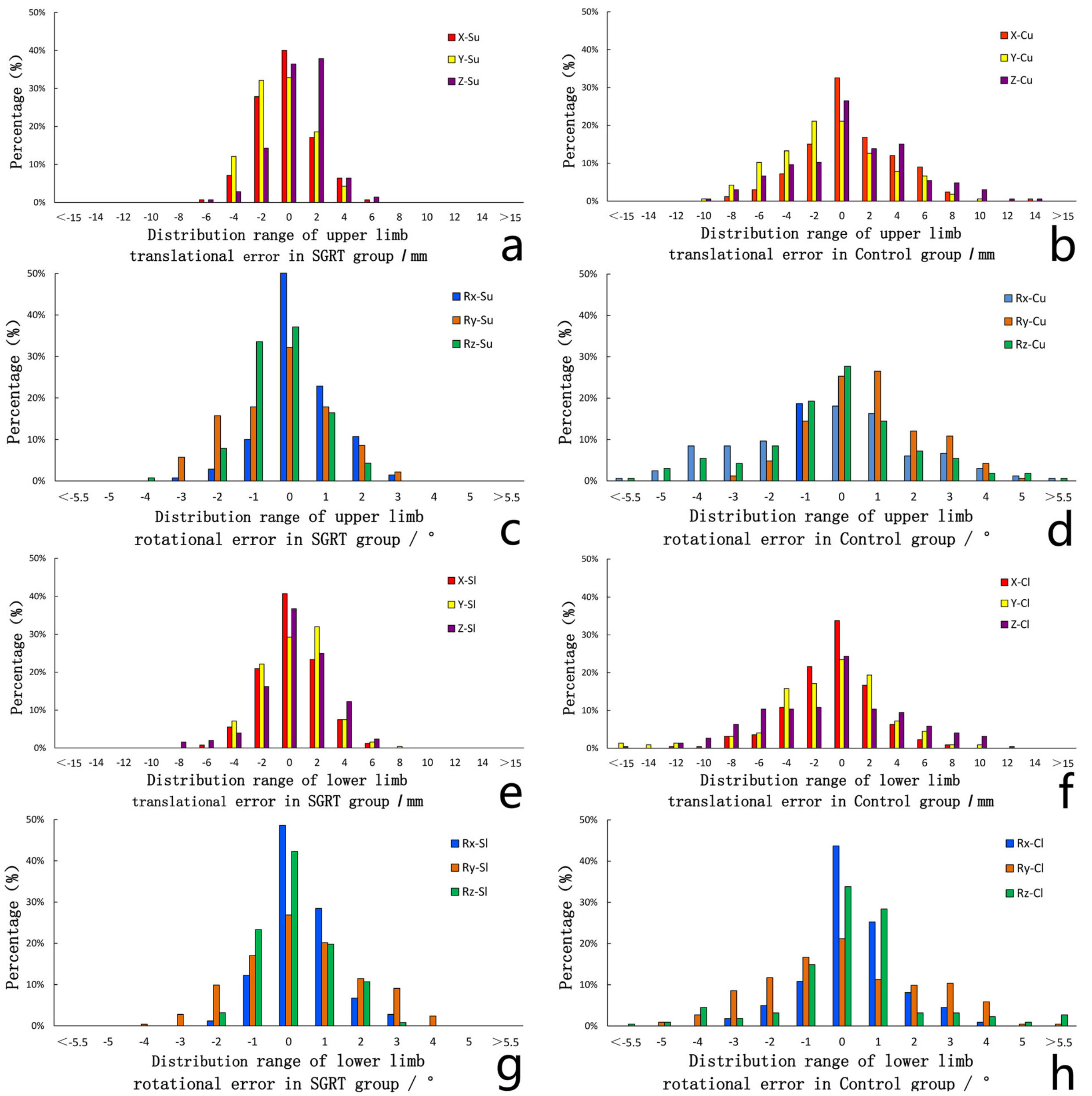

Figure 3 (a-h) Distribution probability histogram of the translational and rotational errors based on treatment group and the target limb.
Abbreviations: Cl = lower limb in the control group; Cu = upper limb in the control group; *Rx* = the sagittal plane; *Ry* = the transverse plane; and *Rz* = the coronal plane; SGRT = surface-guided radiation therapy; Sl = lower limb in the SGRT group; Su = upper limb in the SGRT group; *X* = the left-right direction; *Y* = the superior-inferior direction; *Z* = the anterior-posterior direction.

limb during radiation therapy.[12,22] The different fixation methods used by radiation oncologists precisely indicate their distrust of the fixation device and their lack of recognition of the fixation effect.

Since the advent of SGRT, it has been widely used for tumors of the head and neck, chest, breast, and pelvic cavity, among others.[7-11] However, only a few studies have assessed the positioning reproducibility of the limbs during treatment. Moreover, studies with the inclusion of both upper and lower limb diseases are sparse.[11,12] The AlignRT system used in our study involves the use of stereoscopic imaging and the projection of speckled near-infrared patterns for the acquisition of body surface data.[23,24] Unlike most image-guided techniques, AlignRT allows for real-time monitoring of body motion.[21,25] The application of daily AlignRT during treatment setup beyond the first week in our study not only reduced the need for frequent CBCT imaging, but also allowed for the safe reduction of CTV-PTV margins.

Our study found a significant reduction in both translational and rotational setup errors with SGRT except the left-right translation for upper limb sarcoma. With daily

Table 3 Comparison of lower limb setup errors between the groups

Group		Translational error (mm)			Rotational error (°)		
		X	*Y*	*Z*	*Rx*	*Ry*	*Rz*
SGRT	$\sum$	1.21	1.39	1.48	0.8	1.2	0.7
	σ	1.65	1.71	2.10	0.5	1.1	0.7
Control	$\sum$	1.81	2.93	3.53	0.9	1.8	1.4
	σ	2.60	3.28	3.75	0.8	1.2	1.3
t		−3.560	−3.414	−2.694	−0.175	−1.338	0.444
P		<.001	.001	.007	.861	.182	.657

Abbreviation: SGRT = surface-guided radiation therapy.

optical surface imaging during treatment setup, in addition to daily CBCT for the first 3 to 5 fractions and weekly CBCT thereafter, a uniform 5 mm CTV-PTV margin was deemed feasible in meeting clinical requirements. The clinical benefits of SGRT for limb sarcoma have similarly been investigated by several studies. Dickie et al[12] reported small intrafractional motions of approximately 1 mm translationally and <1° rotationally with weekly optical localization imaging. Based on inter- and intrafractional motion analysis, they also recommended a 5 mm PTV margin.[12] In the study by Gierga et al[11] involving 16 cases of extremity sarcoma, systematic and random translational errors were reported to be minimal, with ranges of 3.3 to 4.3 mm and 2.8 to 4.3 mm, respectively. In their study, optical surface images were acquired daily pre- and posttreatment, and surface registration for the analysis of setup error was performed offline. However, the necessary PTV margins were calculated to be 13, 12, and 10 mm, respectively, which are considerably greater than those calculated in our study (range, 3.8-5.2 mm) and in the study by Dickie et al[12] (range, 4.2-5.2 mm). Such discrepancy may be due to their use of orthogonal megavoltage imaging. The difference in their regime for positioning verification, which was performed only on the first day and weekly thereafter, also may have been a contributing factor. In the Radiation Therapy Oncology Group (RTOG) 0630 trial by Li et al,[13] the omission of daily optical surface imaging resulted in an increase in CTV-PTV margin from 5 to 15 mm.

To our knowledge, our study represents the first in performing separate setup error analyses for upper and lower limb sarcomas. Our findings suggest that positioning of the upper limbs is more prone to translational and rotational shifts as the other study.[3,4] Translational setup errors of 1.6 ± 1.3 mm, 1.1 ± 1.5 mm, and 1.2 ± 1.5 mm in the *X, Y,* and *Z* directions, respectively, were reported in the upper limbs with optical surface guidance. These were similar to those of the lower limbs, which were 1.2 ± 1.7 mm, 1.4 ± 1.7 mm, and 1.5 ± 2.1 mm. As such, our findings imply that similar target volume expansion strategies can be applied to both upper and lower limbs. Based on our results, we suggest CTV-PTV margins of 5.0, 3.8, and 4.1 mm in the *X, Y,* and *Z* directions, respectively, for SGRT of upper limb sarcomas.

Our study had several limitations. First, separate linacs were used for laser-based and optical surface-based imaging. In addition, the treatment groups were assigned according to real-time workload and availability of linacs, rather than by prospective randomization. However, all the technicians were well trained and on regular shift rotation every 3 to 6 months to ensure familiarity of each linac, which to some extent avoids potential difference caused by staff. Furthermore, CBCT was not performed for every fraction due to cost-effectiveness; however, the frequency of CBCT image acquisition was similar between the control and SGRT groups. Although AlignRT allows for image registration and real-time motion detection without radiation, its application is limited to body surface motion and changes. The outline changes due to tissue edema or tumor regression, for example, may thereby affect the accuracy of surface imaging. The potential need for repeat CBCT imaging to obtain the corrected body surface data, and even a repeat of the whole treatment planning process, were recognized throughout the study. As a retrospective analysis, we did not record the actual time of patient's setup, and the time interval calculation used is not accurate to postulate the positioning time between 2 groups.

Conclusion

SGRT with AlignRT can improve the positioning accuracy of patients with extremity soft tissue sarcoma, effectively and safely reduce CTV-PTV margins without the extension of positioning time. Significantly lower setup errors/deviations were generally observed with daily SGRT in both upper and lower limb sarcoma patients. In addition, similar CTV-PTV margin targets of ≤5 mm can be applied to both upper and lower limb diseases.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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