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Preoperative vs postoperative radiation therapy in localized soft tissue sarcoma: Nationwide patterns of care and trends in utilization

Stanislav Lazarev, MD^a, Heather McGee, MD, PhD^a, Erin Moshier, MS^b, Meng Ru, MS^b, Elizabeth G. Demicco, MD, PhD^c, and Vishal Gupta, MD^{a,*}

^aDepartment of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, New York

^bDepartment of Population Health Science & Policy, Icahn School of Medicine at Mount Sinai, New York, New York

^cDepartment of Pathology, Icahn School of Medicine at Mount Sinai, New York, New York

Abstract

Purpose—The timing of perioperative radiation therapy (RT) in the treatment of soft tissue sarcoma (STS) varies among institutions. This study examines patterns of care, trends in utilization, and survival with preoperative versus postoperative RT for primary STS.

Methods and materials—Using the National Cancer Data Base, we identified patients with stage I-III STS who underwent definitive surgery with either preoperative or postoperative RT between 2004 and 2012. Univariate, bivariate, and multivariate analyses were performed to identify factors predicting receipt of preoperative versus postoperative RT. Overall survival (OS) was analyzed using the log-rank test, Kaplan-Meier method, and Cox proportional-hazards model.

Results—This study included 9604 patients: 7246 (75.4%) received postoperative and 2358 (24.6%)-preoperative RT. Chemotherapy was administered to 27.0% patients in the preoperative and 13.0% in the postoperative cohort. Use of preoperative RT increased over time, from 16.8% in 2004 to 29.7% in 2012. Multivariate analysis revealed that preoperative RT utilization increased with the following factors: higher educational attainment, treatment at an academic facility, further distance from facility (>60 miles), receipt of chemotherapy, tumor originating in lower extremities, >10 cm tumors, and myxoid liposarcoma. OS analysis revealed no difference between the 2 treatment cohorts.

Conclusions—Postoperative RT is used much more commonly than preoperative RT in localized STS; however, preoperative RT use has increased in recent years. Multiple demographic and clinicopathologic factors were predictive of preoperative RT use. Consistent with randomized phase 3 data, there was no difference in OS.

*Corresponding author. Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, 1184 5th Ave, Box 1236, New York, NY 10029. Vishal.Gupta@mountsinai.org (V. Gupta).

Conflicts of interest: None.

Introduction

The curative treatment for localized soft tissue sarcomas (STS) is wide surgical excision.¹ Adjuvant radiation therapy (RT) is recommended for patients with high-risk factors, such as high-grade and inadequate margins, to improve local control.² The timing of perioperative RT is often determined by preference of the patients, surgeons, and radiation oncologists. The only phase 3 trial comparing outcomes of preoperative and postoperative RT in STS, conducted by the National Cancer Institute of Canada (NCIC), randomized 190 patients with resectable extremity sarcomas to receive either preoperative or postoperative RT.³ The study revealed a higher incidence of late toxicities and worse limb function with postoperative RT,⁴ but found no difference in local control or survival,⁵ although it was not powered to analyze these endpoints. The analysis was limited mainly to lower extremity sarcomas, which composed about 80% of cases in each cohort.

Preoperative RT advantages include a lower cumulative dose and direct tumor visualization with imaging, which allows better target delineation and a smaller treatment field. Theoretically, there is also a decreased risk of seeding of malignant cells at the time of resection with preoperative RT.⁶ With respect to postoperative RT, its advantages include a lower incidence of acute wound complications³ and availability of complete pathological review of tumor for accurate staging. At the same time, postoperative RT planning is complicated by difficulty of delineating the radiation field and higher RT doses resulting from tumor hypoxia.

A 2013 National Cancer Data Base (NCDB) study evaluating the patterns of trimodality care for primary STS noted an increase in the receipt of neoadjuvant RT from 2000 through 2009.⁷ The main focus of that study was to analyze utilization of 5 different treatment regimens for STS originating in extremities only. In another nationwide retrospective analysis, Sampath and colleagues examined outcomes in 821 patients with localized or metastatic STS after preoperative or postoperative RT and documented a survival benefit with preoperative RT.⁸ In that investigation, the authors did not assess patterns of RT utilization. Given paucity of randomized data and conclusive studies relating to the use of preoperative versus postoperative RT for localized STS originating in all major anatomic sites, we sought to characterize patterns of care and trends in utilization of 2 different perioperative RT approaches using the most up-to-date NCDB registry encompassing 2004 through 2012. Additionally, we aimed to evaluate the association between the long-term overall survival (OS) and timing of RT.

Methods and materials

Data source and patient selection

Data were collected from the NCDB, a nationwide registry that reports 70% of all new cancer cases in the United States annually.⁹ Information on STS diagnosed from January 1, 2004, to December 31, 2012 was derived from a deidentified NCDB file. The subsequent analysis was conducted with the approval of our institution's institutional review board.

Figure 1 illustrates the study cohort. We initially identified 25,642 patients with primary STS who underwent definitive surgery and either preoperative or postoperative RT. The patients that received both preoperative and postoperative RT, intraoperative RT only, and those with undocumented surgery-radiation sequence were excluded. We subsequently excluded benign histologies (dermatofibrosarcoma protuberans), histologies typically treated with chemotherapy (rhabdomyosarcoma, Ewing sarcoma), soft tissue osteosarcomas, and chondrosarcomas. All patients were required to have a documented grade, a confirmed histological diagnosis of STS, dates of diagnosis and last contact, and vital status. We then excluded patients with documented distant metastases, or unknown status of distant metastases, patients who had a surgery performed at a site other than the primary, or only had an excisional biopsy. Furthermore, we restricted our analysis to patients who were alive 30 days following surgery to account for perioperative mortality. Additional ineligibility criteria were radiation modality other than external beam RT, radiation delivered with palliative intent, and interval between surgery and radiation >120 days. We further excluded patients who began curative therapy (either radiation or surgery) >180 days after diagnosis because treatment beyond this point may potentially represent a salvage intent. Finally, we limited our cohorts to patients who received a cumulative dose no higher than 80 Gy to exclude potentially misclassified doses, and removed patients with a cumulative dose <40 Gy preoperatively or 50 Gy postoperatively to exclude potentially palliative cases. For the same reasons, we excluded patients who completed RT in less than 4 weeks preoperatively, or 5 weeks postoperatively, which would theoretically correspond to 40 Gy and 50 Gy of radiation using conventional fractionation once daily 5 days a week. Cases of RT taking longer than 90 days, or those with missing information on the length of RT course, were excluded.

Predictor variables

Potentially relevant demographic variables included age, gender, race, Hispanic origin, insurance status, median household income, education, distance from medical facility, facility type, location, and year of diagnosis. Clinicopathologic characteristics included Charlson-Deyo comorbidity score, primary site, histology, grade, tumor size, receipt of chemotherapy, and start of treatment (either surgery or radiation) in days from diagnosis (<30 days and >30 days). Histologies, coded in NCDB using the International Classification of Disease for Oncology (3rd edition) ICD-O-3 topography codes, were grouped with the help of a surgical pathologist (E.G.D.) and World Health Organization Classification of Soft Tissue Tumours.¹⁰

Statistical analysis

The primary endpoints were receipt of preoperative versus postoperative RT after the diagnosis of localized STS, and trends in utilization of perioperative RT from 2004 through 2012. The secondary endpoint was OS by treatment cohort. Patient characteristics were compared between preoperative and postoperative RT groups using χ^2 test. Multivariable logistic regression models were used to estimate adjusted odds ratios (OR) and 95% confidence intervals (95% CI) to evaluate the association between each variable and treatment status while adjusting for all other variables outlined previously. Preoperative RT was used as the outcome in the regression models. ORs >1.0 indicated an increased

likelihood of receiving preoperative RT, and a decreased likelihood of receiving postoperative RT. To account for the multiple imputations of missing data, logistic regression was performed on each of the 50 imputed datasets. Estimates of corresponding ORs and 95% CIs were then appropriately combined using the MIANALYZE procedure in SAS. The OS interval was measured from the date of diagnosis to the date of last contact or confirmed death. All statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC). Hypothesis testing was 2-sided and conducted at the 5% level of significance.

The Joinpoint Regression Program (version 4.3.1.0) developed by the US National Cancer Institute was used to assess temporal trends in annual preoperative RT utilization rates for all patients combined and by tumor size, facility type, and primary site. The Joinpoint software fits the simplest model to describe the utilization rate trend data, starting with a straight line (0 joinpoints) and then adding more joinpoints to determine whether multiple connecting lines better describe the data points. The software identifies the year(s) when the annual percentage change trends appear to shift upward or downward and whether these trends are statistically significant.

Missing data for the prognostic variables outlined previously were handled by multiple imputation using chained equations.¹¹ Among these variables, facility type and geographical region had the highest frequencies of missing data at 14.1%, followed by race (6.3%) and median income (3.7%). This sequential regression imputation was implemented using IVEware software.¹¹ The process begins for each variable, with missing values being imputed using a univariable logistic, ordinal, multinomial logistic, or predictive mean matching regression model conditional on all of the other variables. The process cycles iteratively through the variables containing missing values until the procedure is stable. We performed 10 repetitions of this cycle to generate 50 imputed datasets. This method is superior to alternatives (complete case or missing data indicator methods) as far as analytic bias is concerned, under the assumption that data are missing at random.¹²

Survival modeling

A landmark analysis addressing potential immortal time bias was performed where only patients alive 180 days following diagnosis were included, which was the latest time by which a patient received postoperative RT; therefore, 9012 patients were included in the survival modeling. OS was analyzed using the log-rank test, Kaplan-Meier method, and Cox proportional-hazards model. All prognostic variables identified here were included in the multivariable Cox proportional-hazards model. To account for the multiple imputations of missing data, Cox regression (for landmark analyses) was performed on each of the 50 imputed datasets, and estimates of corresponding hazard ratios and 95% CIs were then appropriately combined using the MIANALYZE procedure in SAS.

Results

Baseline characteristics

A total of 9604 patients with stage I-III STS met our inclusion criteria: 7246 (75.4%) received postoperative and 2358 (24.6%)-preoperative RT. Chemotherapy was received by 27.0% patients in the preoperative and 13.0% in the postoperative cohort. Table 1 compares baseline characteristics between both cohorts. The median age of the entire cohort was 61 years. Among patients treated in community facilities, 85% had postoperative and 15% preoperative RT, whereas those in academic centers received postoperative RT in 67% versus preoperative RT in 33% of cases. Of 455 head and neck tumors, 92% were irradiated postoperatively versus 8% preoperatively. With regards to limb sarcomas, of 1660 upper extremity cases, 21% had preoperative RT, whereas of 4770 lower extremity cases, preoperative RT was used in up to 31% of patients. Tumors ≤ 5 cm were irradiated preoperatively only in 12% cases, whereas those >10 cm in 36% of cases.

Predictors of receiving preoperative RT

In multivariable analysis, patients receiving preoperative RT were less likely to be Asians (OR, 0.65; 95% CI, 0.48-0.88) or Hispanics (OR, 0.83; 95% CI, 0.73-0.95) (Table 2). Preoperative RT recipients were more likely to have higher educational attainment rates (OR 1.14; 95% CI, 1.02-1.26) or live further (>60 miles) (OR, 1.26; 95% CI, 1.17-1.36). Preoperative RT recipients were also more likely to be treated in academic centers (OR, 1.52; 95% CI, 1.37-1.67), in the South (OR 1.44; 95% CI, 1.31-1.58), or experience a delay in the start of treatment (>30 days from diagnosis) (OR, 1.80; 95% CI, 1.70-1.91). There was no association between patient's age, gender, Charlson-Deyo comorbidity score, insurance status, median household income, and receipt of preoperative RT. Preoperative RT recipients were more likely to have tumors originating in lower extremities (OR, 1.77; 95% CI, 1.58-1.99), but less likely to have sarcomas of the thorax/trunk (OR, 0.68; 95% CI, 0.56-0.81). Patients receiving preoperative RT were more likely to have myxoid liposarcoma (OR, 1.31; 95% CI, 1.10-1.56). Preoperative RT use was increased for tumors larger than 10 cm (OR 1.73; 95% CI, 1.59-1.87). Finally, preoperative RT patients were more likely to receive chemotherapy (OR, 1.38; 95% CI, 1.29-1.48).

Trends in perioperative RT utilization

The use of postoperative RT declined over the study period from 83.2% in 2004 to 70.3% in 2013, whereas preoperative RT utilization increased from 16.8% in 2004 to 29.7% in 2012 (Fig 2). Overall, there was a 7.74% annual percent change increase in preoperative RT use during the study period ($P = .0001$) (Table e1; available as supplementary material online only at www.practicalradonc.org). When stratified by the facility type, there has been a modest increase in preoperative RT utilization among the community hospitals, from 11.5% in 2004 to 19.3% in 2012 ($P < .02$), whereas academic facilities have had a more appreciable increase, from 23.9% to 37.9% ($P < .0008$).

With respect to the primary tumor site, the most noticeable changes in preoperative RT use were seen in extremity or abdominal region sarcomas (Fig 3A). Specifically, from 2004 to 2012, the use of preoperative RT increased from 21.7% to 36.3% ($P = .0003$) for lower

extremity tumors, from 12.6% to 25.4% ($P = .0001$) for upper extremity tumors, and from 17.1% to 36.0% ($P = .008$) for abdominal sarcomas. The use of preoperative RT increased among all tumor sizes over time (Fig 3B). Specifically, when compared between 2004 and 2012, small tumors (≤ 5 cm) had preoperative RT in 6.9% and 17.4% cases ($P = .006$), medium-sized tumors (5.1-10 cm) in 19.9% and 29.9% cases ($P = .0004$), and large tumors (>10 cm) in 24.9% and 40.6% cases ($P = .0003$), respectively.

Survival by treatment cohort

The 2-year OS rates with preoperative versus postoperative RT were 85.7% (95% CI, 84.1-87.1) and 87.6% (95% CI, 86.8-88.4), respectively (eTable 2). Five-year corresponding OS rates were 65.4% (95% CI, 63.0-67.8) and 71.3% (95% CI, 70.1%-72.6). Multivariate analysis found no difference in OS between the 2 cohorts (hazard ratio, 1.05; 95% CI: 0.95-1.16; $P = .33$).

Discussion

To the best of our knowledge, this is the largest nationwide analysis to date directly comparing patterns of utilization of preoperative versus postoperative RT in the context of definitive surgery for localized STS of all major primary sites. Our data show that postoperative RT is used much more frequently than preoperative RT (76% vs 24%, respectively). However, we found a steady increase in the use of preoperative RT from 2004 to 2012, with a concomitant decline in postoperative RT utilization. With the exception of tumors originating in the head and neck and pelvis, the trend toward preoperative irradiation of resectable STS was noted across all primary sites. These gradual changes in practice might be explained, at least in part, by the presentation of findings of the NCIC trial at the 2004 American Society of Clinical Oncology Annual Meeting and their subsequent publication in 2005, which suggested similar local control, but improved late radiation morbidity and functional outcomes with preoperative RT in extremity STS when compared with the postoperative approach.^{4,5} It is likely, therefore, that changes in perioperative sequencing of radiation over the study period reflect oncologists' wish to improve the therapeutic ratio by sparing long-term toxicities and producing good functional outcomes. Notably, before 2004, the standard of care was guided by the evidence of a randomized trial supporting the use of postoperative RT in primary nonmetastatic STS.¹³

Our analysis demonstrated that the most appreciable increase in preoperative RT utilization took place in academic facilities. Furthermore, across the entire cohort, patients receiving preoperative RT were more likely to be treated in an academic center than in the community, in contrast to those receiving postoperative RT. These findings may be due to academic facilities incorporating new data into the clinic more quickly than community practices. Preoperative RT was given more frequently in patients who traveled >60 miles for treatment. This may be due to these patients seeking care at an academic center where preoperative RT was more common.

Although we were not surprised by the trend toward increased use of preoperative RT for STS of the limbs given the NCIC trial, we were intrigued to find that with later years of diagnosis, utilization of the preoperative approach also rose for abdominal tumors, which

comprise both intraabdominal and retroperitoneal sarcomas in this dataset. Our findings coincide with the results of the 2016 NCDB study of retroperitoneal sarcomas, treated with preoperative or postoperative RT versus surgery alone, in which the authors determined that the use of preoperative RT was more frequent in 2007 through 2011 than in 2003 through 2006, $P = .00015$.¹⁴ Given the difficulty of accurate target delineation in the postoperative setting and challenges with meeting normal tissue constraints in the abdomen with high doses of postoperative RT, preoperative RT is likely to be preferred for this tumor location in cases where resection alone is likely to be technically difficult or suboptimal. Postoperative RT should probably be avoided in this subset of patients.

In the present analysis, preoperative RT use increased in tumors >10 cm. Furthermore, when we stratified lesions by size, the most pronounced trend in the preoperative RT utilization over time was also among very large tumors (>10 cm). These findings coincide with results from prior studies demonstrating increased utilization of preoperative RT for large sarcomas.¹⁵ This is not surprising because preoperative irradiation has the potential to downstage bulky tumors and allow more conservative and function-sparing resection. At the same time, smaller lesions are more likely to receive postoperative RT because they may not be imaged preoperatively and are often presumed to be benign; therefore, unless the lesion is more radiosensitive, its size should not factor too much into the decision-making process of perioperative RT timing.

Interestingly, association with increased use of preoperative RT in our investigation was seen both in patients with larger tumors and those receiving chemotherapy. Earlier studies demonstrated that higher grade and large STS benefit the most from chemotherapy as they have a high propensity for distant spread.^{16,17} In fact, in our analysis, patients in the preoperative cohort were more likely to receive chemotherapy than those in the postoperative cohort, 27.0% and 13.0%, $P < .0001$. Unfortunately, the impact of chemotherapy on clinical outcomes is not clear from our data and is beyond the scope of this study.

Although local control benefit of adjuvant RT for resectable nonmetastatic STS has been established in prior studies,^{13,18} its impact on survival is yet to be elucidated. Nevertheless, when RT is offered, its sequencing does not impact survival. The findings of the randomized NCIC trial showed that, at a median follow-up of 6.9 years, there was no difference in long-term survival between patients receiving preoperative or postoperative RT.⁵ Although retrospective in nature, our study further validated the NCIC investigation by using a larger cohort of patients with sarcomas of all major anatomic sites. In our multivariable analysis, we also did not find any statistical difference in OS between the 2 cohorts.

The present investigation has several important shortcomings. First, the NCDB registry does not offer information on certain variables that could have influenced the decision-making process regarding the sequence of perioperative RT, such as patient's performance status, resectability of tumor at presentation, and patient's personal choice. Given coding limitations of the database, we were also unable to partition the anatomic sites of sarcomas in accordance with more common clinical scenarios (ie, separate thorax/trunk tumors into intrathoracic and mediastinal tumors, or abdominal, into retroperitoneal, intra-abdominal,

and abdominal wall tumors). As a result, we were unable to assess the influence of the more specific anatomic compartments on the choice of perioperative RT. Additionally, lack of information on radiation toxicities, wound complications, and functional outcomes limit this analysis. Furthermore, the nonrandomized allocation of treatment cohorts makes it challenging to provide a robust analysis of survival; therefore, the lack of significant variation in survival that was noted in our study could possibly reflect a patient selection bias. Finally, although NCDB uses standardized methods of data collection, there is still a possibility of coding errors; hence, reliance of data documentation by a wide range of facilities cannot be verified.

In summary, this study shows that postoperative RT is given much more commonly than preoperative RT for primary STS; however, utilization of the preoperative approach has increased in recent years. This is not meant to ascertain that preoperative irradiation should be the standard of care for localized sarcomas. The decision regarding the optimal timing of RT has to be made by a multidisciplinary sarcoma team on a case-by-case basis after accounting for numerous patient- and treatment-related factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Exclusion criteria and treatment group allocation. RT, radiation therapy.

Figure 2.

Trends in preoperative RT utilization by year of diagnosis. This figure shows that there was a significant 7.74% annual percent change (APC) increase ($P = .0001$) in preoperative RT utilization (APC, 7.74; 95% confidence interval, 5.58-9.94) over the study period. Overall, the use of preoperative RT increased from 16.8% in 2004 to 29.7% in 2012. Abbreviation as in Fig 1.

Figure 3. Trends in preoperative RT utilization stratified by (A) primary site and (B) tumor size. Abbreviation as in Fig 1.

Abbreviations: APC = Annual Percent Change. The figure above shows the trend in preoperative RT utilization by year of diagnosis. Overall, the use of preoperative RT increased over the study period, from 16.8% in 2004 to 29.7% in 2012. For the overall cohort, there was a significant 7.74% increase (p-value = 0.0001) in preoperative RT utilization from 2004 to 2012 (APC: 7.74, 95% CI 5.58 - 9.94).

Figure 4.
Adjusted Cox regression model curves

Table 1

Comparison of baseline characteristics between preoperative and postoperative RT cohorts, 2004-2012, imputed missing data (N = 9604)

Characteristic	Preoperative RT (n = 2358) No. (%)	Postoperative RT (n = 7246) No. (%)	P
Age, y			
60	1140 (25)	3397 (75)	.2158
>60	1218 (24)	3849 (76)	
Sex			
Female	1046 (25)	3178 (75)	.6703
Male	1312 (24)	4068 (76)	
Race			
White	2067 (25)	6330 (75)	.0003
Black	226 (27)	609 (73)	
Asian	47 (15)	264 (85)	
Other	18 (30)	43 (70)	
Charlson-Deyo comorbidity score			
0	1970 (24)	6085 (76)	.8556
1	322 (25)	970 (75)	
2	66 (26)	191 (74)	
Hispanic origin			
No	2254 (25)	6818 (75)	.0058
Yes	104 (20)	428 (80)	
Insurance status			
Uninsured	74 (25)	218 (75)	.6941
Private	1245 (25)	3764 (75)	
Government	1039 (24)	3264 (76)	
Median household income, \$			
<30,000	251 (24)	779 (76)	.0059
30,000-45,999	1102 (26)	3123 (74)	
46,000 +	1005 (23)	3344 (77)	
Education (% no high school diploma)			
29	303 (24)	967 (76)	.6288
14-28.9	1097 (25)	3293 (75)	
<14	958 (24)	2986 (76)	
Distance from facility, miles			
60	1799 (22)	6403 (78)	<.0001
>60	559 (40)	843 (60)	
Year of diagnosis			
2004	147 (17)	725 (83)	<.0001
2005	192 (19)	797 (81)	
2006	189 (20)	773 (80)	
2007	243 (23)	831 (77)	

Characteristic	Preoperative RT (n = 2358) No. (%)	Postoperative RT (n = 7246) No. (%)	P
2008	240 (23)	825 (77)	
2009	334 (29)	809 (71)	
2010	314 (27)	838 (73)	
2011	362 (30)	852 (70)	
2012	337 (30)	796 (70)	
Facility type			
Community	595 (15)	3401 (85)	<.0001
Academic	1639 (33)	3348 (67)	
Other	124 (20)	497 (80)	
Facility location			
West	303 (17)	1439 (83)	<.0001
Midwest	673 (24)	2092 (76)	
South	927 (30)	2172 (70)	
Northeast	455 (23%)	1543 (77)	
Start of treatment (either surgery or radiation), days from diagnosis			
30	1346 (19)	5895 (81)	<.0001
>30	1012 (43)	1351 (57)	
Primary Site			
Head and neck	37 (8)	418 (92)	<.0001
Upper extremity	343 (21)	1317 (79)	
Lower extremity	1464 (31)	3306 (69)	
Thorax/trunk	155 (13)	1027 (87)	
Abdomen	103 (25)	317 (75)	
Pelvis	220 (24)	695 (76%)	
Other/NOS	36 (18)	166 (82)	
Histology			
Liposarcoma, well-differentiated	58 (16)	307 (84)	<.0001
Liposarcoma, myxoid	259 (34)	494 (66)	
Liposarcoma, pleomorphic	79 (25)	238 (75)	
Liposarcoma, dedifferentiated	45 (15)	258 (85)	
Liposarcoma, NOS	42 (16)	219 (84)	
Leiomyosarcoma	254 (22)	924 (78)	
Undifferentiated pleomorphic sarcoma	538 (21)	1992 (79)	
Malignant peripheral nerve sheath tumor	66 (16)	339 (84)	
Synovial sarcoma	107 (32)	226 (68)	
Sarcoma NOS	211 (24)	669 (76)	
Other	699 (31)	1580 (69)	
Grade			
Low	688 (23)	2336 (77)	.0054
Intermediate/high	1670 (25)	4910 (75)	
Chemotherapy			

Characteristic	Preoperative RT (n = 2358) No. (%)	Postoperative RT (n = 7246) No. (%)	P
No	1731 (22)	6300 (78)	<.0001
Yes	627 (40)	946 (60)	
Tumor size			
5 cm	381 (12)	2702 (88)	<.0001
5.1-10 cm	906 (26)	2607 (74)	
>10 cm	1071 (36)	1937 (64)	

NOS, not otherwise specified; RT, radiation therapy.

Table 2

Multivariable logistic regression analysis of predictors of preoperative RT utilization

Characteristic	Multivariable OR (95% CI)	P
Age, y		
60	Ref	
>60	1.05 (0.98-1.12)	.2018
Gender		
Female	Ref	
Male	1.00 (0.95-1.06)	.9388
Race		
White	Ref	
Black	0.99 (0.79-1.24)	.9047
Asian	0.65 (0.48-0.88)	.0045
Other	1.42 (0.89-2.27)	.1374
Charlson-Deyo comorbidity score		
0	Ref	
1	0.95(0.83-1.10)	.5066
2	1.02 (0.82-1.26)	.8797
Hispanic origin		
No	Ref	
Yes	0.83 (0.73-0.95)	.0080
Insurance status		
Uninsured	Ref	
Private	1.09 (0.96-1.23)	.1645
Government	1.07 (0.94-1.22)	.2867
Median household income, \$		
<30,000	Ref	
30,000-45,999	1.08 (0.99-1.17)	.1011
46,000+	0.98 (0.88-1.10)	.7167
Education (% no high school diploma)		
29	Ref	
14-28.9	0.99 (0.91-1.07)	.7907
<14	1.14 (1.02-1.26)	.0144
Distance from facility, miles		
60	Ref	
>60	1.26 (1.17-1.36)	<.0001
Facility type		
Community	Ref	
Academic	1.52 (1.37-1.67)	<.0001
Other	0.95 (0.81-1.12)	.4727
Facility location		
West	Ref	

Characteristic	Multivariable OR (95% CI)	P
Midwest	1.06 (0.96-1.16)	.2382
South	1.44 (1.31-1.58)	<.0001
Northeast	0.98 (0.88-1.10)	.7206
Start of definitive treatment, days from diagnosis		
30	Ref	
>30	1.80 (1.70-1.91)	<.0001
Primary site		
Head and neck	Ref	
Upper extremity	1.38 (1.19-1.60)	<.0001
Lower extremity	1.77 (1.58-1.99)	<.0001
Thorax/trunk	0.68 (0.56-0.81)	<.0001
Abdomen	1.23 (0.97-1.55)	.0880
Pelvis	1.16 (0.98-1.38)	.0820
Other/NOS	1.02(0.72-1.44)	.9199
Histology		
Liposarcoma, well-differentiated	Ref	
Liposarcoma, myxoid	1.31 (1.10-1.56)	.0027
Liposarcoma, pleomorphic	1.56 (1.38-1.76)	<.0001
Liposarcoma, dedifferentiated	1.45 (1.21-1.73)	<.0001
Liposarcoma, NOS	1.05 (0.80-1.38)	.7059
Leiomyosarcoma	0.55 (0.40-0.76)	.0003
Undifferentiated pleomorphic sarcoma	0.70 (0.51-0.98)	.0408
Malignant peripheral nerve sheath tumor	1.21 (1.03-1.43)	.0226
Synovial sarcoma	1.06 (0.93-1.20)	.3649
Sarcoma NOS	0.75 (0.57-0.99)	.0384
Other	1.73 (1.33-2.24)	<.0001
Grade		
Low	Ref	
Intermediate/high	1.02 (0.95-1.09)	.6279
Chemotherapy		
No	Ref	
Yes	1.38 (1.29-1.48)	<.0001
Tumor size, cm		
5	Ref	
5.1-10	1.11 (1.03-1.20)	.0048
>10	1.73 (1.59-1.87)	<.0001

CI, confidence interval; OR, odds ratio; ref, reference. See Table 1 for other other abbreviation.