Radiation therapy in childhood STS:

Report of Italian-German RMS ‘79, RMS ’88 and RMS ’96 protocols.

Giovanni Scarzello
U.O.A. di Radioterapia.
Istituto Oncologico Veneto – I.R.C.C.S.

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Associazione Italiana Ematologia Oncologia Pediatrica

STSC Soft Tissue Sarcoma Committee

RMS '79	182
RMS '88	317
RMS '96	516

Chemotherapy	21
Surgery	12
Radiotherapy	7

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Patients are staged based on histology, primary tumor size, nodal status, location and the presence of distant metastases.

STAGE	SITE	T stage	N stage	M stage
I	**Favourable:** orbit, H-N, GU, biliary tract	Any	N0-N1	MO
II	**Unfavourable:** PM, B-P, limbs, trunk, peritoneum	T1a-T2a	N0	MO
III	**Unfavourable:** PM, B-P, limbs, trunk, peritoneum	T1a-T2a T1b-T2b	N1 N0-N1	MO
IV	Any	Any	Any	M1

Chemotherapy Principles

Multi-agent CT is used in the treatment of all patients with STS.

Active agents including vincristine, dactinomycin and cyclophosphamide (VAC) are the backbone of CT.

Variations on VAC based on the clinical group and site of disease are given based on the results of the previous IRS and RMS studies.

Surgery: an integral component of the STS local management .
Extent of disease: one of the most significant prognostic factors predicting outcome - guides the grouping classification defined by the Intergroup RMS studies.

I R S surgical-pathological grouping system

GROUP	
I	Completely resected localised disease without nodal involvement (N0) A. Confined to organ or muscle B. Infiltration outside organ or muscle
II	Gross total resection A. Microscopic residual disease and N0 B. Resected involved regional lymph nodes C. Microscopic residual disease and resected involved regional lymphnodes
III	Incomplete resection with gross residual disease A. After biopsy B. After major surgical resection
IV	Distant metastases at initial diagnosis

The treatment algorithm for STS is based on risk stratification, which incorporates group, stage, histology and age of initial diagnosis.

I R S surgical-pathological grouping system

Low risk	**Stage 1/group I-III with embryonal or botyroid histology or stage 2-3/groups I-II with embryonal or botyroid histology**
Intermediate risk	**Stage 2-3/group III patients with embryonal or botyroid histology; stage 1-3 patients with alveolar or undifferentiated histology**
High risk	**Stage 4/group IV**

RMS '79: RADIOTHERAPY

IRS I	**No RT**
IRS II	**40-45 Gy**
IRS III < 6 y	**40-45 Gy if T < 5 cm**
	45-50 Gy if T > 5 cm
IRS III > 6 y	**45-50 Gy if T < 5 cm**
	50-55 Gy if T > 5 cm

RMS '88: HART

IRS I	FH		No RT
	UH		40 Gy
IRS II			40 Gy
IRS III	FH	CR	No RT
	UH	CR	40 Gy
IRS III		R> 2/3	40 Gy
		R<2/3	54.4 Gy

RMS '96: HART

All R0 patients No RT			
FH	**R> 2/3**		**32 Gy**
		boost	**44.8 Gy**
		boost	**10 Gy**
UH	**Not R0**		**44.8 Gy**
FH	**R<2/3**		**44.8 Gy**

Outcome

5 year OS at 8 year minimum FU

RMS ‘79	**54.4 %**
RMS ‘88	**68.8 %**
RMS ‘96	**74.8 %**

Conclusions

A correct risk group stratification allows a therapy reduction in selected patients without compromising results.

HART has not improved OS and DFS.

A long term assessment at a median FU of 23 years has shown a 10% OS decrease because of 6 second tumors and 3 late effect related deaths. So modern protocols must imply long term follow-up to confirm the results and have to relate the treatment to late effects.