



IRCCS Azienda Ospedaliera Universitaria San Martino - IST
Istituto Nazionale per la Ricerca sul Cancro

“SIMPOSIO AIRO-AIEOP *Sarcomi delle parti molli dell’età pediatrica*”

“Tossicità attese e management”

Establishing and Enhancing Services
for Childhood Cancer Survivors
LONG-TERM FOLLOW-UP PROGRAM
RESOURCE GUIDE

Clinical Practice Subcommittee/Survivorship
in collaboration with the Late Effects Committee



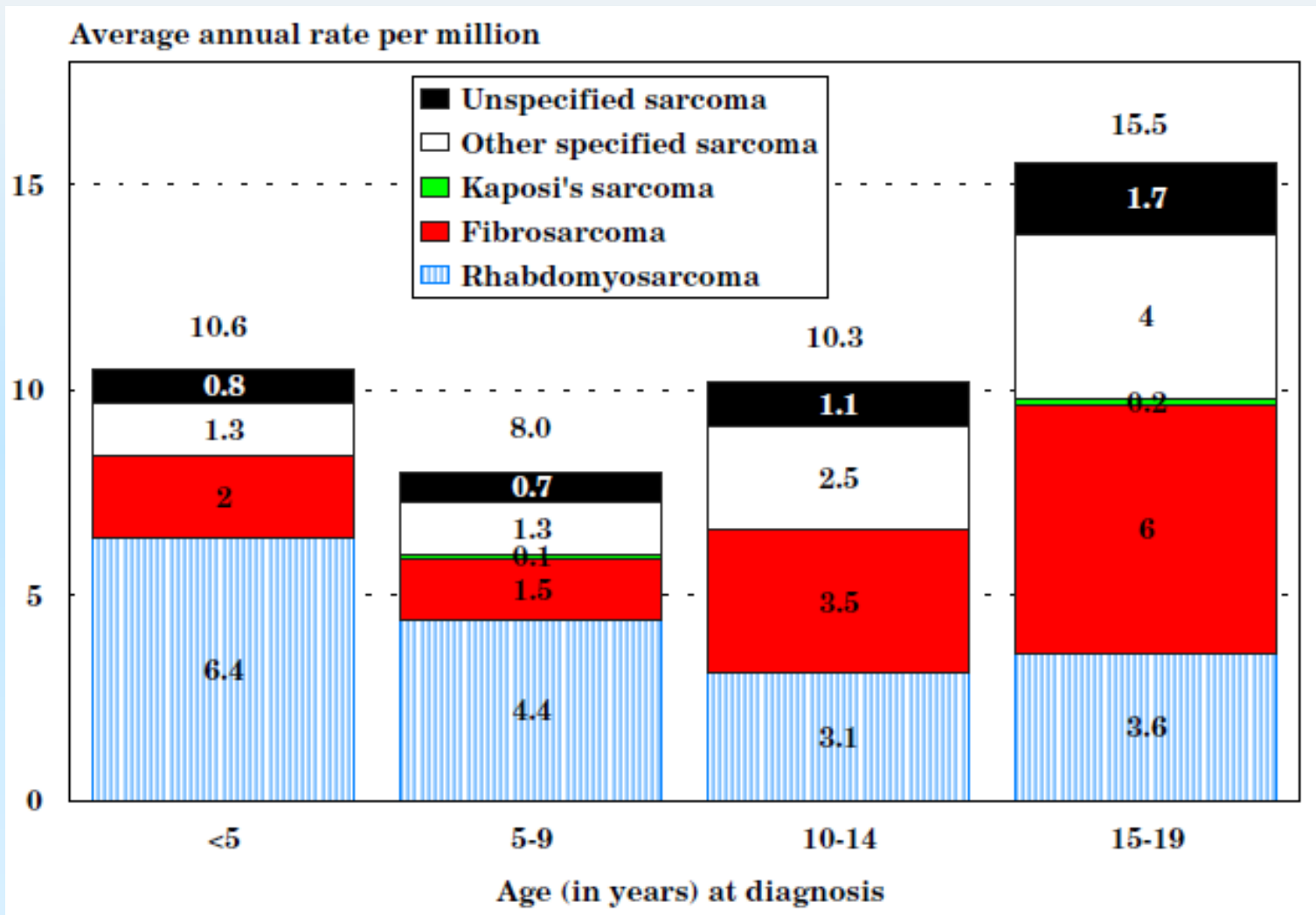
A recent report compared the health status of 10,397 survivors of childhood cancer treated from 1970 to 1987 with 3,034 of their siblings. Among the survivors, 62% had at least one chronic health condition, and 27% had a serious or life-threatening condition, such as stroke, heart disease, or kidney failure. Survivors were 54 times more likely to have a major joint replacement, 15 times more likely to have congestive heart failure or to develop a second cancer and 10 times more at risk for cognitive problems than their siblings. In fact, only about one in three survivors remained free of long-term problems related to their cancer diagnosis or treatment.

- Oeffinger et al. 2006



SOFT TISSUE SARCOMAS

James G. Gurney, John L. Young, Jr., Steven D. Roffers, Malcolm A. Smith, Greta R. Bunin





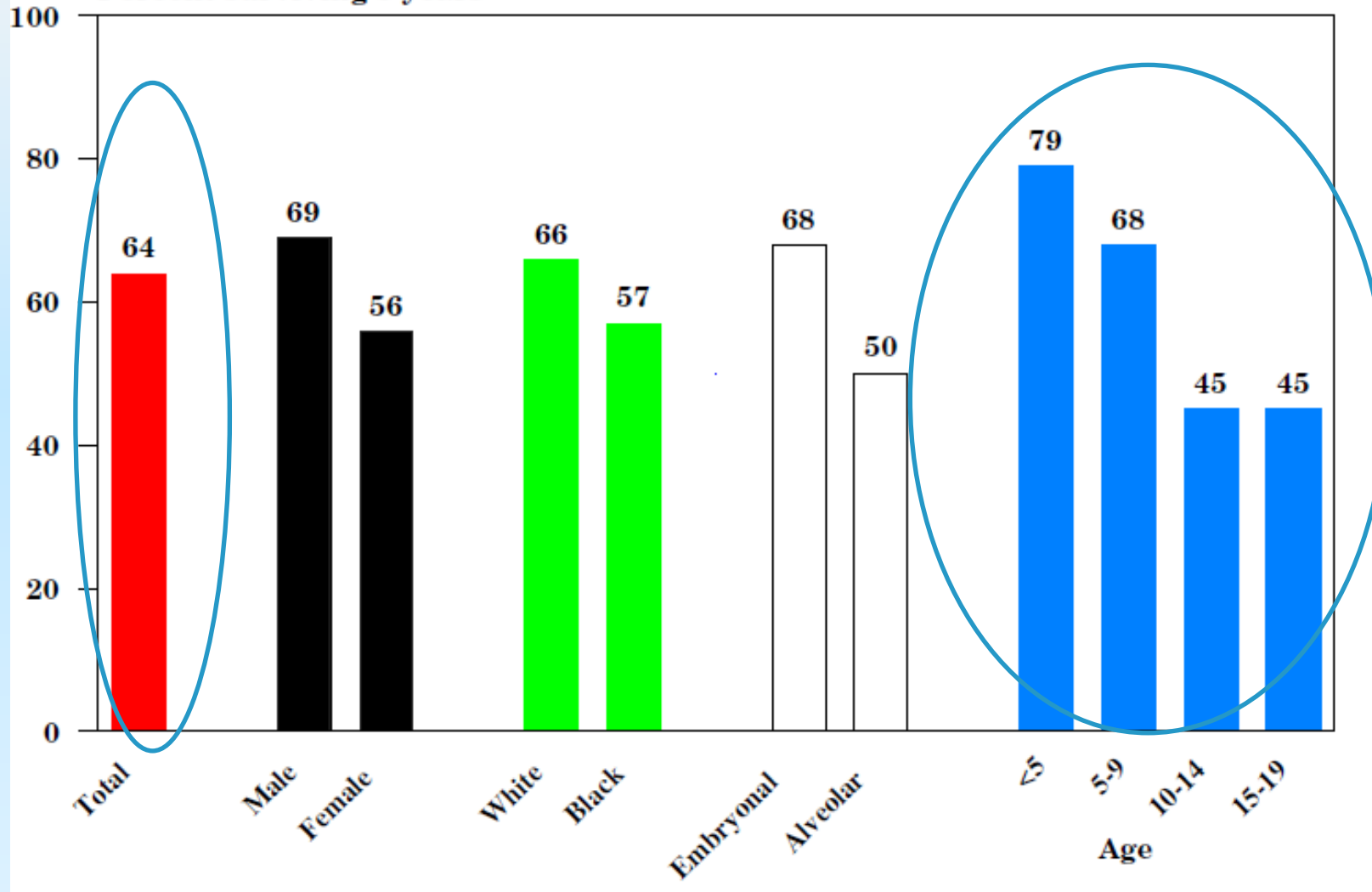
SOFT TISSUE SARCOMAS

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Rhabdomyosarcoma

Percent surviving 5 years





Childhood Cancer Survivor Study

Chronic Conditions: STS

			Maximum Grade																
			Any chronic condition		1:Mild		2:Moderate		3:Severe		4:Disabling		5:Fatal ¹		Multiple health conditions (>=2) ²		Multiple health conditions (>=3) ²		
			All cases	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Both sexes	All cases		988	634	64.2	166	16.8	163	16.5	235	23.8	54	5.5	16	1.6	381	38.6	256	25.9
	Treatment	Surgery only	148	87	58.8	22	14.9	20	13.5	9	6.1	.	.	42	28.4	27	18.2		
		Chemotherapy, no radiation	171	98	57.3	21	12.3	32	18.7	8	4.7	1	0.6	46	26.9	29	17.0		
		Radiation, no chemotherapy	56	23	41.1	10	17.9	6	10.7	1	1.8	.	.	10	17.9	8	14.3		
		Chemotherapy and radiation	484	357	73.8	72	14.9	84	17.4	149	30.8	31	6.4	14	2.9	234	48.3	160	33.1
		Unknown	129	76	58.9	16	12.4	26	20.2	28	21.7	5	3.9	1	0.8	49	38.0	32	24.8



Long-Term Medical Effects of Childhood and Adolescent Rhabdomyosarcoma: A Report From the Childhood Cancer Survivor Study

Adverse medical conditions for **606 RMS** survivors 3,701 siblings of cancer survivors. The relative risk (RR) for developing sequelae among survivors compared with siblings was greatest **within 5 years after diagnosis**. RR was **elevated more than 5 years after diagnosis** for several conditions (RR, 95% CI) as follows:

1. eye (cataract, impairment visual disturbances ,very dry eyes)

2. endocrine impairment (growth hormone deficiency , hypothyroidism ,need for medications to induce puberty)

3. Cardiopulmonary

4. Neurosensory and neuromotor impairment

5. Tumours



Effetti Tardivi Muscolo Scheletrici

Strahlenther Onkol 2013 · 189:529–534
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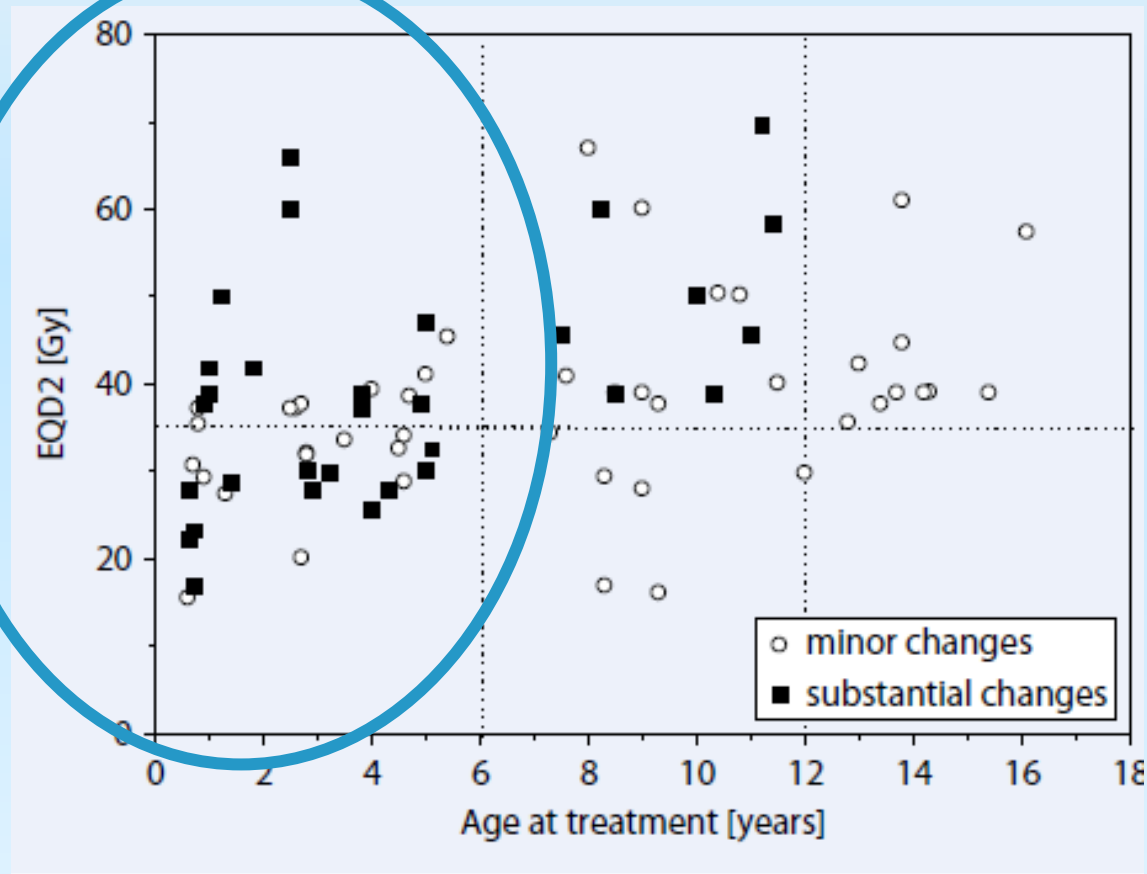
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³ Kinder- und Jugendmedizin, Chemnitz

Late bone and soft tissue sequelae of childhood radiotherapy





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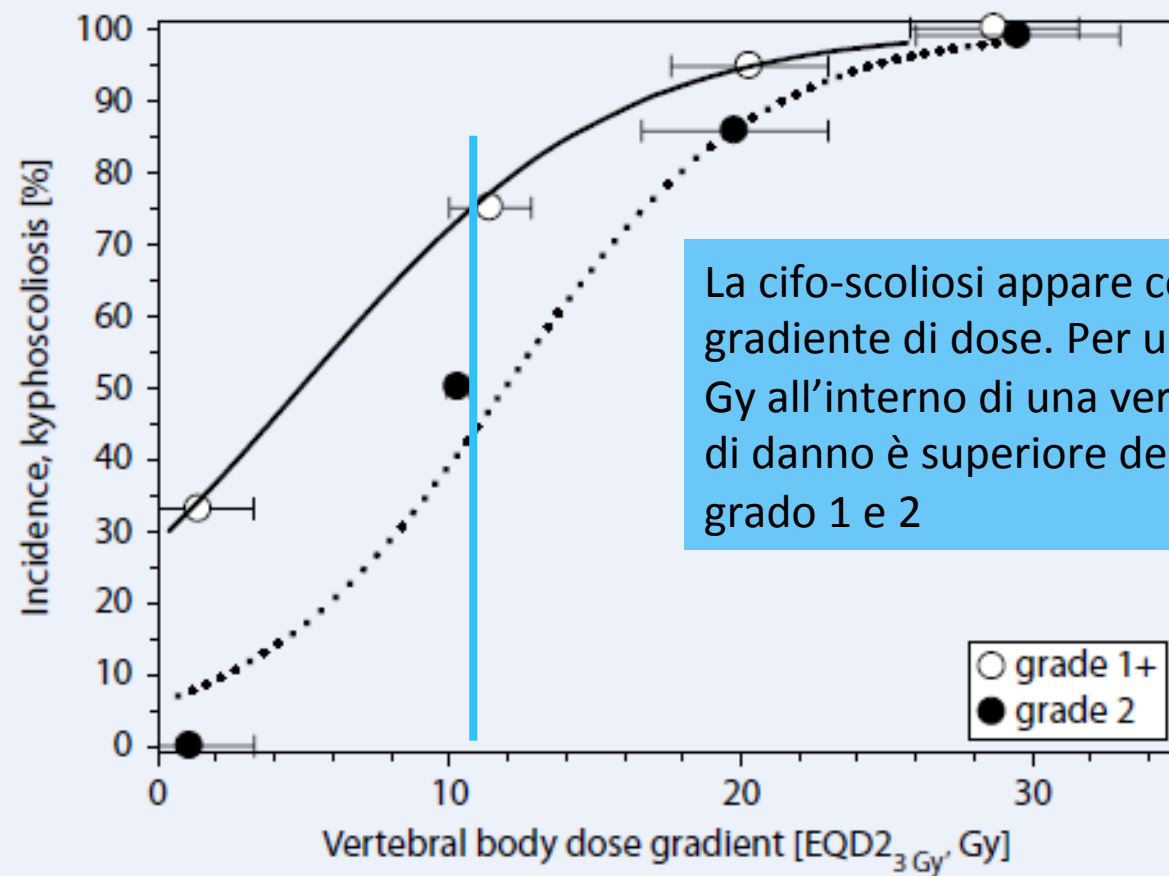
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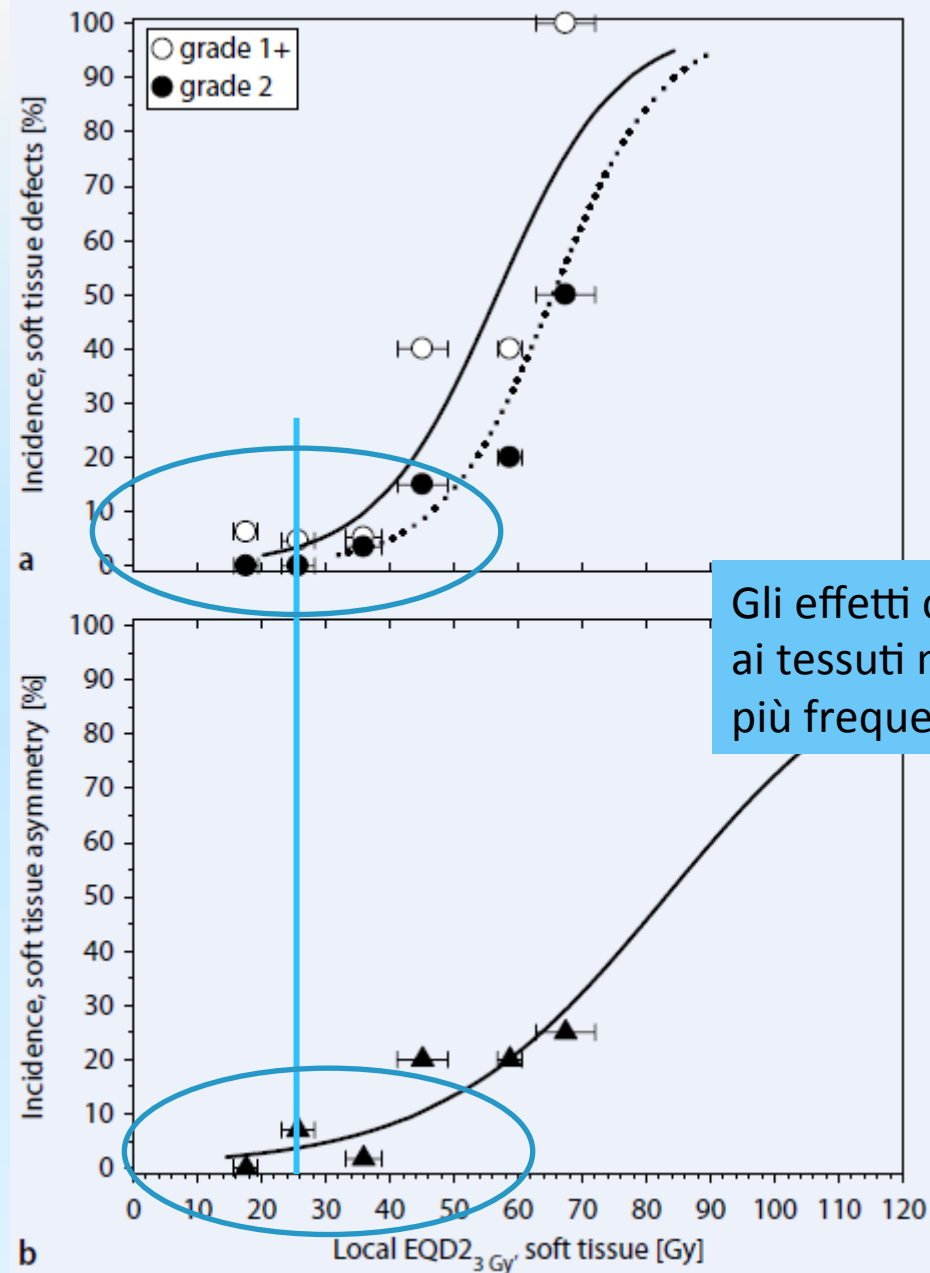
Late bone and soft tissue sequelae of childhood radiotherapy



La cifo-scoliosi appare correlata al gradiente di dose. Per un gradiente di 10 Gy all'interno di una vertebra l'incidenza di danno è superiore del 70% -30% per grado 1 e 2



Effetti Tardivi Muscolo Scheletrici



Gli effetti collaterali tardivi ai tessuti molli appaiono più frequenti a dosi alte.



Effetti Tardivi Pelvici

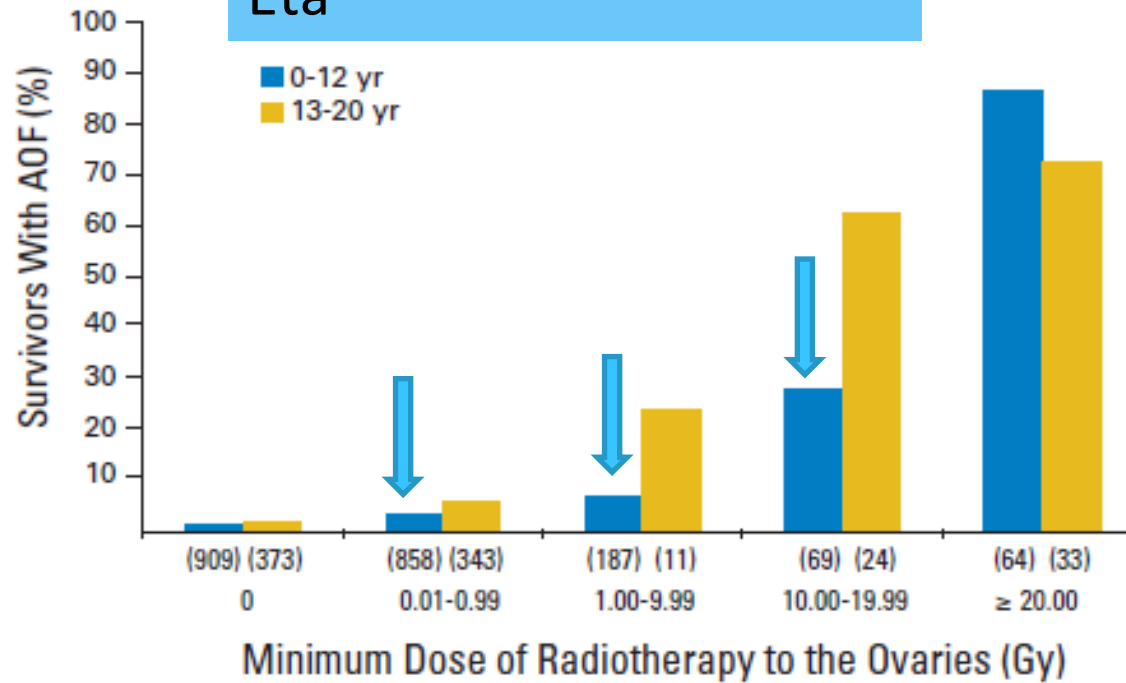
VOLUME 27 · NUMBER 14 · MAY 10 2009

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

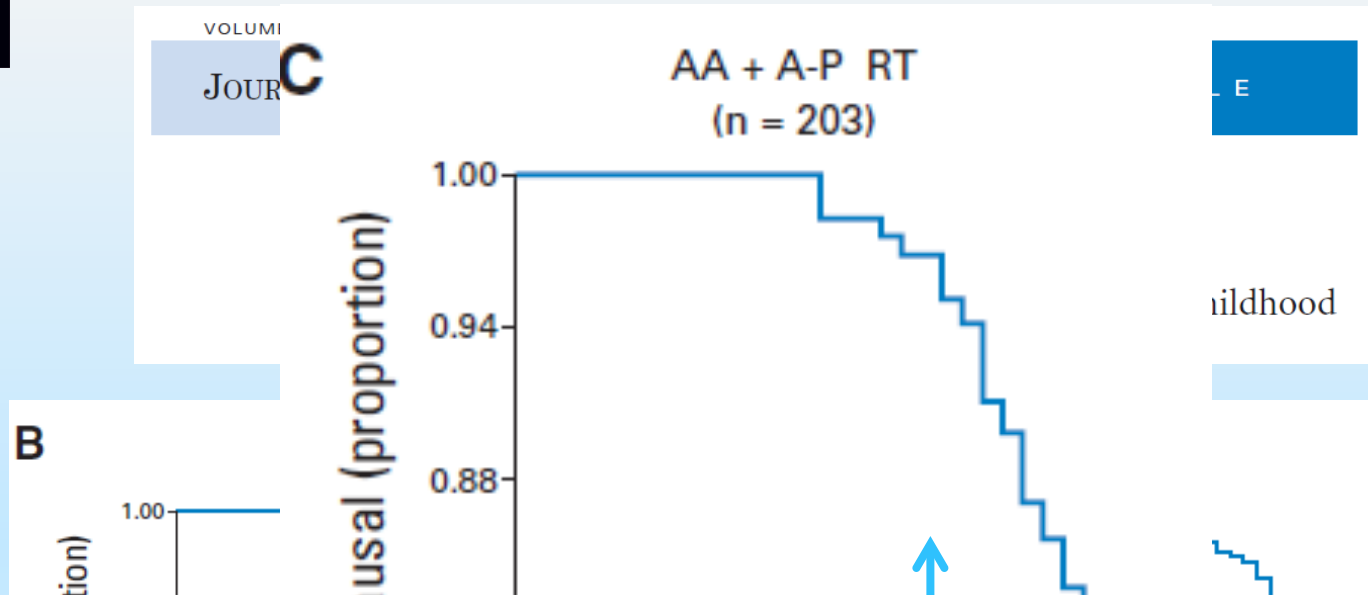
Dose ≥ 10 Gy
Agenti alchilanti
Età

Outcomes After
Results From the Childhood





Effetti Tardivi Pelvici



GRAVIDANZA:

- Aumento di aborti spontanei
- Riduzione del volume uterino
- Riduzione dello spessore dell'endometrio
- Riduzione alla risposta ormonale dell'endometrio
- Aumento di parti prematuri
- Basso peso alla nascita
- Doxorubicina aumentava il rischio di basso peso alla nascita.



available at www.sciencedirect.com



journal homepage: www.ejconline.com



Testicular function of survivors of childhood cancer: A comparative study between ifosfamide- and cyclophosphamide-based regimens ☆

International Journal of
Andrology

international journal of andrology ISSN 0105-6263

International Journal of Andrology © 2010 |



ORIGINAL ARTICLE

High risk of azoospermia in men treated for childhood cancer

Azoospermia nel 66%

Alti livelli di FSH nel 56%

Fattori di rischio :ciclofosfamide, ifosfamide, radioterapia

Le gravidanza di donne con partners lungo sopravvivenuti erano caratterizzate ad un numero maggiore di nati morti RR=0.79. L'uso della Dactinomicina aumentava in rischio RR=0.68

I figli dei maschi lungo sopravvivenuti trattati con CT non alchilanti presentavano un peso < 2.5 Kg alla nascita



Effetti Tardivi Pelvici

Pediatr Blood Cancer 2009;52:439-446

REVIEW

Late Effects on the Urinary Bladder in Patients Treated for Cancer in Childhood: A Report From the Children's Oncology Group

Esposizione	Effetto	Fattore di rischio	Potenziamento
Section 11: Cyclophosphamide and Ifosfamide	Hemorrhagic cystitis, bladder fibrosis, dysfunctional voiding.	Higher cumulative doses (decreased incidence with use of Mesna), combined	Cyclophosphamide dose ≥ 3 gm/m ² ; pelvic radiation
Alto rischio di cistite emorragica > di 30 Gy su tutto il volume vescicale > di 60 Gy su porzione della vescica			
Alto rischio di fibrosi \geq di 45 Gy su tutto il volume vescicale			
Potenziamento del danno		Ciclofosfamide e ifosfamide	
≥ 30 Gy to whole abdomen, pelvis, sacral spine		(≥ 30 Gy to entire bladder, ≥ 60 Gy to portion of bladder)	cyclophosphamide and/or ifosfamide
Section 81: Radiotherapy ≥ 30 Gy to whole abdomen, pelvis, sacral spine	Bladder fibrosis, dysfunctional voiding, vesicoureteral reflux, hydronephrosis	Higher radiation dose (≥ 45 Gy); radiation to entire bladder; combined with: Cyclophos phamide, Ifosfamide, Vincristine	



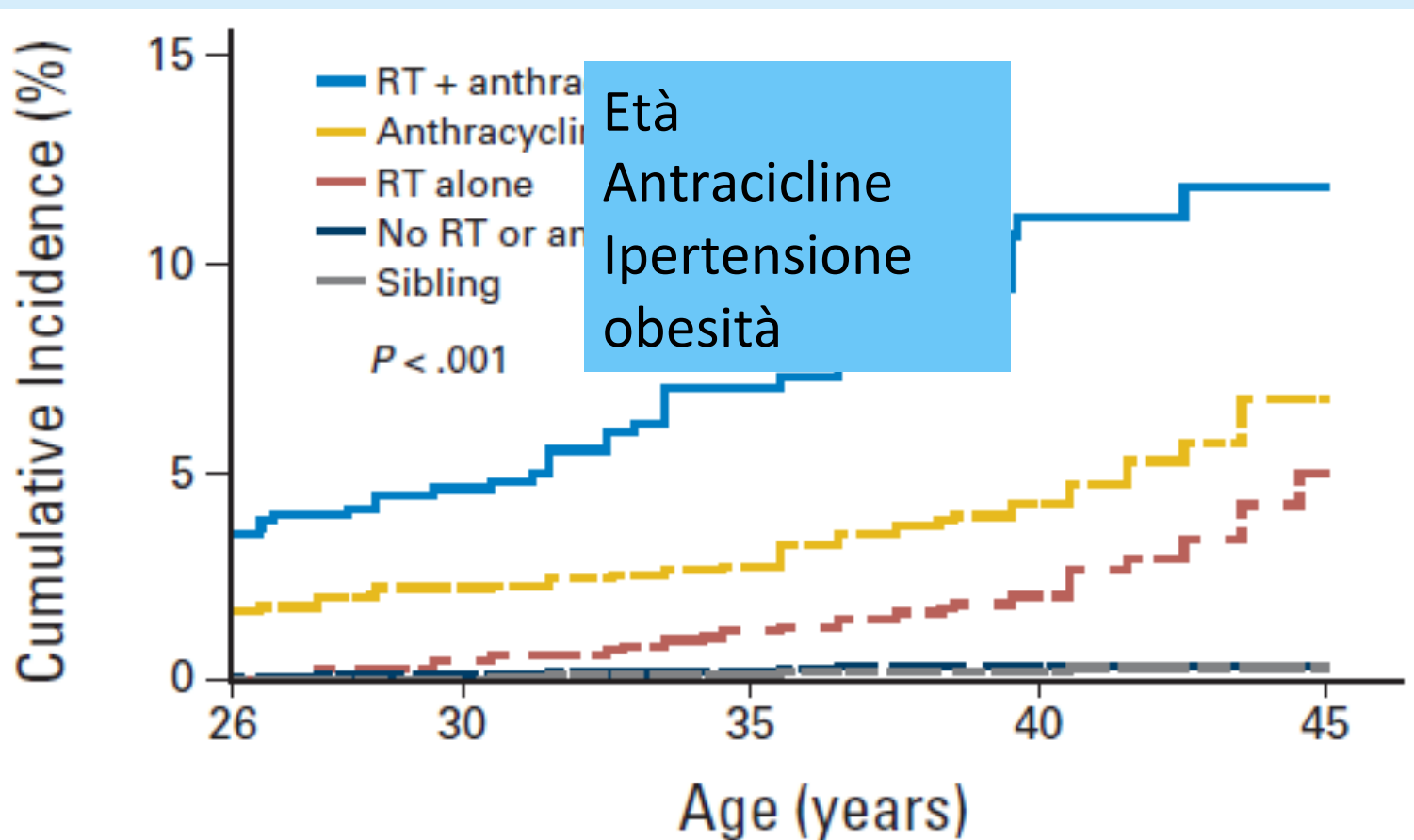
Effetti Tardivi Cardiaci e Polmonari

VOLUME 31 · NUMBER 29 · OCTOBER 10 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Modifiable Risk Factors and Major Cardiac Events Among Adult Survivors of Childhood Cancer





Effetti Tardivi Cardiaci e Polmonari

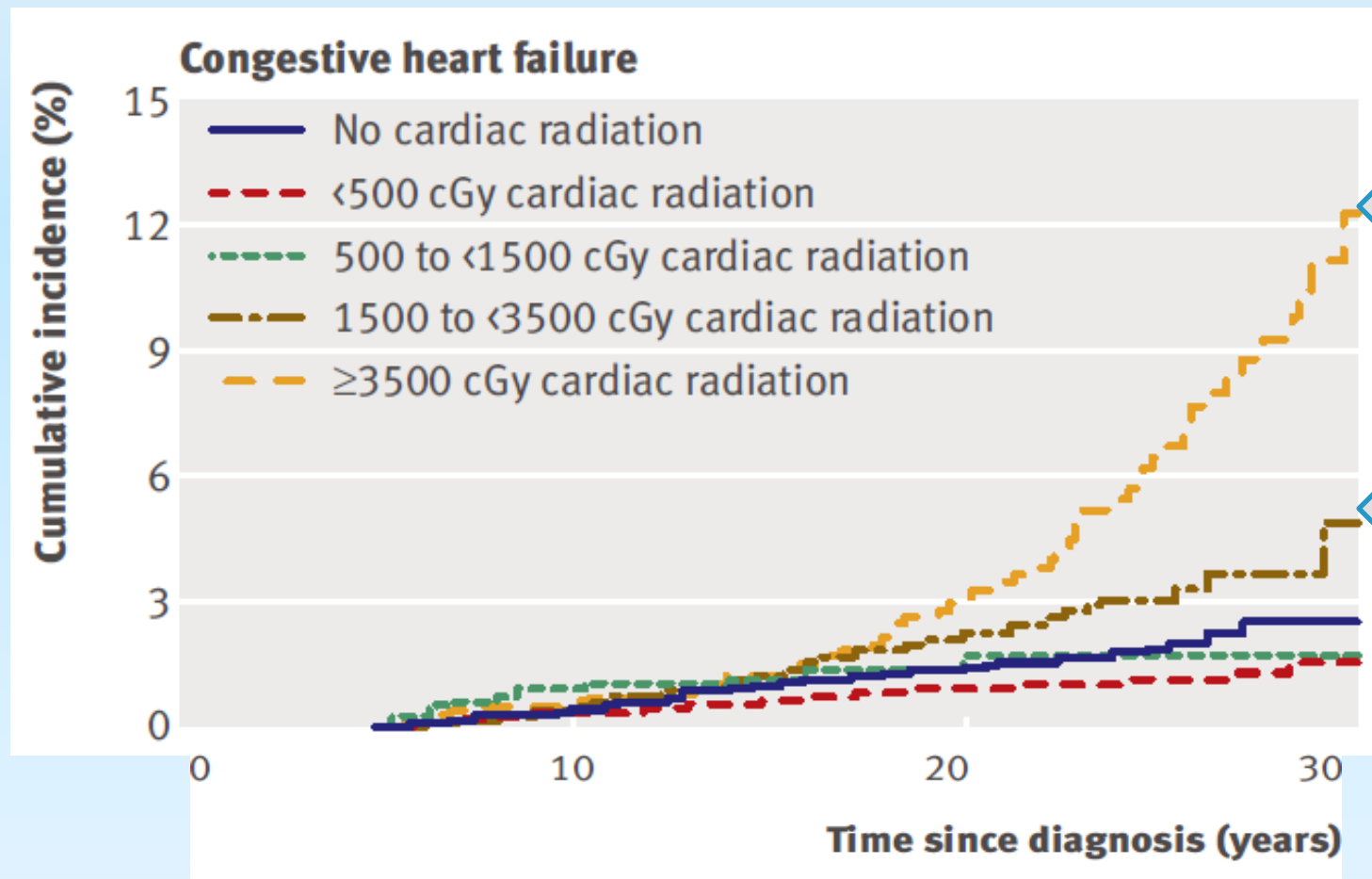
BMJ

RESEARCH

BMJ 2009;339:b4606

Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: retrospective analysis of the Childhood Cancer Survivor Study cohort

Setting 26 institutions that participated in the Childhood Cancer Survivor Study. Participants 14 358, five year survivors of cancer





Effetti Tardivi Cardiaci e Polmonari

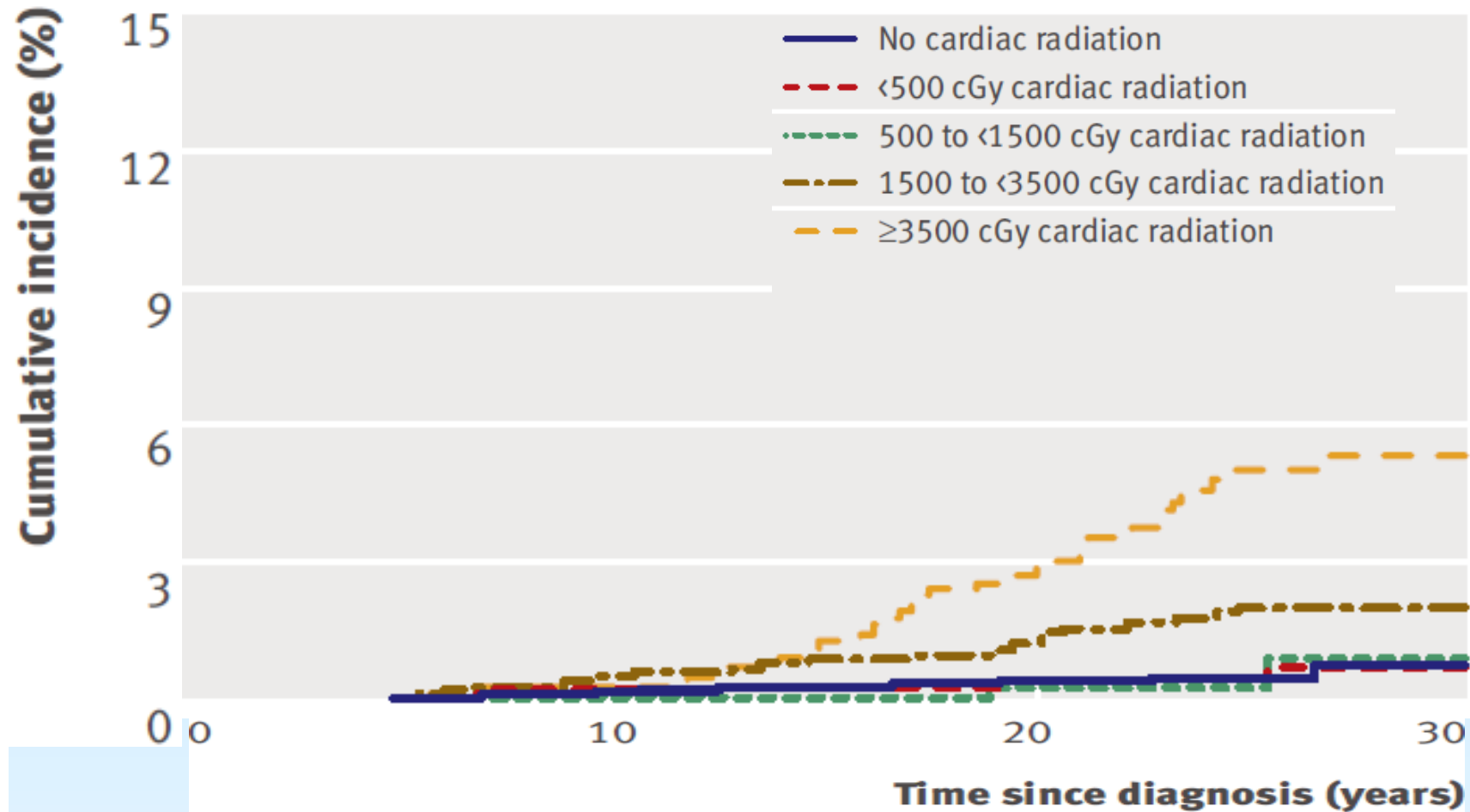
BMJ

RESEARCH

BMJ 2009;339:b4606

Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: retrospective analysis of the Childhood Cancer Survivor Study cohort

Myocardial infarction





Effetti Tardivi cardiaci e polmonari



NIH Public Access

Author Manuscript

Radiat Res. Author manuscript; available in PMC 2011 December 1.

Published in final edited form as:

Radiat Res. 2010 December ; 174(6): 840–850. doi:10.1667/RR1903.1.

Long-Term Effects of Radiation Exposure among Adult Survivors of Childhood Cancer: Results from the Childhood Cancer Survivor Study

Assessment of the CCSS cohort demonstrated that cardiac radiation therapy of **15 Gy** or more increased the risk of congestive heart failure, myocardial infarction, pericardial disease and valvular abnormalities by two- to sixfold compared to non exposed survivors

Effetti Tardivi testa e collo

Pediatr Blood Cancer 2005;44:643-653

Long-Term Medical Effects of Childhood and Adolescent Rhabdomyosarcoma: A Report From the Childhood Cancer Survivor Study

Head-neck tumor sites /
non-head-neck tumor site
RR

Surgery+radiatio
+chemotherapy/ surgery
+chemotherapy

RR

Eye impairment

Cataract (N = 55)	8.0
Visual disturbances (N = 51)	6.4
Very dry eyes (N = 73)	5.4

6.2
6.3
10.0

Endocrine impairment

Hypothyroidism (N = 46)	6.1
Growth hormone deficiency (N = 62)	6.0
Medications to induce puberty (N = 33)	0.5
Osteoporosis (N = 17)	0.4

5.9
8.7
6.6
2.6



Pediatr Blood Cancer 2005;44:643–653

**Long-Term Medical Effects of Childhood
and Adolescent Rhabdomyosarcoma:
A Report From the Childhood Cancer Survivor Study**

Danni sensoriali (vertigini, acufeni, sordità)	37%
Danni motori (disturbi della masticazione, deglutizione, crisi epilettiche)	26%



Seconde neoplasie



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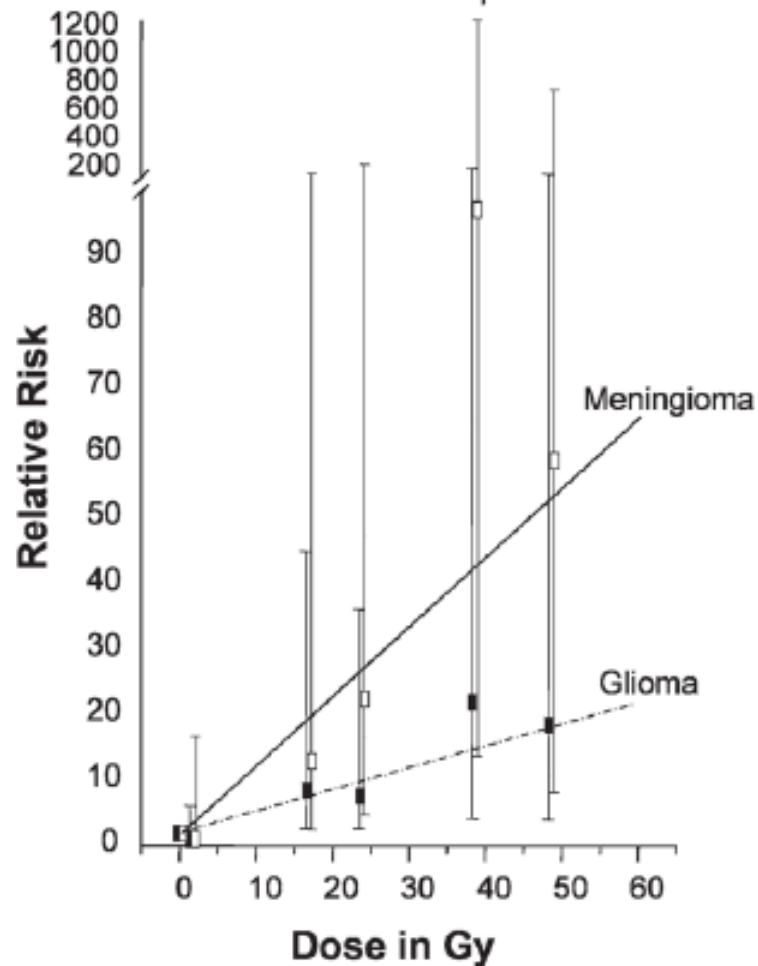
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Central Nervous System Second Neoplasms



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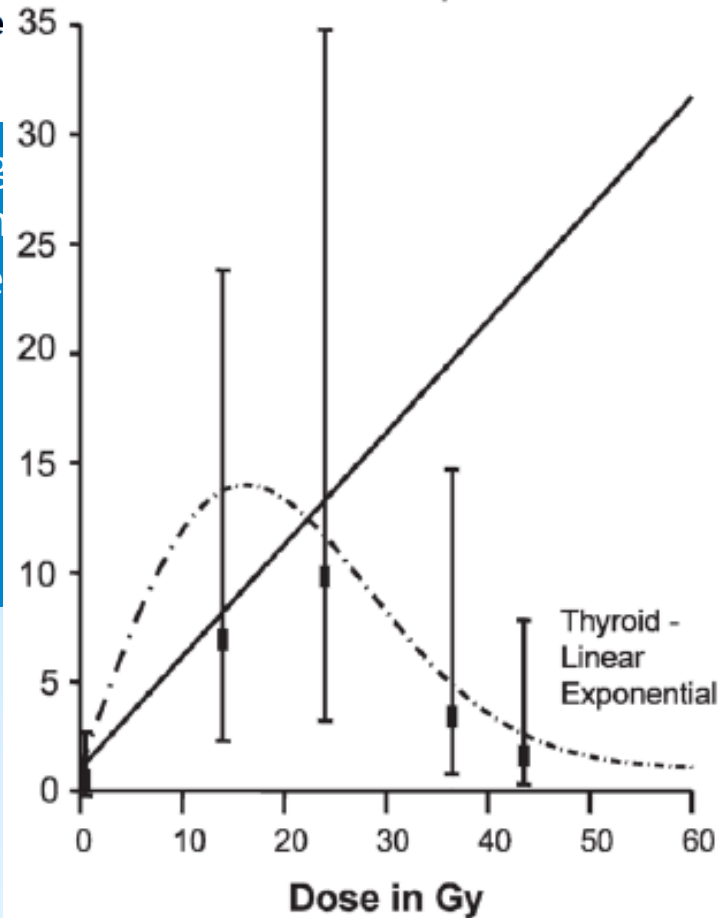
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Thyroid Second Neoplasms



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Seconde neoplasie

2012 American Association for Cancer Research.

Research Article

Cancer
Epidemiology,
Biomarkers
& Prevention

Chemotherapy and Thyroid Cancer Risk: a Report from
the Childhood Cancer Survivor Study



Thirty years after the first childhood cancer treatment, the cumulative incidence of thyroid cancer was 1.3% for females and 0.6% for males. Among patients with thyroid radiation doses of 20 Gy or less treatment with alkylating agents was associated with a significant 2.4-fold increased risk of thyroid cancer ($p < 0.002$).

Chemotherapy risks decreased as radiation dose increased, with a significant decrease for patients treated with alkylating agents. No chemotherapy-related risk was evident for thyroid radiation doses more than 20 Gy.



Conclusioni

**CHILDREN'S
ONCOLOGY
GROUP**

The world's childhood cancer experts

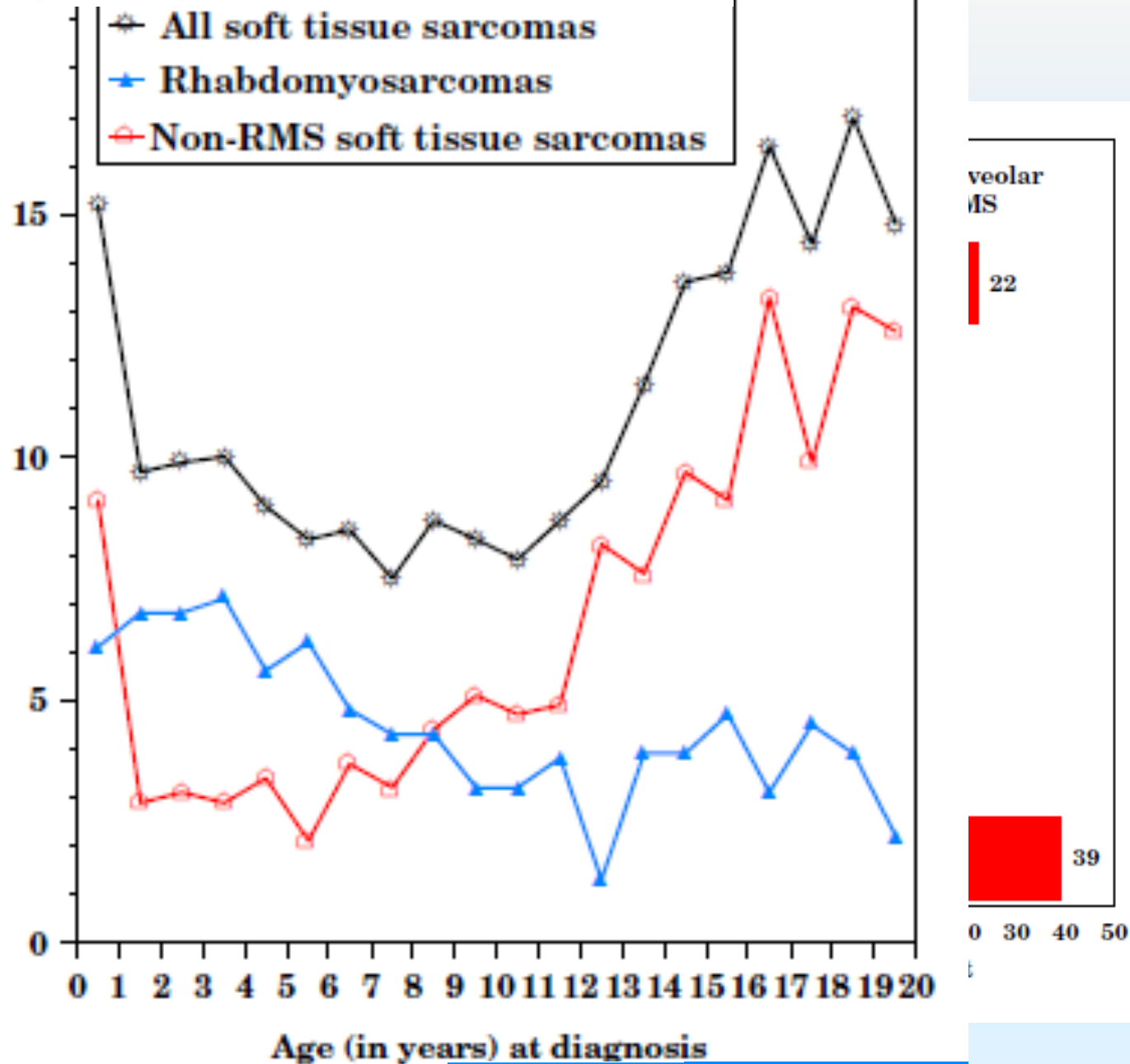
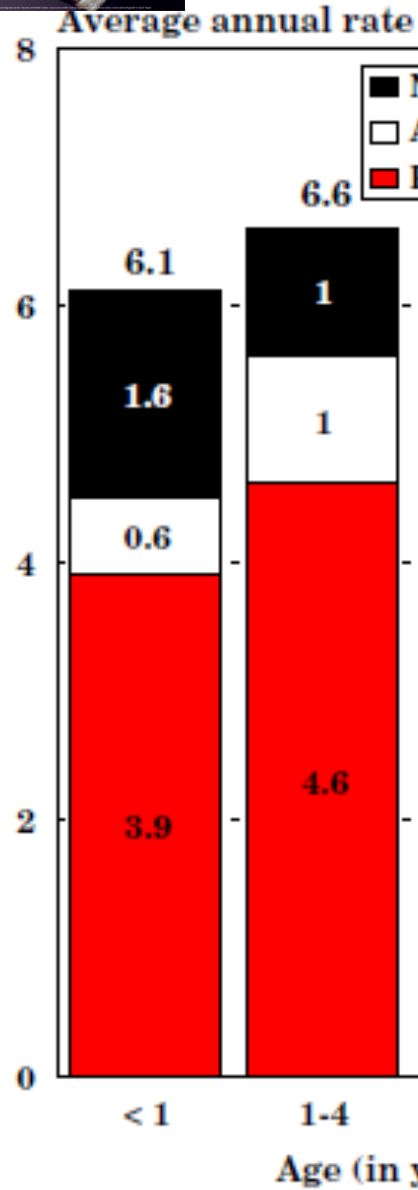
Riduzione di dose degli alchilanti
Individuazione di pazienti a cui è possibile evitare la RT
Riduzione della dose di RT
Constraints RT





SOFT TISSUE SARCOMAS

James G. Gurney, John L. Young, Jr., Steven D. Roffers, Malcolm A. Smith, Greta R. Bunin





**CHILDREN'S
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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

Risk Group	Subgroups	Pathology	Post surgical Stage (IRS Group)	Site	Node Stage	Size & Age
Low Risk	A	Favourable	I	Any	N0	Favourable
Standard Risk	B	Favourable	I	Any	N0	Unfavourable
	C	Favourable	II, III	Favourable	N0	Any
	D	Favourable	II, III	Un favourable	N0	Favourable
High Risk	E	Favourable	II, III	Unfavourable	N0	Unfavourable
	F	Favourable	I, II, III	Any	N1	Any
	G	Unfavourable*	I, II, III	Any	N0	Any
Very High Risk	H	Unfavourable	I, II, III	Any	N1	Any

Low risk per il COG include anche i standard risk del gruppo EPSSG
La stratificazione EPSSG non include i pazienti metastatici



Pediatr Blood Cancer 2005;44:643-653

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1. eye (cataract, impairment visual disturbances ,very dry eyes)

2. endocrine impairment (growth hormone, hypothyroidism need for medications to induce puberty)

Myelodysplasia (C, I



* No therapy
C Cyclophosphamide
D Doxorubicin
I Ifosfamide
RT Radiation therapy