Postoperative Radiation Therapy in the Soft-tissue Sarcoma

Yeon Shil Kim, M.D., Hong Seok Jang, M.D., Sei Chul Yoon, M.D., Mi Ryeong Ryu, M.D., Ki Moon Kang, M.D., Su Mi Chung, M.D., Hoon Kyo Kim, M.D.*, Yong Koo Kang, M.D.†

Department of Therapeutic Radiology, Internal Medicine*& Orthopedic Surgery †

College of Medicine, The Catholic University, Seoul, Korea

Purpose: The major goal of the therapy in the soft tissue sarcoma is to control both local and distant tumor. However, the technique of obtaining local control has changed significantly over the past few decades from more aggressive surgery to combined therapy including conservative surgery and radiation and/or chemotherapy. We retrospectively analyzed the treatment results of the postoperative radiation therapy of soft tissue sarcoma and its prognostic factor.

Materials and Methods: Between March 1983 and June 1994, 60 patients with soft tissue sarcoma were treated with surgery and postoperative radiation therapy at Kang-Nam St. Mary's hospital. Complete follow up was possible for all patints with median follow up duration 50 months (range 6 - 162 months). There were 28 male and 32 female patients. Their age ranged from 6 to 83 with a median of 44 years. Extremity (58%) was the most frequent site of occurrence followed by trunk (20%) and head and neck (12%). Histologically malignant fibrous histiocytoma (23%), liposarcoma (17%), malignant schwannoma (12%) constitute 52% of the patients. Daily radiation therapy designed to treat all areas at a risk for tumor spread upto dose of 4500-5000 cGy. A shrinking field technique was then used and total 55-65 Gy was delivered to tumor bed. Twenty-five patients (42%) received chemotherapy with various regimen in the postoperative period. Results: Total 41 patients failed either with local recurrence or with distant metastasis. There were 29 patients(48%) of local recurrence. Four patients (7%) developed simultaneous local recurrence and distant metastasis and 8 patients (13%) developed only distant metastasis. Local recurrence rate was rather higher than of other reported series. This study included patients of gross residual, recurrent cases after previous operation, trunk and head and neck primary. This feature is likely explanation for the decreased local control rate. Five of 29 patients who failed only locally were salvaged by re-excision and/or re-irradiation and remained free of disease. Factors affecting local control include histologic type, grade, stage, extent of operation and surgical margin involvement, lymph node metastasis (p < 0.05). All 21 patients who failed distantly are dead with progressive disease at the time of this report. Our overall survival results are similar to those of larger series. Actuarial 5 year overall survival and disease fresurvival were 60.4 %, 36.6% respectively. Grade, stage (being close association with grade), residual disease (negative margin, microscopic, gross) were significant as a predictor of survival in our series (p < 0.05).

<u>Conclusion</u>: Combined surgery and postoperative radiation therapy obtained 5 year survival rate comparable to that of radical surgery.

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20 (33%), 15 (25 %), 12 (20%), 7 (12%) (ma lignant fibrous histiocytoma) 14 (23%), (lipos a r-(ne urovacoma) 10 (17%), (malignant schscular bundle) (connective tissue) wannoma) 7 (12%) (aggressive fibromatosis) 8 (15%) Table 1. Tumor Histologic Subtype Versus Grade at Presentation Grade Histologic subtype I II III Unknown Total 가 Liposarcoma 가 MFH Malig. schwannoma (amputation) (radical Leiomyosarcoma Angiosarcoma compartmental resection)가 Fibrosarcoma 3 20% $Rhabdomyos\,a\,ccom\,a$ Aggressive fibromatosis Othe rs 1982 National Cancer Institute (NCI) pro-Total 27 3 24 spective randomized trial11 multimodality Table 2. Tumor Size Versus Grade treatment 가 Maximum diameter(cm) multimodality treatment Grade Less than 5 5 to 10 More than 10 Total 가 I II가 3 7 Ш 10 7 24 Unknown 3 3 6 Total American Joint Committee on Cancer(AJCC) 1. I 26 (43%), ID 3 (5%), III, IV가 18 (30%), 8 (13%) 1983 1994 grade I, . II, III가 27 (45%), 3 (5%), 24 (40%) Kaposi's sarcoma juve nile rhabdo myo-80% (8/10) grade I sarcoma(30 가 grade III 57% (8/14) 0.9:1 44 (le iomyos arcoma), (angiosarcoma), 6-83) 25 (42%) (rhabdomyosar coma) grade III (Table 1).

Table 1- 3

5cm

(43%), 5-10cm 18 (30%), 10cm

26

(27%) . (Table 2). 5 (8.3%) 7;
2.
S5
, 가 (Table 4).3.
6 162 50 . 7†
가 Kaplan-Meier method
metastasis free survival) . aggressive fibromatosis 8
52 . 13 ,
(Logrank, Wikoxon test) , , , ,
0.05 .

Table 3. Patients Characteristics

Characteristics		No. of Patients (%)	
Age		6 - 83 yrs (Median 44 yrs)	
Sex	ma le fe ma le	28(47) 32(53)	
Presentation	primary recurrent	35(58) 25(42)	
Site	upper extremity lower extremity trunk retroperitoneum head and neck	15(25) 20(33) 12(20) 6(10) 7(12)	
Stage	I II III IV undetermined	26(43) 3(5) 18(30) 8(13) 5(8)	
T Stage	T 1 T2	26(43) 34(57)	
N Stage	NO N1	55(92) 5(8)	
M Stage	MO M1	55(92) 5(8)	

Table 4. Treatment Characteristics

Characteristics	No. of patients	(%)
Operation type	intrales ional excision	5(8)
• • •	marginal excision	36(60)
	wide excision	19(32)
Surgical margin	negative margin	23(38)
0	microscopic(+)	21(35)
	gross residual	16(27)
Radiation dose	< 50 Gy	6(10)
	50-60 Gy	25(42)
	> 60 Gy	29(48)
Chemotherapy	yes	25(42)
	no	33(55)
	undetermined	2(3)

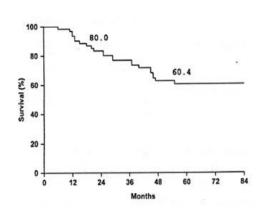


Fig. 1. Overall survival of 60 soft tissue sarcoma patients treated with postoperative radiation therapy.

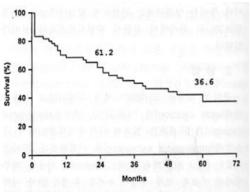


Fig. 2. Disease free survival of 60 soft tissue sar-coma patients treated with postoperative radiation therapy.

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20 (33%),
     7 (12%),
                            가
가 14 (23%) .
                               3,
                         13 ,
              . 5
          가
         1
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60.4%, 36.6% 132 (Fig. 1, 2). 40% (24/60)가 10 (17%)가 43.3% (26/60) 가

, AJCC (surgical margin) M stage (Table 5).

5 0%, 33.3%, 50%, 55.1%, 60 %, 71.4%, 75%, (p=0.0118). 100% grade I, II, III 5 84.3%, 66.7%, 37.5% (p=0.0001). 가 5 가 5 37.5%

(negative surgical margin) (microscopic positive margin)(70.3% vs 68.6%)

5cm 5cm 5 (72.5% vs 49.4 %, p=0.1459). 가

50.8%

68.0%

47.0%

1. 41 (68%) 29 (48%), 가 4 8 (13%), 5 가 (7%) 29 2 가) 48.7% 9 5

1

Table 5. Analysis of Overall Survival

Va ria ble s	No. of patients	5YOSR*	Univariate	p value
Presentation	primary	35	62.5	0.5860
	re curre nt	25	57.3	
Site	upper extremity	14	71.4	0.1417
	lower extremity	21	64.5	
	trunk	12	55.6	
	retrope ritone um	6	55.6	
	head and neck	7	14.3	
Histology	liposarcoma	10	60.0	0.0118
	MFH	14	55.1	
	ma lig.s chwa nnoma	7	7 1.4	
	le io myos arcoma	2	50.0	
	angiosarcoma	3	33.3	
	fibrosarcoma	4	75.0	
	rhabdomyosarcoma	3	0	
	A. fibromatos is	8	100	
Stage	I	26	87.5	0.0001
	П	3	66.7	
	Ш	18	50.0	
	IV	8	0	
Grade	I	27	84.3	0.0001
	П	3	66.7	
	Ш	24	37.5	
Tumor size	< 5 cm	26	72.5	0.1459
	5 - 10 cm	18	49.4	
	> 10 cm	16	55.6	
N stage	No	55	66.1	0.0002
	N1	5	0	
M stage	Mo	55	66.5	0.0015
	M1	5	0	
OP type	intralesional excision	5	40.0	0.1260
	marginal excision	36	63.2	
	wide excision	19	61.8	
Surgical margin	(-)	23	68.6	0.0504
-	(+)	21	70.3	
	gross residual	16	37.5	
RT dose	< 50 Gy	6	83.3	0.3833
	50 - 60 Gy	25	56.0	
	> 60 Gy	29	58.7	
OP-RT interval	< 6 wks	36	68.8	0.2630
	> 6 wks	22	49.6	
СтетоТх	ye s	25	40.0	0.0004
	no	33	78.1	

^{*:5} year overall survival rate

(p=0.3551).

, AJCC , , , , , 88.9%, 75%, , , , , (surgical 57.1%, 50%, 28.6% margin) (Table 6). 5

Table 6. Analysis of Local Control

Variables	No. of patients	5YLCR*	Univariate	p value
Presentation	primary	35	53.9	0.3956
	re curre nt	25	41.5	
Site	upper extremity	14	33.1	0.3551
	lower extremity	21	54.8	
	trunk	12	50.0	
	retroperitoneum	6	41.7	
	head and neck	7	21.4	
Histology	liposarcoma	10	88.9	0.0003
	MFH	14	28.6	
	ma lig.schwa nnoma	7	57.1	
	le io myos a rcoma	2	0	
	angiosarcoma	3	Ö	
	fibrosarcoma	4	50.0	
	rhabdomyosarcoma	3	0	
	A. fibromatos is	8	75.0	
Stage	I	26	72.7	0.0001
Stage	I	3	0	0.0001
	Ш	18	37.5	
	IV	8	18.8	
Grade	I	27	73.1	0.0001
o i u u u	I	3	0	0.0001
	Ш	24	27.4	
Tumor size	< 5 cm	26	50.8	0.7117
	5- 10 cm	18	42.9	
	> 10 cm	16	55.6	
N stage	No	55	53.5	0.0008
Ü	N1	5	0	
M stage	Мо	55	52.5	0.0890
C	M1	5	0	
OP type	intra les ional excision	5	20.0	0.00 15
	marginal excision	36	44.2	
	wide excision	19	66.4	
Surgical margin	(-)	23	68.1	0.0001
-	(+)	21	49.1	
	gross residual	16	18.8	
RT dose	< 50 Gy	6	83.3	0.4344
	50 - 60 Gy	25	48.8	
	> 60 Gy	29	40.6	
OP-RT interval	< 6 wks	36	60.0	0.1613
	> 6 wks	22	39.1	
CmemoTx	yes	25	24.1	0.0009
	no	33	66.7	

^{*: 5} year local control rate

*: 5 year local control rate $\varphi = 0.0003$).

5 grade I, II, III7 73.1%, . (intrales ional excision) 가 0%, 27.4% \(\psi = 0.000 \, 1 \). 가

5	20%	(marginal	가 가		,
excision)	(wide excision)			-1	
44.2%	66.4% $(p = 0.0015).$			가	,
가	5		20%		
68.1%,	49.1%				
	18.8% (p=0.000 1).				
16			MD Audonou		1960
			M.D. Anderson	Cancer Center	Suit ²)
(Table 7).					
4.					
	ıl		•		
12 7	35.0%(21/60) 가				
	9 가	•			
. 5					
	3가		. 1982	NCI Rosenbe	e rg ¹⁾
,	,		randomized trial		
			가 (0/16 vs 4/27)	5	81%, 78%
			5	88%, 89%	가 .
	(Table 8).			가 43	
			71	randomized	tria l
			가 .	가	
			,	71	가
	가				
			5	5	
			60.5% 36.6% .		,
가 가	(pseudocapsule)		,		
71	(pseudocapsule)		기	<u> </u>	5
				Herbert ³⁾	
Table 7 Local E	Zailum Assarding to Padiation			4)	가
Table 7. Local Failure According to Radiation Dose and Resection Margin				52% (15/29)가	
	No. of local failure/No. of	treated		12	
Radiation dose	(+) margin (-) margin	Total			
< 50 Gy	1/ 2	1/ 5		5 (8.3%)	
50-60 Gy > 60 Gy	4/ 9 2/ 9 4/10 4/11	6/ 18 8/2 1			1

Total

9/21

6/23

15/44

Table 8. Analysis of Distant Metastasis Free Survival

Variables	No. of patients	5YDMFS R*	Univariate	p value
Presentation	primary	31	73.7	0.04 16
	recurrent	21	41.7	
Site	upper extremity	13	61.5	0.7289
	lower extremity	18	53.9	
	trunk	9	45.0	
	retroperitoneum	5	50.0	
	head and neck	7	68.6	
Histology	liposarcoma	10	64.3	0.0003
	MFH	14	53.6	
	ma lig .s chwa nno ma	7	85.7	
	leiomyosarcoma	2		
	angiosarcoma	3		
	fibrosarcoma	4	75.0	
	rhabdomyosarcoma	3	0	
	othe rs	9	53.6	
Stage	I	18	83.5	0.0001
	П	3		
	Ш	18	45.8	
	IV	8	0	
Grade	I	19	78.9	0.0546
	II	3		
	Ш	24	36.5	
Tumor size	< 5 cm	23	66.3	0.4581
	5 - 10 cm	16	55.5	
	> 10 cm	13	51.9	
N stage	No	47	64.8	0.0005
	N1	5	20.0	
M stage	Mo	47	67.6	0.0001
	M1	5	0	
OP type	intra les ional excision	5	0.08	0.9451
	marginal excision	30	63.0	
	wide excision	19	51.5	
Surgical margin	(-)	22	63.1	0.3607
	(+)	16	58.6	
	gross residual	14	60.2	
RT dose	< 50 Gy	6		0.1097
	50 - 60 Gy	21	64.2	
	> 60 Gy	25	45.7	
OP-RT interval	< 6 wks	30	57.7	0.6754
	> 6 wks	20	60.0	
СтетоТх	yes	25	46.6	0.1343
	no	25	69.1	

^{*:5} year distant metastasis free survival rate

5 48.7% Lindberg⁵⁾ 71 27% (16/60) 5 70-80% 71 . 42% (25/60) , , ,

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가
                                                          , AJCC
                          가
                                                          Ue da9)
                가 32% (19/60)
                          2
                                                   NCL<sup>10)</sup> MGH<sup>6)</sup>
                 48%
                                                                                          5cm
                                                    T1 5cm
                                                                           T2
                                                     72.5% 51.7%
                                                                                           p =
                                                0.0640)
               MGH Suit, Pao Pao
                           88.9%
                                                     Pao, Potte r<sup>10)</sup>
                                                                                  가
                     Pao<sup>7)</sup>
                                                                                     (5
                      80% (8/10)
    grade I
                                                70.3%, 68.6%).
                                                     5
                                                                 37.5%
                                                    가
                            . 40.7%
       21.4%, 41.7%, 50.0%
                      フト (p =0.355 1)
Lindbe rg5)
                       . UCSF Leibe f<sup>5)</sup>
He rbe rt<sup>3)</sup>
                                                                 가
                                                            . Suit Tepper
                       35% (2 1/60)
                                                                             10-20%
                                      Linbe rg<sup>5)</sup>
                                                                     11)
                     20-40%
              가
                        , M stage
       0%, 53.6%
                     가
                 grade III
                                                           가
100% (3/3), 57.1% (8/14)
Le ibe l<sup>8)</sup> He rbe rt<sup>3)</sup>
                              가
                                                                     NCI randomized trial<sup>1)</sup>
             grade III
                                                          doxorubicin, cyclophos pha mide
          grade I, II
                               7%
53%
                                                                                         (95%,
       grade III 5
                                                74%)
                                                               (92%, 60%)
                                                                               가가
                                 78.9%, 100%
36.5%
        grade I, II
           Suit 6)
                      가
   가
  2.5cm 6%, 15-20cm
                                 60%, 20 cm
                                                                                      grade III,
   80%가
  5cm , 5-10cm, 10cm
                                                                                 high LET
          66.3%, 55.5%, 51.9%
                                 가
                                가
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- 1. Rosenberg SA, Tepper J, Glatstein E, et al. The treatment of soft tissue sarcoma of the extremities. Ann Surg 1982; 196:305-315
- 2. Suit HD, Russel W, Martin RG et al.

 Management of patients with sarcoma of soft tissue and extremity. Cancer 1973; 31:1247-1255
- 3. Herbert SH, Corn BW, Solin LJ, et al.
 Limb preserving treatment for soft tissue sarcomas of
 extremities: The significance of surgical margin. Cancer
 1993; 72:1230-1238
- Kim WD, Oh DH, Ha SW. Postoperative radiotherapy in the treatment of soft tissue sarcoma.
 1995; 13:69-77
- 5. Lindberg RD, Martin RG, Romsdahl MM et al.

 Conservative surgery and postoperative radiation therapy in 300 adults with soft tissue sarcoma.

 Cancer 1981; 47:2391-2397

- Suit HD, Mankin HJ, Wood WC, et al. Treatment of Mo soft tissue sarcoma. J Clin Oncol 1988; 6:854-862.
- Pao WJ, Pilepich MV. Postoperative radiotherapy in the treatment of extremity soft tissue sarcomas. Int J Radiat Oncol Biol Phys 1982; 8:263-273
- 8. Leibel SA, Tranbaugh RF, Wara WM, et al. Soft tissue sarcoma of the extremities: Survival and pattern of failure with conservative surgery and postoperative irradiation compare to surgery alone. Cancer 1982; 50:1076-1083
- Ueda T, Aozasa K, Tsujimoto M et al. Multivariate analysis for clinical prognostic factors in 163 patients with soft tissue sarcoma. Cancer 1988; 62:1444-1450
- 10. Potter Da, Kinsella T, Glastein E et al. High grade soft tissue sarcoma of the extremities. Cancer 1986; 58:190-205
- 11. Suit HD & Tepper JE. Impact of improved local control on survival in patients with soft tissue sarcoma. Int J Radiat Oncol Biol Phys 1986; 12:699-700

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가
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      : 1983 1994 60 7h
50 . 7h 35 (58%) 7h 12
                                 14 (23%),
 (20%), 7 (12%)
  10 (17%), 7 (12%) . 6

7 grade I, II, III7 27 (45%), 3 (5%), 24 (40%) .

19 (32%) , 36 (60%) , 5 (8%)

28.8-80Gy 25
                         20 (25%), 7 (12%),
           가 14 (23%) .
           5
                                     . 2 5
   68.0% 48.7%
           , AJCC ,
                               5
            (p < 0.05) .
              89
60.4%, 36.6%
              , AJCC ,
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