

XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLOGNA,
27-29 OTTOBRE 2023

PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti



Associazione Italiana
Radioterapia e Oncologia clinica

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HOPE to be PAST

A Multifactorial Approach To Permanent Alopecia Management in Paediatric Neuroncology Patients after Craniospinal Irradiation

Camilla Satragno

Dipartimento di Medicina Sperimentale (DIMES), Università degli studi di Genova

Disclosure

Ongoing collaboration with Tecnologie Avanzate
no other disclosure to declare

Background

a) Epidemiology

- Brain tumors are the 3rd most frequent tumors in childhood
- **1st cause of solid tumours in paediatric age**
- Posterior Cranial Fossa tumor account for 40%, especially <10 years

b) Radiotherapy indications

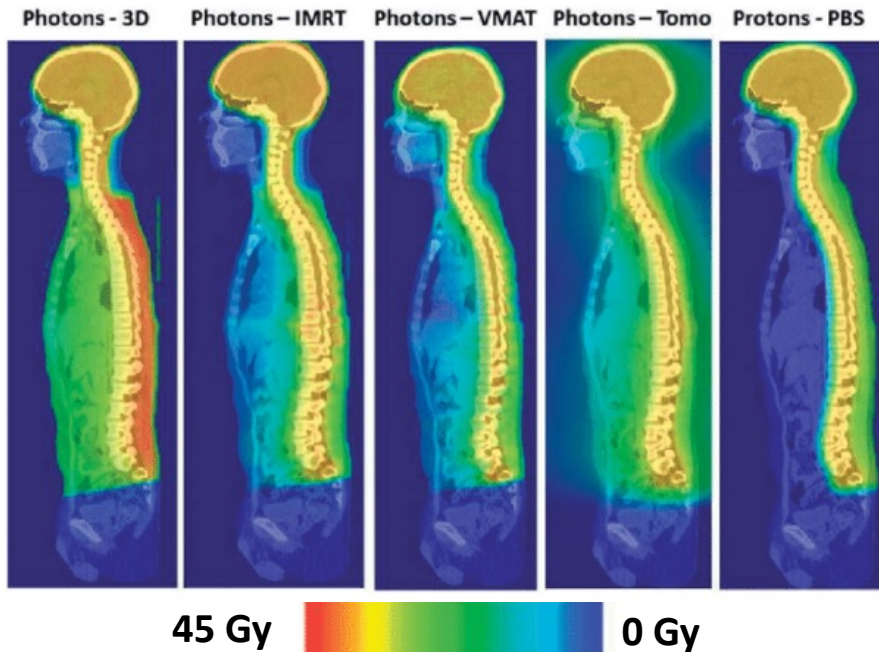
- **First-line: Medulloblastoma, ependymoma, germ cell tumours, high grade glioma**
- Second-line: low-grade glioma, craniopharyngioma

CSI Dose

- 39 Gy 1.30 Gy x 2 day
- 36 Gy 1.8 Gy day
- 36 Gy 1 Gy x 2 day
- 24 1.6 Gy day
- 23.40 1.8 Gy day
- 18 1.8 Gy day

Boost

- Tumour bed up to 68 Gy
- Brain M+ 45-54 Gy

Background

CSI

Medulloblastoma

Ependymoma if
metastaticGerm cell tumour
if metastatic

CSI Toxicity

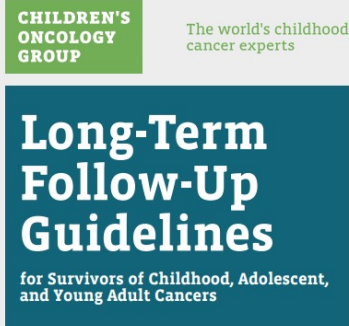
- High risk of late side effects (neurocognitive, endocrinological and psycho-social).
- **Permanent alopecia** remains a late **irreversible** effect, with a negative impact on the patient's **quality of life and on social life**.
- Hair follicles have a *high radiosensitivity*.
- To date, there are **no treatments** (post-therapy) to resolve this late toxicity.
- The only definitive curative treatment is **prevention**.

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Scarring, Disfigurement, and Quality of Life in Long-Term Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Karen E. Kinahan, Lisa K. Sharp, Kristy Seidel, Wendy Leisenring, Aarati Didwania, Mario E. Lacouture, Marilyn Stovall, Anand Haryana, Leslie L. Robison, and Kevin R. Krull



How to prevent?

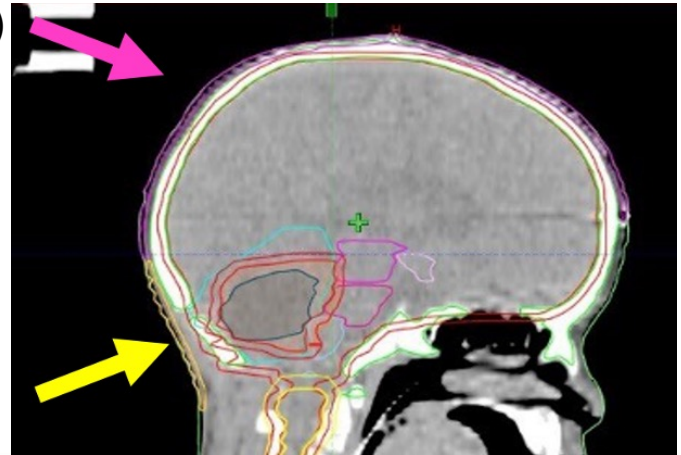
- Say Goodbye to alopecia with **PAST**: *the Pediatric Atlas - based Scalp segmentation Technique* that may help to prevent hair loss in craniospinal irradiation.
- **HOPE**: *Hair loss Outcome Prediction and Evaluation.*

Materials and Methods

- We **dearchived** the CT scans and treatment plans of patients undergoing CSI in our hospital.
- We performed scalp contouring based on an *internal contouring protocol*, the Alopecia_Hope (A_H) contouring protocol, and through *automatic scripting on our TPS* (RayStation version 12A-SP1).
- We have identified 2 volumes:

Whole scalp (WS)

Posterior cranial
fossa scalp (PCFs)



Materials and Methods

- Randomly selected patients for the creation of the atlas and tester patients were chosen.
- Patients with **significant bone changes** after neurosurgery were excluded.
- The **total and average contouring time** and the percentage of time saved were recorded.
- **The accuracy** of atlas contouring was assessed using the *standard similarity metrics of 3D DICE similarity coefficient (DSC) and mean distance of agreement (MDA)*.

Results

52 scans, 8 testers

Median contouring time with the guidelines,
the A_H protocol and automatic scripting:
19 minutes

The contouring time by the automatic atlas
was 11 min and the mean time of the expert
correction was 4.5 min

Metric (Mean)	WS	PCFS
DICE	0,76 ± 0,05	0,77 ± 0,04
Sensitivity	0,77 ± 0,05	0,80 ± 0,08
Specificity	0,78 ± 0,09	0,75 ± 0,16

Considering the work done by the atlas is in background,
this resulted in a time savings of 80% for the operator.

How to prevent?

- Say Goodbye to alopecia with **PAST**: *the Pediatric Atlas - based Scalp segmentation Technique* that may help to prevent hair loss in craniospinal irradiation.
- **HOPE**: *Hair loss Outcome Prediction and Evaluation.*

Materials and Methods

- Selected paediatric patients who underwent CSI from 2006 to 2021
- **PAST protocol** used for scalp contouring
- Clinical-pathological-therapeutic data was used, focusing on **age at diagnosis**, use of **high-dose thiotepa**, **endocrinological damage**, use of **replacement therapies** and **vitamin D deficiency**
- Timing of onset of alopecia from the end of RT was taken into account
- Toxicity was studied according to CTCAE both on **whole scalp (WS)** and **posterior cranial fossa (PCF) scalp**

Materials and Methods

- **Several dosimetric variables** taken into account^{1,2,3,4}
- **Automatic scripting** to recalculate scalp doses based on previous treatment's plan
- Receiver characteristic curve (**ROC**) and area under the curve (**AUC**) to identify dosimetric **cut-offs**
- We repeated the analysis **stratifying** the whole scalp cohort also according to thiotepa administration and number of RT fractions per day

¹Lawenda et al, Int. J. Radiation Oncology Biol. Phys. 2004; ² Min et al, Radiation & Oncology 2014;

³Scoccianti et al, Front Oncol 2020; ⁴ Satragno et al, Journal of Neurooncology 2022

RESULTS

- **48** patients were selected
- Mean **age at diagnosis** 8.6 years
- Median **follow-up** 4.5 years (1-12 years)
- **CSI mean dose** 29.49 Gy
- **PCF mean dose** 52.29 Gy
- **Alopecia G0** in 26/48 (**54%**) patients

Factors associated with Alopecia WS

		Absent	Present	p
Age at diagnosis		9.1 ± 5.31	8.0 ± 3.85	0.65
Sex	Female	10 (38.5%)	8 (36.4%)	0.88
	Male	16 (61.5%)	14 (63.6%)	
Thiotepa	No	16 (61.5%)	6 (27.3%)	No vs Yes: 0.010*
	Pre RT	5 (19.2%)	4 (18.2%)	
	Post RT	5 (19.2%)	12 (54.5%)	
Number of fractions/days	1/day	21 (80.8%)	9 (40.9%)	0.004*
	2/day	5 (19.2%)	13 (59.1%)	

ROC and AUC for alopecia WS

Variables	AUC	Cut-off	Sensitivity, %	Specificity, %
V3000cGy WS	0.70 (0.55 – 0.85); 0.019	15.26%	81.8%	53.8%
V3500cGy WS	0.75 (0.60 – 0.89); 0.003	12.22%	77.3%	73.1%
V4000cGy WS	0.75 (0.61 – 0.89); 0.003	6.31%	68.2%	76.9%
V4300cGy WS	0.74 (0.60 – 0.88); 0.004	3.27%	68.2%	76.9%
D0.03cc WS	0.76 (0.62 – 0.90); 0.002	5520.33	54.5%	88.5%
D0.01cc WS	0.75 (0.61 – 0.89); 0.004	5689.28	50.0%	92.3%
D2% WS	0.75 (0.61 – 0.89); 0.003	4062.04	81.8%	65.4%

An AUC of 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding¹

Thiotepa and fractions/day in alopecia WS

Variables	Tiothepa	AUC
Total dose to PCF tumor bed	No	0.64 (0.42 – 0.85)
	Yes	0.70 (0.48 - 0.93)
D0.03cc WS	No	0.63 (0.39 – 0.87)
	Yes	0.79 (0.59 – 0.99)
V4000cGy WS	No	0.65 (0.38 – 0.93)
	Yes	0.76 (0.51 – 1.00)
V4300cGy WS	No	0.61 (0.35 – 0.88)
	Yes	0.73 ((0.49 – 0.98)
D0.01cc WS	No	0.58 (0.35 – 0.81)
	Yes	0.78 (0.59 – 0.99)
D2% WS	No	0.60 (0.25 – 0.84)
	Yes	0.78 (0.53 – 1.02)

Variables	Daily fractions	AUC
D0.03cc WS	1/die	0.64 (0.42 – 0.86)
	2/die	0.74 (0.46 – 1.02)
D0.01cc WS	1/die	0.63 (0.41 – 0.85)
	2/die	0.75 (0.48 – 1.03)

An AUC of 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding¹

Factors associated with Alopecia PCF

		Alopecia PCF								p
		No				Yes				
		Standard Mean	Deviation	Count	Column N %	Standard Mean	Deviation	Count	Column N %	
Age at diagnosis		9.1	5.31			8.0	3.85			0.65
Sex	Female			10 (38.5%)				8 (36.4%)		0.88
	Male			16 (61.5%)				14 (63.6%)		
Thiotepa	No			16 (61.5%)				6 (27.3%)		0.010*
	PreRT			5 (19.2%)				4 (18.2%)		
	PostRT			5 (19.2%)				12 (54.5%)		
Number fractions/die	1/die			21 (80.8%)				9 (40.9%)		0.004*
	2/die			5 (19.2%)				13 (59.1%)		

ROC and AUC in alopecia PCF

Variables	AUC	Cut-off	Sensitivity, %	Specificity, %
V3500cGy PCF	0.74 (0.59 – 0.89);0.004	41.19%	72.7%	80.8%
V4000cGy PCF	0.74 (0.59 – 0.88); 0.005	20.31%	63.6%	84.6%
V4300cGy PCF	0.73 (0.58 – 0.87); 0.007	10.85%	63.6%	80.8%
D0.01 cc PCF	0.72 (0.58 – 0.87): 0.009	4394.91	81.8%	57.7%
D0.03cc PCF	0.72 (0.58 – 0.89); 0.009	4360.03	77.3%	57.7%
D2% PCF	0.71 (0.56 – 0.86); 0.013	5014.67	54.5%	84.6%
D50% PCF	0.74 (0.59 – 0.89); 0.005	3280.19	72.7%	80.8%

An AUC of 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding¹

Conclusions

- The PAST atlas: reliable and time-saving tool for scalp contouring
- The HOPE study:
 - dose-effect relationship for chronic alopecia
 - bifractionated radiotherapy and high doses of chemotherapy
 - endocrinological damage and surgery do not seem related to alopecia
 - the identified constraints can be a guide for scalp sparing CSI
 - further studies on larger cohorts are needed

Thanks for the attention!

Radioterapia pediatrica, IRCCS
Ospedale San Martino

Dott.ssa **S. Barra**
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Dott. **A. Ferrero**

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Università degli studi di
Genova, Dip. Statistica
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Neuroncologia pediatrica,
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*Eleonora e tutti i nostri
piccoli pazienti.*

satragno.camilla@gmail.com