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Heavy Ion Therapy Research Integration

The role of surgery in paediatric soft tissue sarcomas

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Soft tissue sarcomas in children

Rabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children 14 years old and younger.

Non Rabdomyosarcoma Soft Tissue Sarcomas (NRSTS) is more common in adolescents and young adults.
In infants NRSTS, such as infantile fibrosarcoma and malignant hemangiopericytoma, constitute a distinctive set of histologies.

In the USA, 850-900 children and adolescents are diagnosed each year / 350 RMS.

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RMS

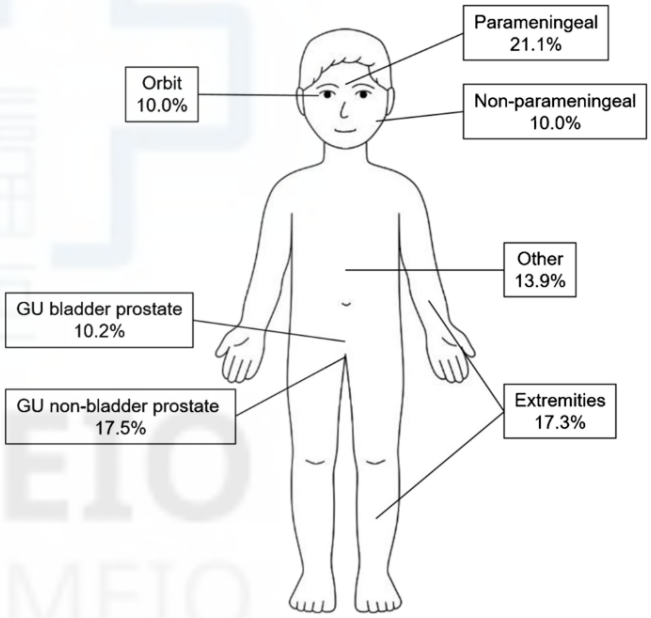
50% of all soft tissue sarcomas in children < 15 years old.

Incidence: 4.6 per million per year (steady over the past 30 years.

Bimodal peak age (2-5, 15-19 years old).

Slightly more common in boys than in girls (3:2).

More common in caucasian children (12:5).



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Etiology

Association with Li-Fraumeni syndrome (germline mutations in p53), Neurofibromatosis (mutations in NF1), Beckwith-Wiedemann syndrome.

Chromosomal translocation, gains, losses

Weak association with congenital anomalies, especially in boys.

Sometimes are seen as second malignant neoplasms after radiation therapy.

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Cytogenetic abnormalities in soft tissue sarcomas

Diagnosis	Cytogenetic abnormality	Genes involved
Alveolar RMS	t(2;13) or t(1;13)	FKHR on chromosome 13 and PAX3 (chromosome 2) or PAX7 (chromosome 1)
Infantile fibrosarcoma	t(12;15)	TEL (ETV6) on chromosome 12 and NTRK3 (TRKC) on chromosome 15
Dermatofibrosarcoma Protuberans	t(17;22)	PDGF β-chain on chromosome 17 and collagen type Ia on chromosome 22
Synovial sarcoma	t(X;18)	SYT on chromosome 18 and SSX-1 or SSX-2 on the X chromosome
Liposarcoma	t(12;16)	FUS gene on chromosome 16 and CHOP gene on chromosome 12
Myxoid chondrosarcoma	t(9;22)	EWS on chromosome 22 and TEC gene on chromosome 9
Alveolar soft part sarcoma	t(X;17)	Unidentified genes, esp. at chromosome band 17q25

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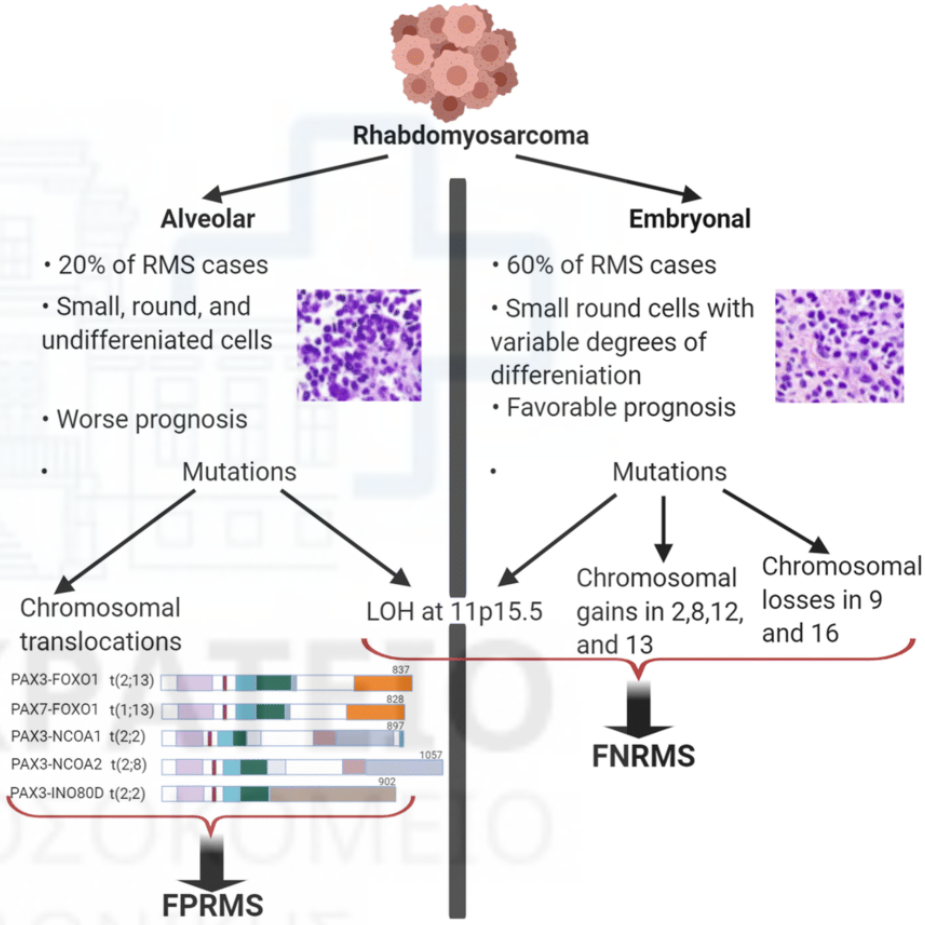
Histologic subtypes

Embryonal

Alveolar

Spindle cell

Pleiomorphic



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TNM Staging System

Stage	Sites	T	Size	N	M
1	Orbit	T_1 or T_2	a or b	N_0 or N_1 or N_x	M_0
	Head and neck				
	Genitourinary/not bladder or prostate				
	Biliary tract				
2	Bladder or prostate	T_1 or T_2	a	N_0 or N_x	M_0
	Extremity				
	Cranial parameningeal				
	Other				
3	Bladder or prostate	T_1 or T_2	a	N_1	M_0
	Extremity		b	N_0 or N_1 or N_x	M_0
	Cranial parameningeal				
	Other				
	All	T_1 or T_2	a or b	N_0 or N_1	M_1

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Abbreviations: a, ≤5 cm in diameter; b, >5 cm in diameter, N0, regional lymph nodes not involved; N1, regional nodes clinically involved with neoplasm; Nx, clinical status of regional nodes unknown; M0, no distant metastasis; T1, confined to anatomic site of origin; T2, extension or fixation to surrounding tissue.

Intergroup Rhabdomyosarcoma Study (IRS) Clinical Grouping System

Group	Definition
Group I	Localized disease completely resected
Group IIa	Gross total resection with microscopic residual disease
Group IIb	Regionally involved lymph nodes, completely resected with the primary
Group IIc	Regional disease with involved nodes, totally resected with microscopic residual disease or histologic evidence of involvement of the most distant lymph node in the dissection
Group III	Incomplete resection
Group IV	Distant metastases

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Risk stratification in rhabdomyosarcoma

Histology	Clinical group	Stage	Risk group
Embryonal	I, II, III	1	Low
Embryonal	I, II	2, 3	Low
Embryonal	III	2, 3	Intermediate
Embryonal	IV	4	High
Alveolar	I, II, III	1, 2, 3	Intermediate
Alveolar	IV	4	High

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The role of surgery in RMS

Because of the importance of clinical grouping in determining treatment and prognosis, implementing surgical principles is crucial.

The basic principle of **radical resection** with tumour-free margins should be followed as long as sacrifice of surrounding normal tissue does not result in unacceptable loss of function or is not feasible.

Open excisional or incisional biopsy / endoscopic biopsy for genitourinary RMS.

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Loeb DM, Thornton K, Shokek O. Pediatric soft tissue sarcomas. Surg Clin North Am. 2008;88:615–627,

The role of surgery in RMS

If the initial surgical procedure is a biopsy or an “unplanned” excision, the question of **primary re-excision** often arises.

Wide re-excision is the current recommendation in such cases, unless this results in unacceptable loss of function or an unacceptable cosmetic result. Pretreatment re-excision results in a lower clinical group and a more favourable prognosis.

When local radiotherapy is the primary local treatment modality, a residual persistent mass is common and is not associated with patient outcome. For that reason, second-look surgeries are not routinely recommended.

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Pathologic confirmation of clinically positive **lymph nodes** is essential, because this has a direct impact on the extent of radiotherapy.

Children's Oncology Group (COG) currently recommends aggressive regional lymph node sampling in RMS of the extremities.

Prophylactic regional node dissection is not recommended.
Staging ipsilateral retroperitoneal nerve-sparing template node dissection is required for all boys >10 years of age with paratesticular RMS or patients <10 years old with radiographically positive nodes.

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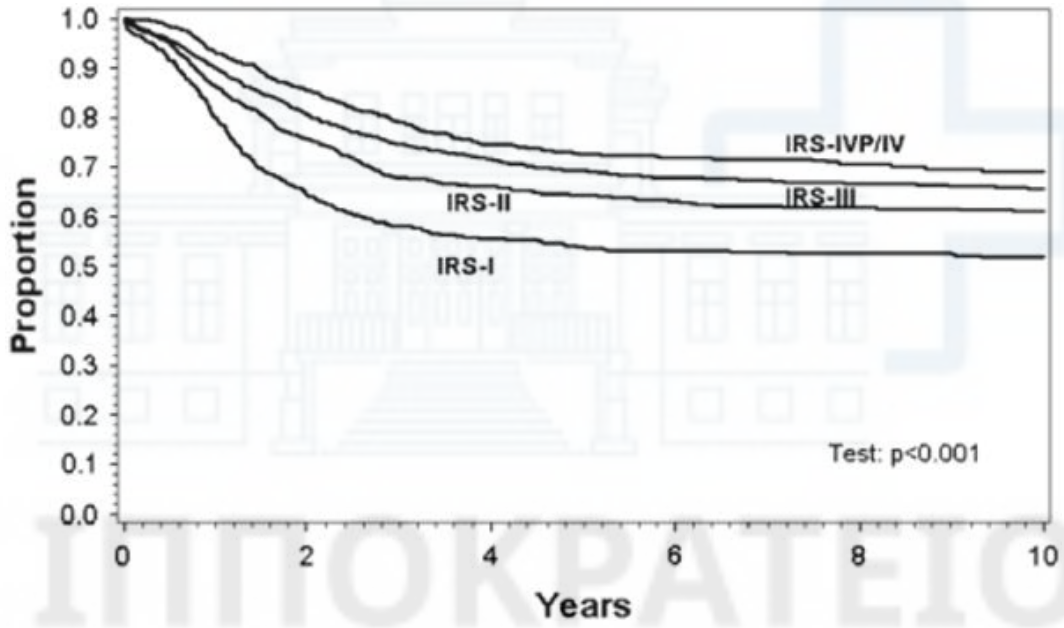
Survival IRS-I through IRS-IV.



Improvement in survival with successive clinical trials.

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NRSTS

International Classification of Childhood Cancer

1. the fibrosarcoma category

2. Kaposi's sarcoma

3. "other specified" soft tissue sarcomas (synovial sarcoma, angiosarcoma, hemangiopericytoma, leiomyosarcoma, liposarcoma and extraosseous Ewing's sarcoma)

4. "unspecified" soft tissue sarcomas.

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Histologic subtypes of NRSTS in pediatric patients

Histology	Normal counterpart	Incidence
Fibrosarcoma	Fibroblast	0.6
Infantile fibrosarcoma	Fibroblast	0.2
Malignant fibrous histiocytoma	Fibroblast	0.8
Dermatofibrosarcoma protuberans	Fibroblast	1.0
Malignant peripheral nerve sheath tumor	Schwann cell	0.6
Kaposi's sarcoma	Blood vessels	0.1
Liposarcoma	Adipocyte	0.1
Leimyosarcoma	Smooth muscle	0.3
Synovial sarcoma	Synovial cells	0.7
Hemangiosarcoma	Blood vessels	0.2
Malignant hemangiopericytoma	Vessel pericytes	0.1
Alveolar soft part sarcoma		0.1
Chondrosarcoma	Chondrocytes	0.1

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Gurney J, Young JL Jr, Roffers SD, et al. Cancer incidence and survival among children and adolescents: United States SEER Program 1975–1995. Vol NIH Pub. 99-4649. Bethesda (MD): National Cancer Institute, SEER Program; 1999.

Risk stratification in NRSTS and treatment proposal according to the Children's Oncology Group (NCT00346164)

Risk group	Factors				Proposed treatment
	Grade	Size	Stage	Initial resectability	
Low	Low	Any	Nonmetastatic	Gross resection	Observation
	High	< 5 cm	Nonmetastatic	Without microscopic margins	Observation
	High	< 5 cm	Nonmetastatic	With microscopic margin	Adjuvant radiation therapy
Intermediate	High	> 5 cm	Nonmetastatic	Gross resection	Adjuvant chemotherapy and radiation therapy
	High	> 5 cm	Nonmetastatic	Unresected	Neoadjuvant chemoradiotherapy, surgery, adjuvant chemotherapy with or without radiation therapy
High	Low	Any	Metastatic	Gross resection	Observation
	High	Any	Metastatic	Gross resection	Adjuvant chemotherapy and radiation therapy
	High	Any	Metastatic	Unresected	Neoadjuvant chemoradiotherapy, surgery, adjuvant chemotherapy with or without radiation therapy

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The role of surgery in NRSTS

A biopsy is necessary to establish the diagnosis.

Core Needle Biopsy : the diagnostic procedure of choice.
In most cases adequate to obtain diagnostic tissue, excellent accuracy, high sensitivity and specificity, low morbidity.

Biopsies should be obtained by a trained surgical oncologist or radiologist and preferably at a multidisciplinary sarcoma treatment center.

The biopsy site should be chosen so that it lies in the field of future resection.

Open biopsy is indicated when a diagnosis cannot be provided by a core needle biopsy.

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The role of surgery in NRSTS

Surgery remains the cornerstone of treatment for NRSTS.

The goal of surgical excision is complete removal of the mass with a 1-2cm margin of surrounding normal tissue. Closer margins should prompt consideration of re-excision.

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The role of surgery in NRSTS

When complete tumour resection risks compromising the integrity of distal structures, adjuvant chemotherapy or radiation therapy may be required.

Amputation should be reserved for cases of major artery or nerve involvement, sufficiently extensive bone involvement, or recurrence after previous resection with adjuvant radiation therapy.

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To sum up…

Although surgery for RMS and NRSTS is becoming less mutilating, the surgeon plays a critical role in initial biopsy and staging, primary re-excision and appropriate wide local resection.

Therefore, the surgeon should be an early participant in the multimodal approach to treatment.

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Thank you

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