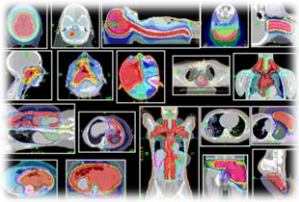
Gemona 5 ottobre 2018
Palmanova, 30 novembre 2018

Novità in Radioterapia in Età Pediatrica





Maurizio MASCARIN (MD)

Elisa Coassin (MD), Irene Bassi, (TSRM), Giulio Pruch (TSRM) Federica Fedrigo (IP),
Paola Pase (IP), Andrea Schicariol (TSRM), Luana Tassan (IP)

AYA and Pediatric Radiation Oncology Unit

C.R.O. Centro di Riferimento Oncologico – Aviano (Italy)

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CRO Aviano - Cancer Center

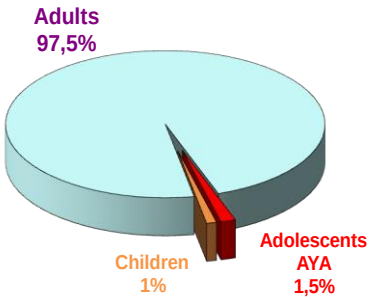
Activities of RT-Department
- ❖2,100 new patients / year
- ❖42,000 treatments / year
- ❖160 patients / day

Human resources RT:
- ✓Physician 14
- ✓Physicist 7; Dosimetrist 2
- ✓Informatics 2
- ✓Radiotherapist 19

Children, Adolescents and Young Adults

Italian population:
Total 60.589.485

- **Italy ≤ 14 years:** 8.182.584 Children
- **Italy 15-24 years:** 5.895.353 Adolescent
- **Italy 24-29 years:** 3.884.123 Young Adult
- **Italy 30-39 years:** 7.393.662 adult



Cancer Incidence

Age 0-14 years: 175 cases/million/years (≈ **1380 new cases**)
Age 15-19 years: 270 cases/million/years (≈ **804 new cases**)
Age 20-24 years: 352 cases/million/years (≈ **1096 new cases**)
Age 25-29 years: 547 cases/million/years (≈ **1944 new cases**)

I tumori in FVG 1995-2005, Agenzia Reg Sanità - ISTAT 2012
AIRTUM, E&P 2008; AIRTUM 2014
Bleyer A et al SEER 1975-200

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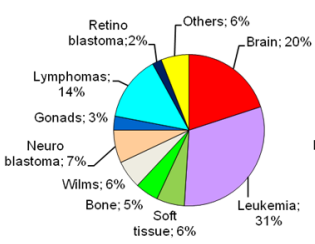
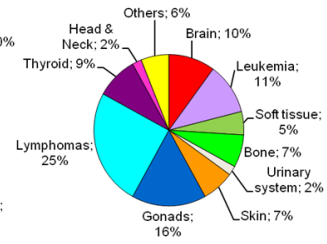
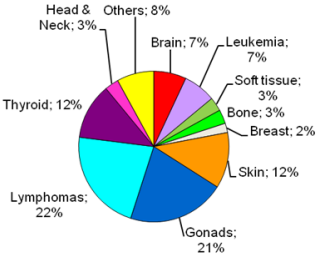
Age related cancer subtypes



Age 0-14 years



Age 15-19 years



Age 20-24 years

I tumori in FVG 1995-2005, Agenzia Reg Sanità - ISTAT 2017
AIRTUM, E&P 2008; AIRTUM 2014

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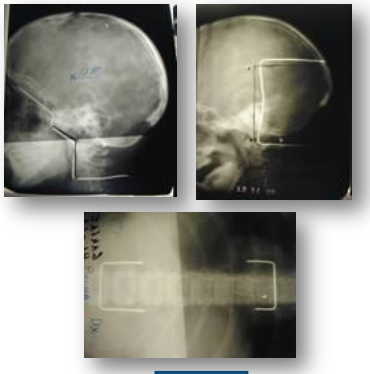
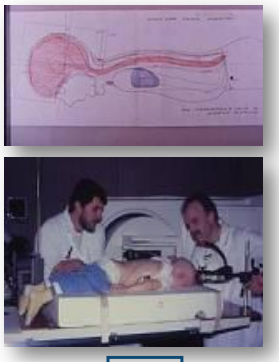
CRO History of Radiotherapy in children

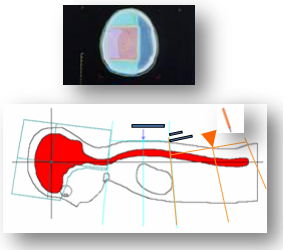


1975
Cobalto

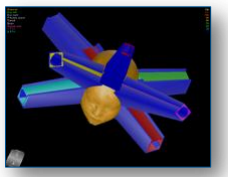


1985
Acc. Lineare

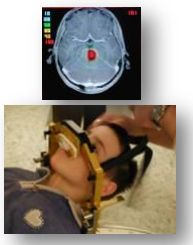
CRO History of Radiotherapy in children



1995
PC planning

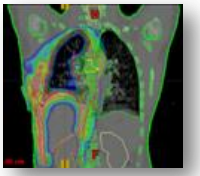


2000
3D conformal

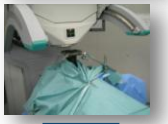


2001
Stereotassi

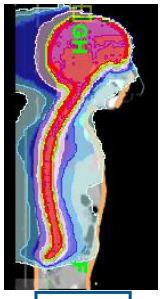
CRO History of Radiotherapy in children



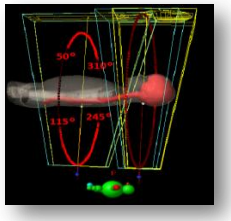
2005
IMRT
IGRT



2005
IORT



2006
TOMO



2012
ArcTherapy

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Linear Accelerator 6MV

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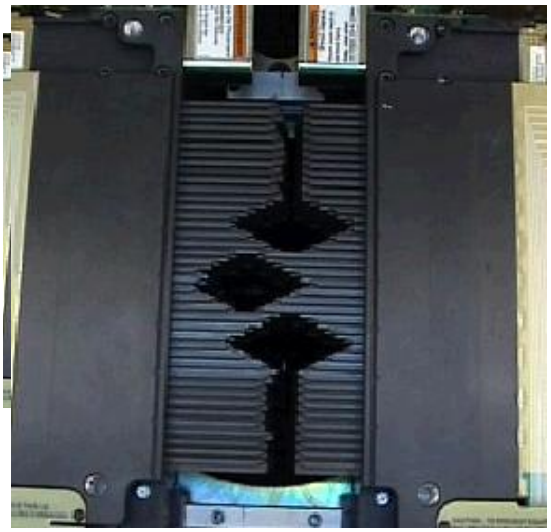
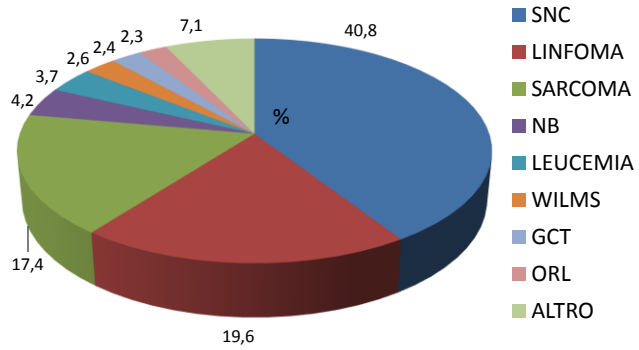
Multi Leaf Collimator



TomoTherapy

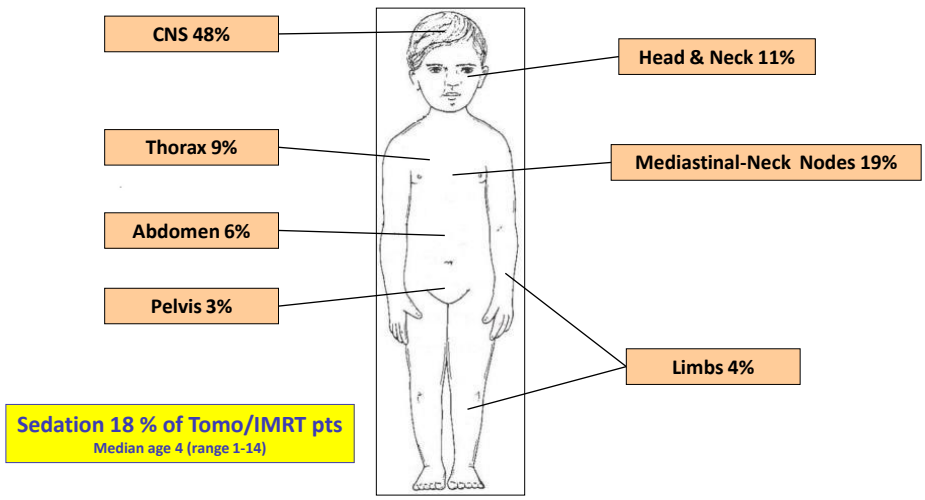
CRO Aviano – RT in Pediatric-AYA Patients

PAZIENTI ≤ 18 anni DAL MAGGIO 1995 AL MAGGIO 2018: 622 ped



CRO Aviano – Tomo/IMRT in Pediatric-AYA Patients

(pts recruited from June 2005 to May 2018: **299 Tomo/IMRT**)



222 TOMO pts (+77 IMRT). Median age 14 years

Radiotherapy in Pediatric Tumors

- 2% del totale dei pz di un reparto RT
- Circa 2/3 dei bambini con tumore solido avranno bisogno prima o poi della RT

DEFINIZIONE DEL PROBLEMA

- Problema delegabile?
- Paziente è "NON TIPICO"

DIFFICOLTÀ DI APPROCCIO

- Obiettivi della cura.
- Rischio degli effetti collaterali

QUALITA' DELLA VITA

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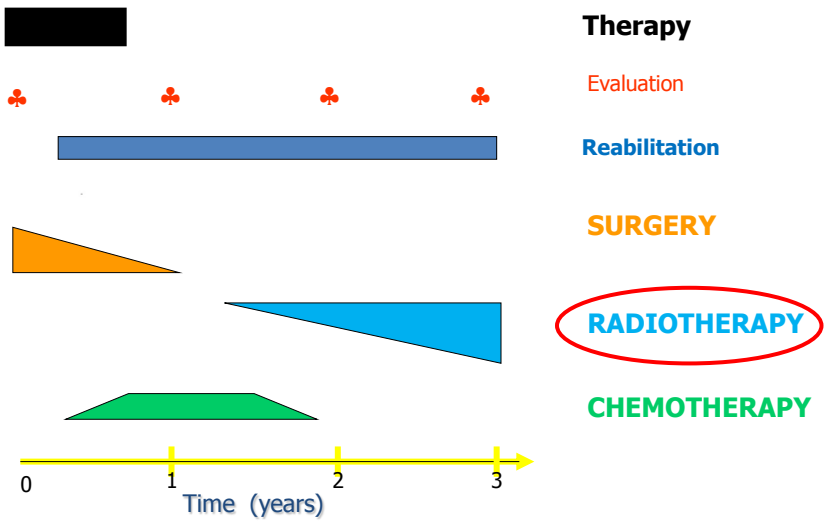
Pediatric Tumors and Outcome



Clinical assesment

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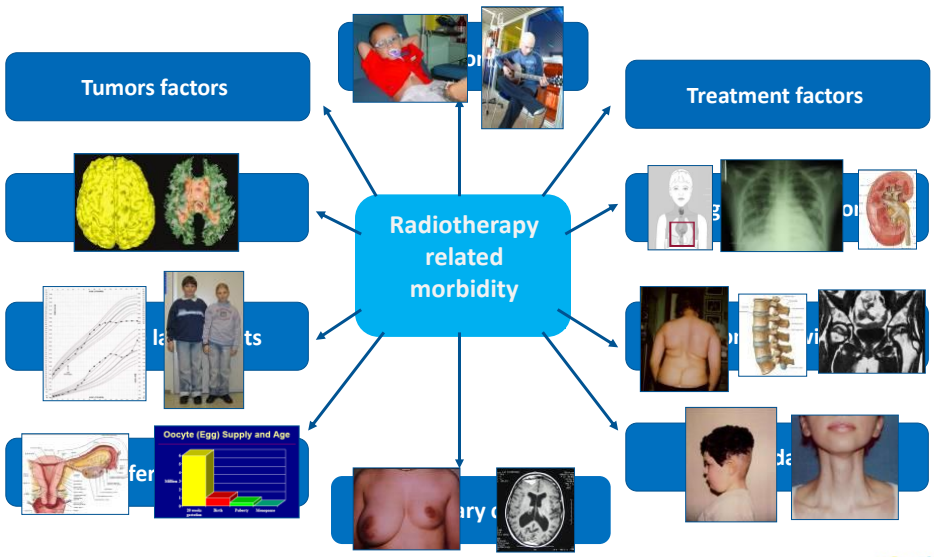
Risk-adapted radiotherapy



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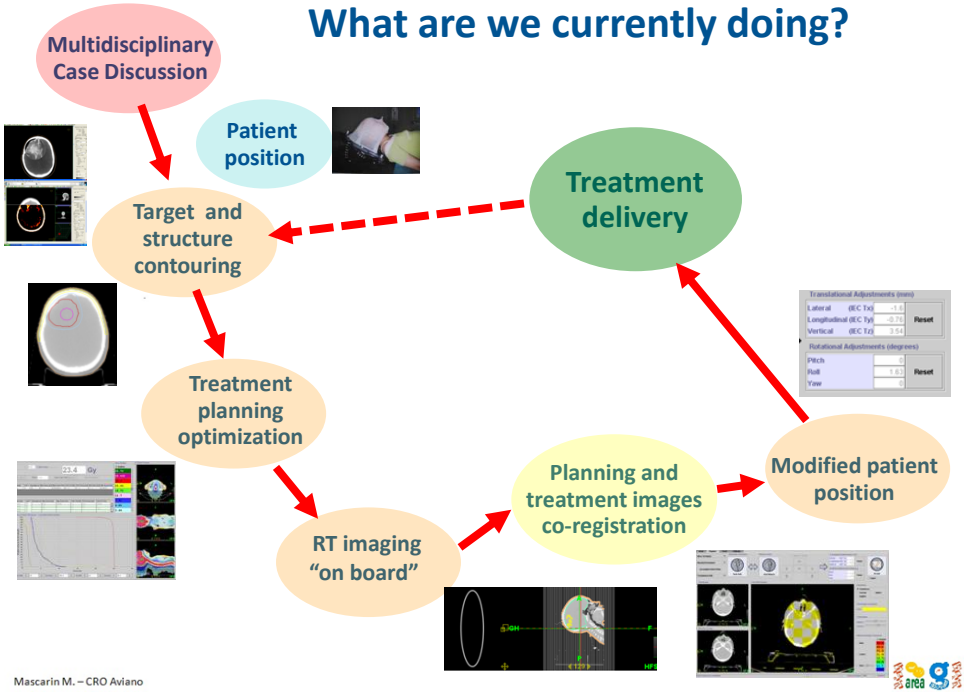
Risk-adapted therapy

Mascarin M. – CRO Aviano

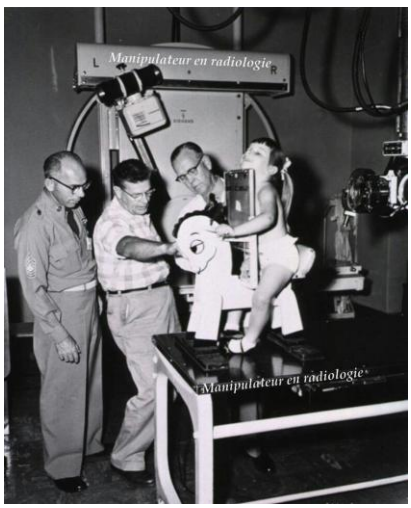
What are we currently doing?



Immobilization

Immobilization

Immobilization



1959

https://www.google.it/search?sa=G&hl=it&q=maquina+de+raio+x+antigas&tbm

Immobilization

Halperin 1950

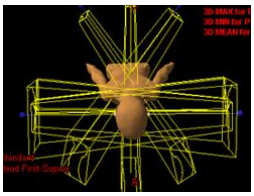
Immobilization

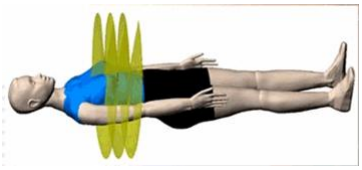
1980

Immobilization

2000

“old” prone position, “new” supine position





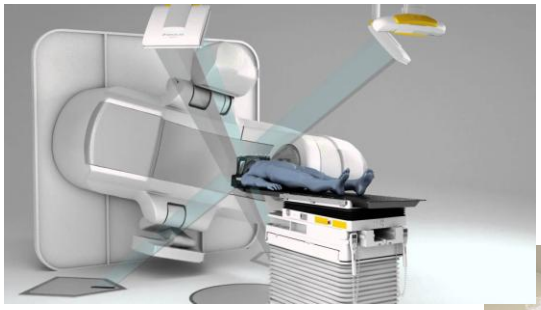
Prone

Supine

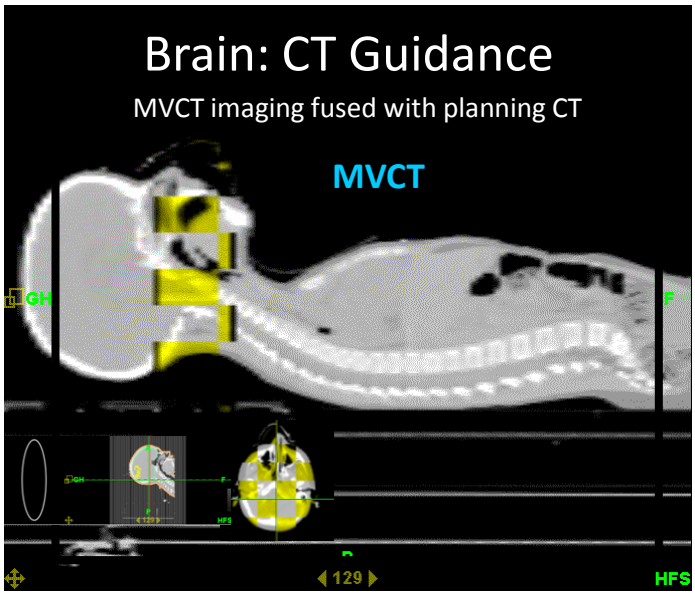
Immobilization

Mask + shoulder

IGRT Image Guided Radiotherapy



IGRT and Tomo



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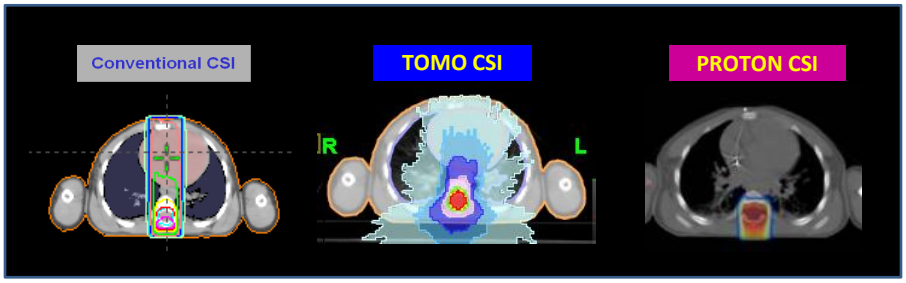
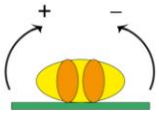
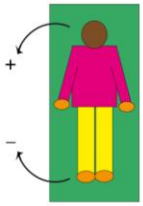
IGRT and technology selection



ROLL

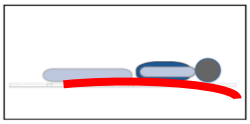


JAW



PITCH

BED deflection



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Sedation - Pt positioning - Immobilization

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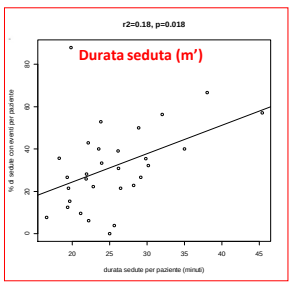
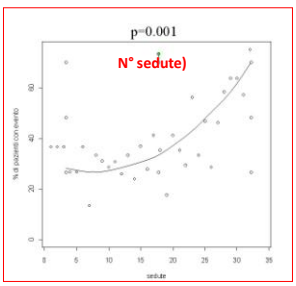
Sedation with propofol in Pediatric Radiotherapy

In **783 sedazioni con Propofol** per RT ped:

- **nessuna complicazione maggiore,**
- **2 desaturazioni (0,25%),**
- 92 variazione della frequenza cardiaca (11,7%),
- 173 complicanze minori vie aeree (22%).





Vi è un aumento degli eventi collaterali durante la sedazione all'aumentare della durata della stessa (28 vs 24 m') e all'aumentare del numero progressivo delle sedazioni (>15).

LA SEDAZIONE CON PROPOFOL IN RADIOTERAPIA PEDIATRICA Mascarin M, Giergji M, Fantin D, Bortolussi R, Fabiani F, Bertuzzi C, Gigante M,Capone D, Fedrigo F, Pase P, Ros L, Bassi I, Pacenzia R, D'Ecclesia G, Bulian P,De Cicco M , Proceeding Congresso Nazionale AIEOP 2010

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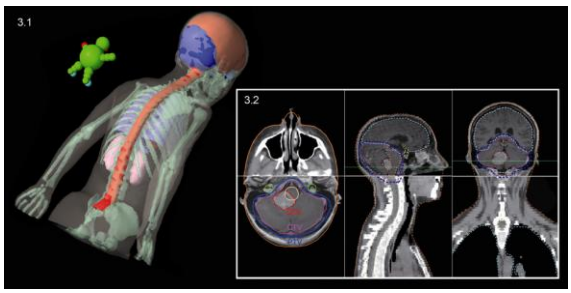
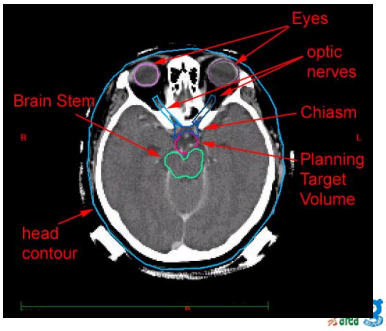
30

Target Definition

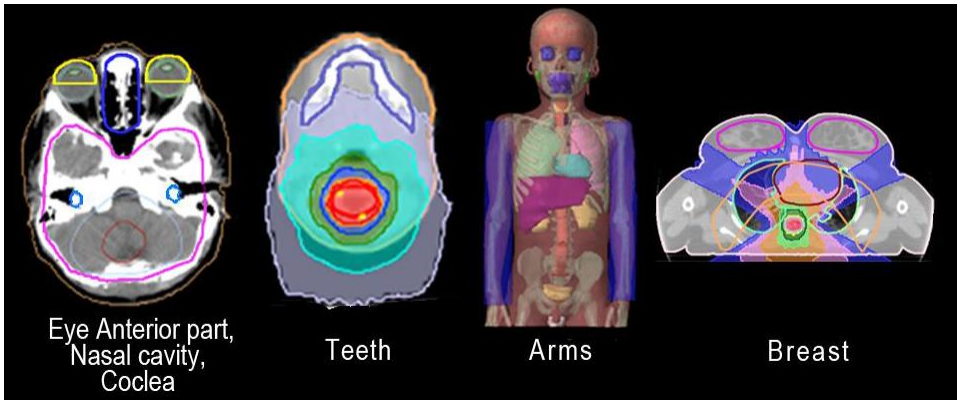
Definition of tumor treatment volume and OAR



Mascarin M et al in Posterior Fossa Tumors in Children. M. Özek , G. Cinalli, W. Maixner, C. Sainte-Rose. Editors, Springer Ed, pp363380 2015



OAR Organ at Risk



Some extra structures were generated ("tune structures") to obtain a better optimization around the target

If OARs are not contoured, the process "doesn't matter"

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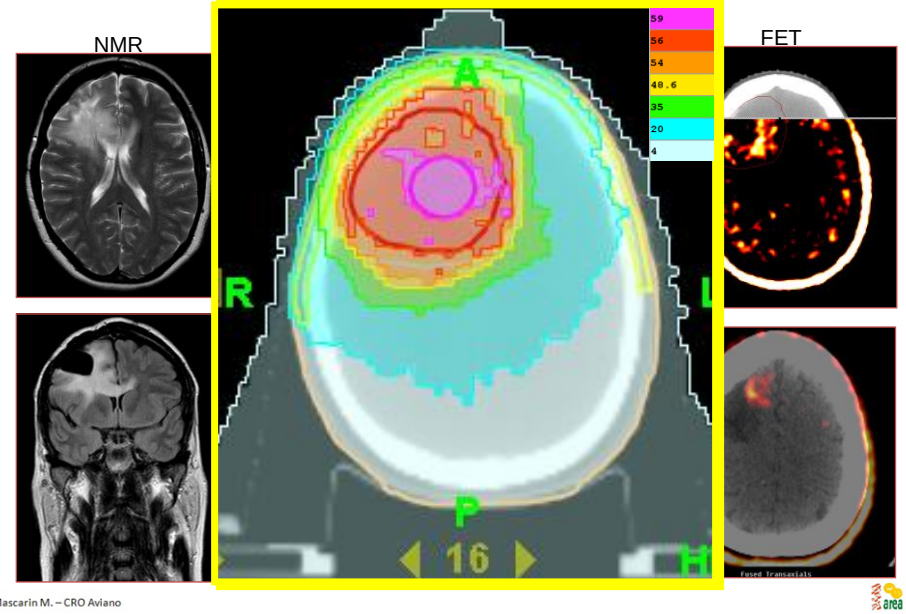
Mascarin M et al. **Helical Tomotherapy in Children and Adolescents: Opportunities and Issues, Cancers 2011**

From multimodality co-registration to IMRT (Intensity Modulation Radiation Therapy)



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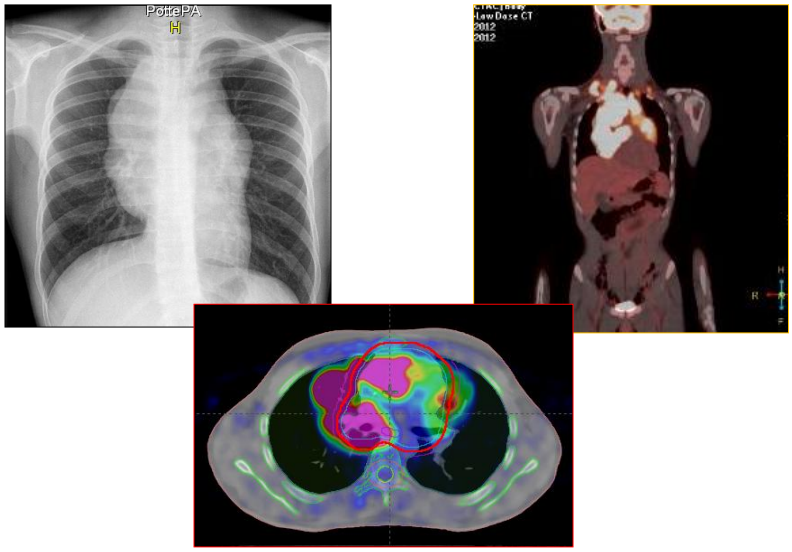
Tumor shrinking



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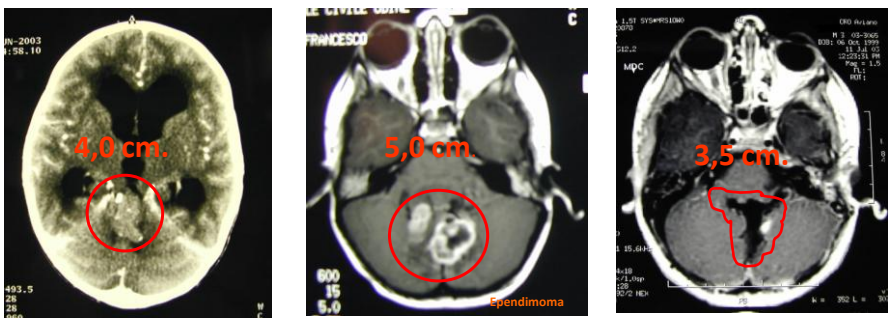
Comparison between diagnostic PET and CT/RT-simulation after chemotherapy

"Tumor shrinking"



TC pre-operatoria

RNM pre-operatoria

RNM post-operatoria

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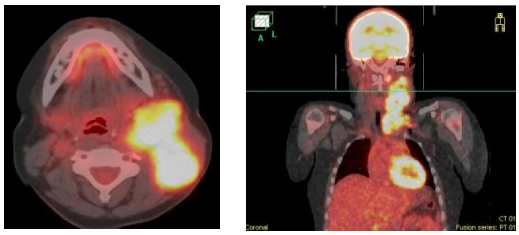
Could Radiotherapy Volumes safely reduced?

EURONET PHL C2
Radiotherapy volumes "**DECOPDAC21**"

RT volumes planned on disease burden at the chemotherapy course (ISRT - INRT modified).

Initial PET/CT



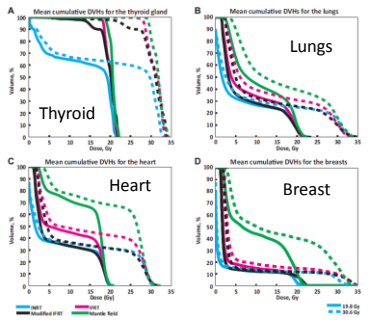
LRA-qPET
At the end of CT

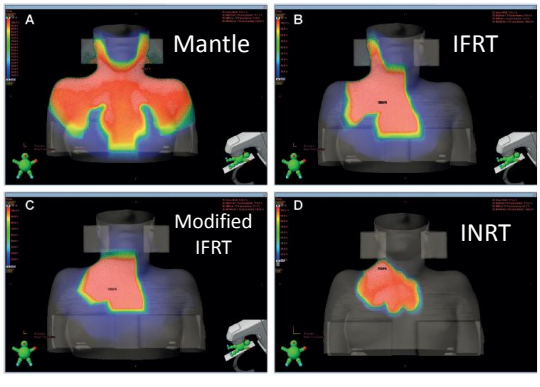
Could Radiotherapy Volumes safely reduced?

Pediatr Blood Cancer 2014;61:717–722

The Impact of Involved Node, Involved Field and Mantle Field Radiotherapy on Estimated Radiation Doses and Risk of Late Effects for Pediatric Patients with Hodgkin Lymphoma

M.V. Maraldo, MD,[1*] M. Jørgensen, MD,[1,2] N.P. Brodin, PhD,[1,3] M.C. Aznar, PhD,[1,4] L.R. Vogelius, PhD,[1] P.M. Petersen, MD, PhD,[1,2,5] A.K. Berthelsen, MD,[1,6] C.B. Christensen, MD,[6] L.L. Hjalgrim, MD, PhD,[7] and L. Specht, MD, DMSc[1,2,5]

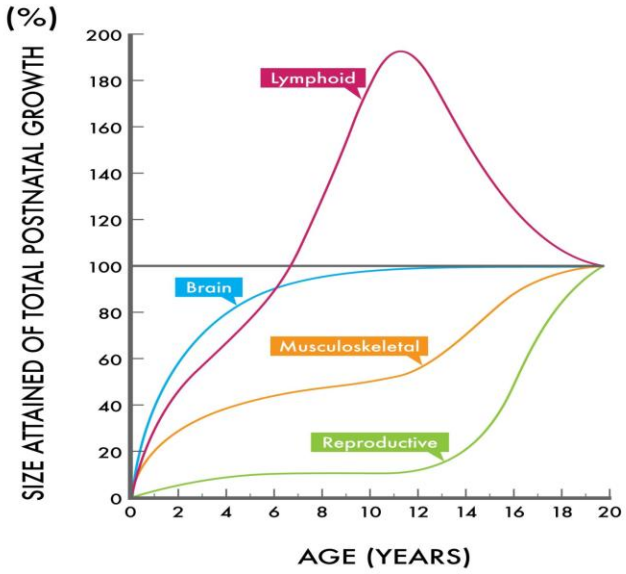




Mantle fields
IFRT
Modified IFRT
ISRT

Involved Node Radiotherapy should be considered for pediatric patients with Hodgkin lymphoma since it is estimated to substantially lower the risk of severe long-term complications.

Postnatal tissue growth



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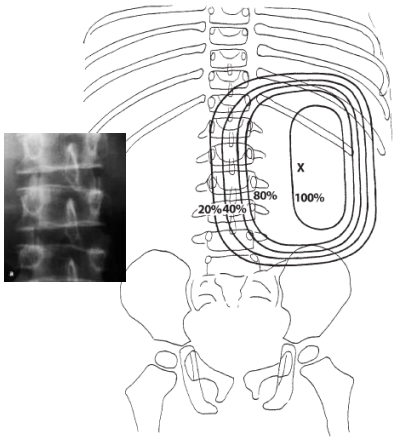
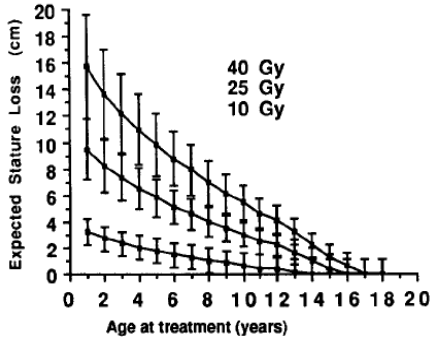
Pathophysiology of Bone Growth Damage

Younger age, higher radiation dosage, and asymmetric bone radiation volume influences the detrimental effects of RT.



J. Pfeil. Orthopäde 2002, 31:2-10
Gawade PL et al. A Systematic Review of Selected Musculoskeletal Late Effects in Surviv CC. Curr Pediatr Rev. 2014



Skeletal Loss for a radiotherapy field from T10-11 to L4-5
using a hypothetical male patient with IAS equal to **176.8 cm. Each** point corresponds to an age when irradiated, **a dose in Gray,** and **SL ± 1 SD.**

Silber et al, JCO 1990

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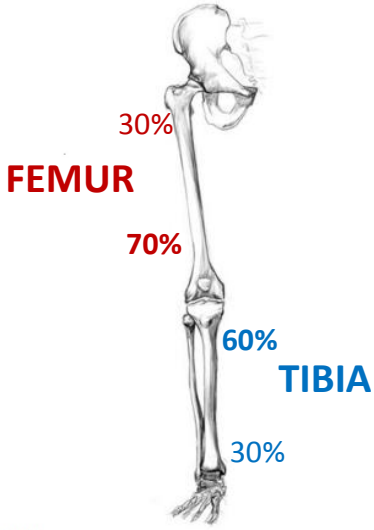
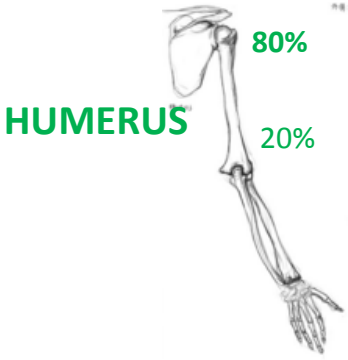
Legs

Bone Development & Growth in Children





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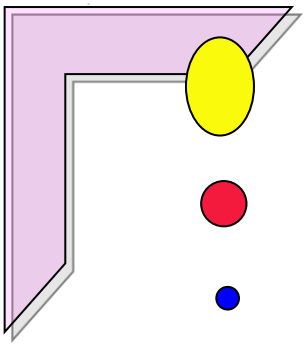
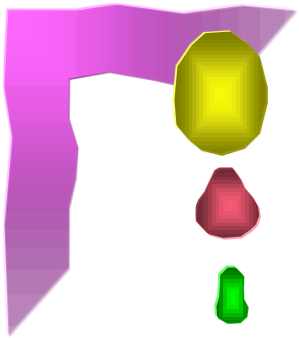
"4D Radiotherapy"

take account of **Spatial-Temporal Evaluation of the Target** during the imaging, planning and delivery of the radiotherapy.





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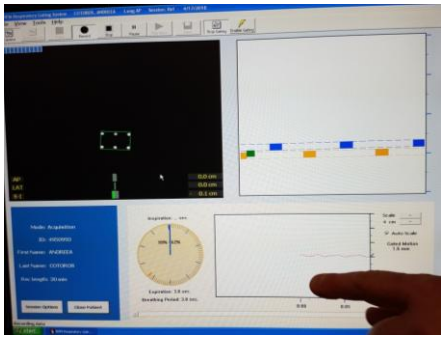
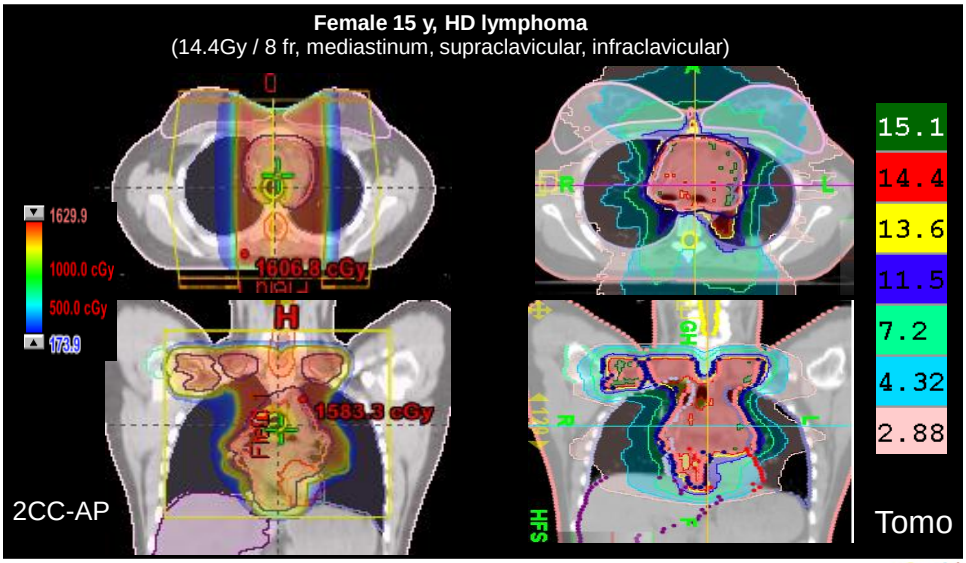
“4D Radiotherapy” ?



Dose Distribution

Dose distribution
Traditional vs High conformal RT



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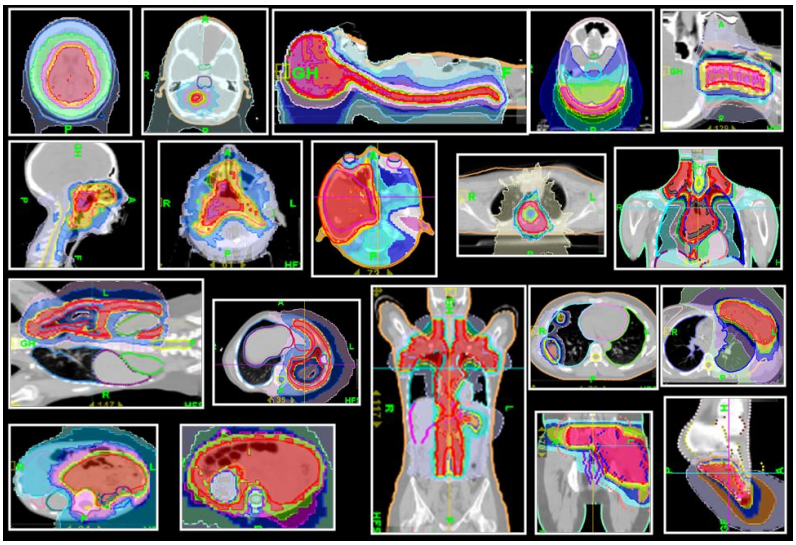
Indications for HT



Mascarin M, Giugliano FM, Coassin E. Cancers 2011.

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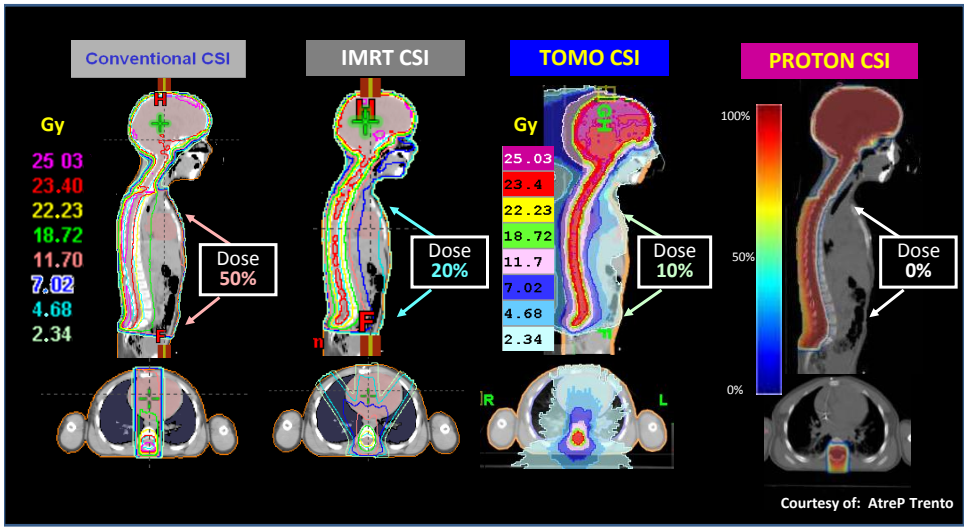
Craniospinal Irradiation

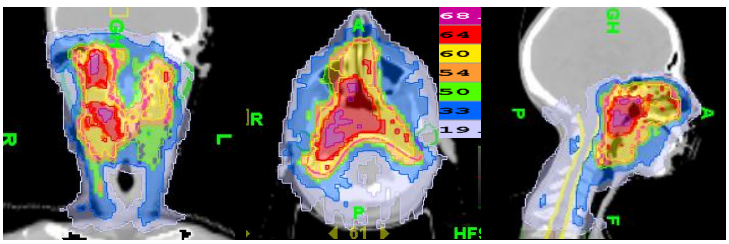
Craniospinal irradiation



Mascarin M et al in Posterior Fossa Tumors in Children. M. Özek , G. Cinalli, W. Maixner, C. Sainte-Rose. Editors, Springer Ed, pp363380 2015

Head and Neck

TOMO in Nasopharynx Carcinoma



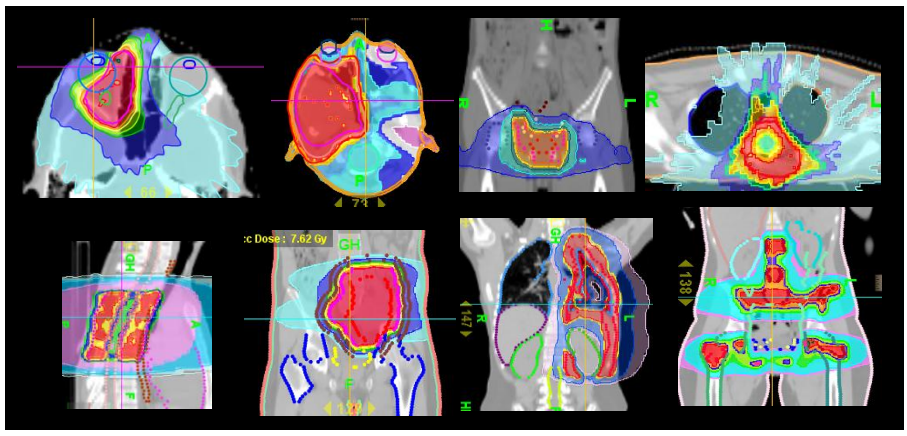
Female 14 y, Nasopharynx carcinoma

- NO multiple fieds, different energies, junctions
- Easy delivering different doses at different volumes:
  - sequential boost, SIB
  - SIB lower doses surrounding high dose PTV than sequential boost
  - HT-SIB better homogeneity and sparing of OAR
- Reduced incidence of high grade toxicity, delayed onset moderate toxicity → prevention of treatment breaks → reduction in the total RT time

Mascarin M, Coassin E. Tomotherapy in Children. Pediatric Radiation Oncology. Editors: Merchant, Thomas E., Kortmann, Rolf-Dieter; Eds. Springer, April 2018.

Sarcoma (soft tissue / bone)

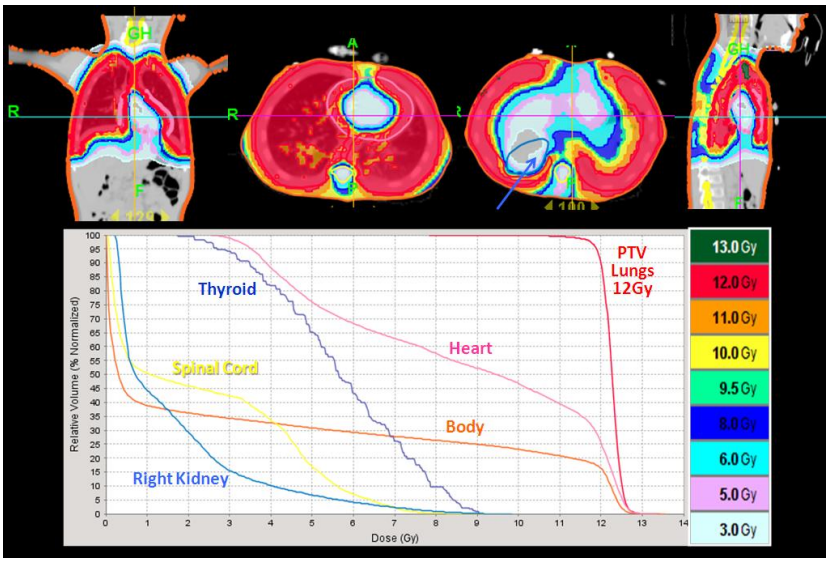
Sarcoma (soft tissue/bones)



Mascarin M, Coassin E. Tomotherapy in Children. Pediatric Radiation Oncology. Editors: Merchant, Thomas E., Kortmann, Rolf-Dieter; Eds. Springer, April 2018.

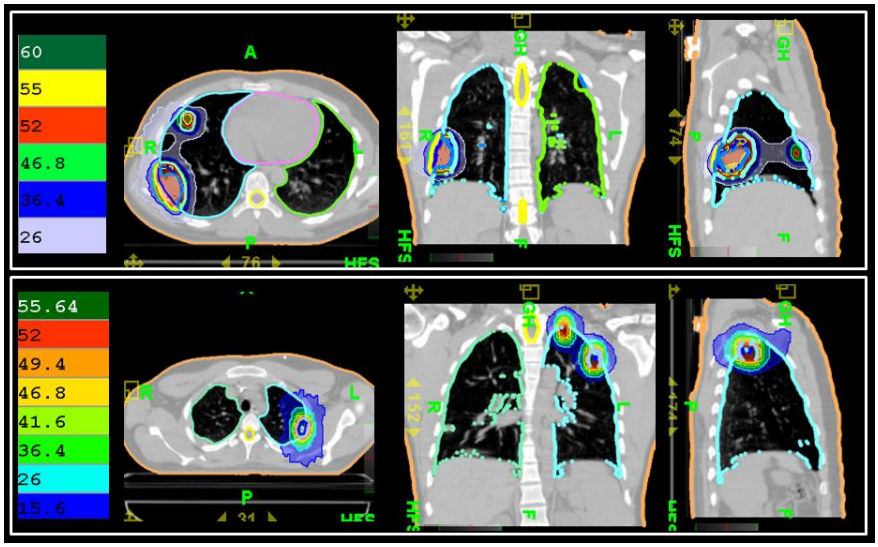
Lung irradiation

Whole lung irradiation



Mascarin M, Coassin E. Tomotherapy in Children. Pediatric Radiation Oncology. Editors: Merchant, Thomas E., Kortmann, Rolf-Dieter; Eds. Springer, April 2018.

Lung stereotactic irradiation



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Mascarin M, Coassin E. Tomotherapy in Children. Pediatric Radiation Oncology. Editors: Merchant, Thomas E., Kortmann, Rolf-Dieter; Eds. Springer, April 2018.

Whole abdominal irradiation

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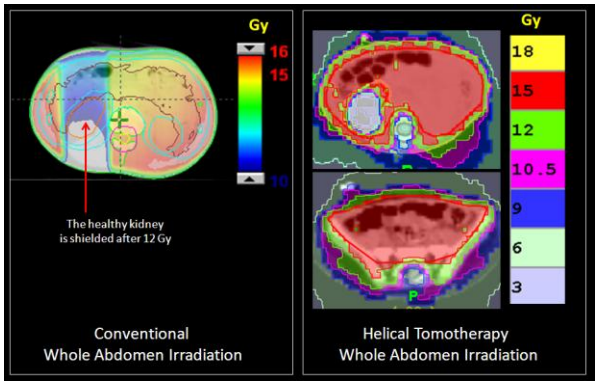
Whole abdominal irradiation



- **Adequate coverage**
- **Limited dose to residual kidney, spinal cord, bone marrow**
- **Reduced dose to small bowel**
- **Homogeneous dose along vertebral bodies**

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Mascarin M, Coassin E. Tomotherapy in Children. Pediatric Radiation Oncology. Editors: Merchant, Thomas E., Kortmann, Rolf-Dieter; Eds. Springer, April 2018.

Palliations

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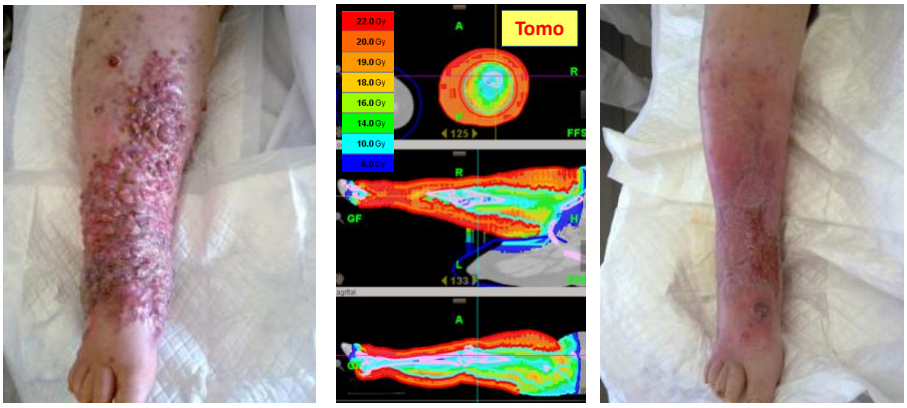
Palliative Intent



Female, 22y, alveolar rhabdomyosarcoma, Site: Leg, PRO during CT, **RT20Gy/5fr.**

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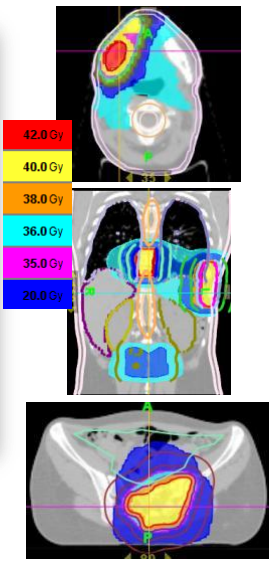
Improve the Quality of Life

High School exit examination



Female, 18 y, stage IV° Ewing/PNET

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What are we currently doing?

Video TSRM

Proton therapy

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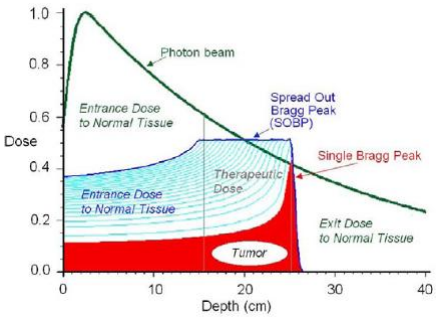
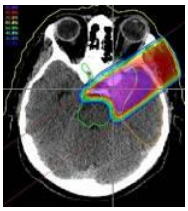
PROTON Therapy

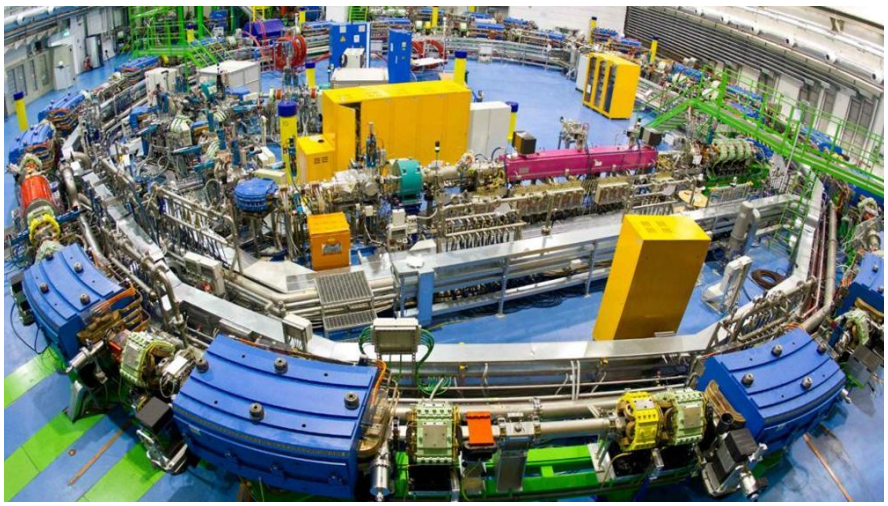


Hoffman EK et al.. Journal of Child Neurology, 24, 11:1387-1396; 2009

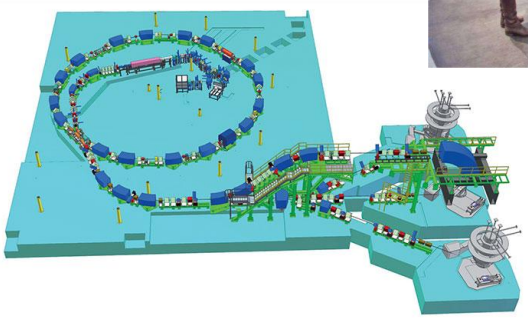
- **Protons Stop!!**
- **Photons don't stop.**
- **Proton dose at depth (target) is greater than dose at surface.**
- **Photon dose at depth (target) is less than dose at d_{max}.**



PROTON Therapy (CNAO Pavia)

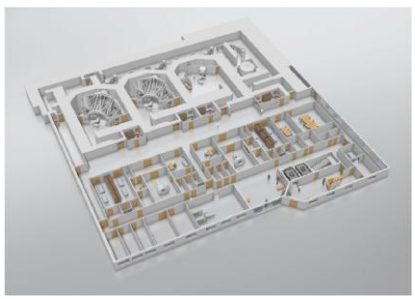


PROTON Therapy (CNAO Pavia)



Mas

PROTON Therapy (IBA Trento)



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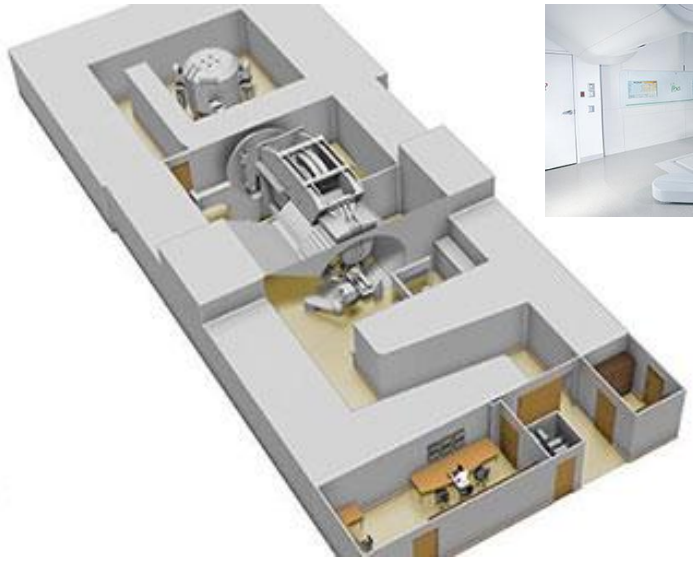
PROTON Therapy (IBA)



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PROTON Therapy (MEVION)

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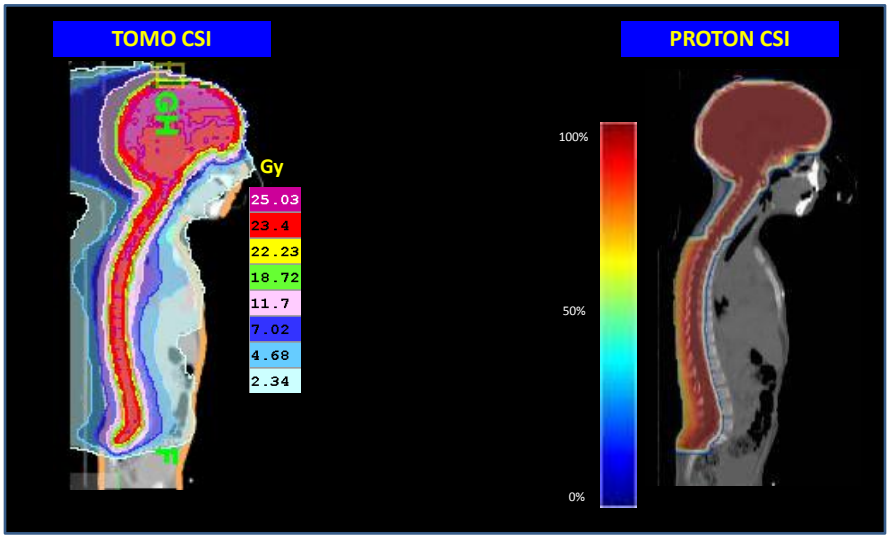
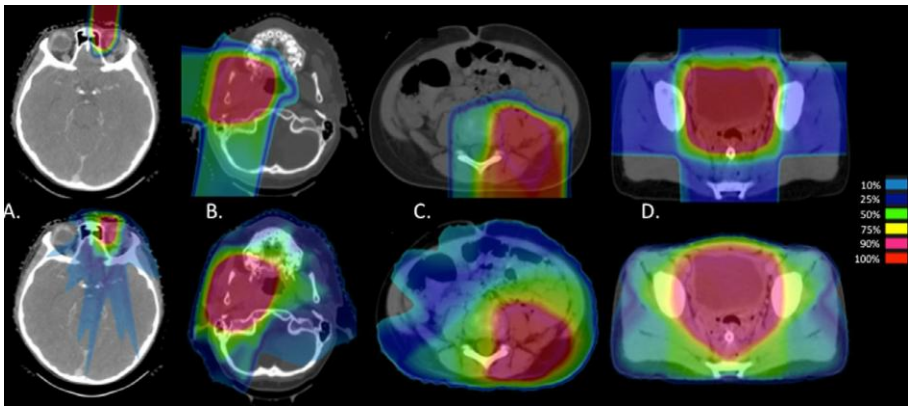
TomoTherapy vs Proton Therapy in CSI



Mascarin M et al in Posterior Fossa Tumors in Children. M. Özek , G. Cinalli, W. Maixner, C. Sainte-Rose. Editors, Springer Ed, pp363380 2015
Proton Plan Courtesy ATREP Trento

Dosimetric comparison of proton and IMRT in pediatric RMS on a prospective phase II study



Ladra et al, Radiother Oncol 113:77-83, 2014

PROTON Therapy

Both Proton and Tomo/IMRT provided satisfactory conformation and OARs sparing in complex pediatric cases.

Proton demonstrated superior target coverage, homogeneity, conformity, and OARs sparing.

In some situations (small volumes, shallow depths) Tomo provided comparable results.

Learning curve, not only for technology but also in pediatric oncology subset.

The "value" of radiotherpay process

HIGH TECH: "new technologies"
HIGH TOUCH: "special patient"

§ persone/giorno di trattamento RT

RT*	Ricavi €	Simulation	Contouring	Planning	Treatment §	*Anesthesia*
Mammella	4420	20'	30'	60'	10'	no
Prostata	5170	30'	30'	60'	12'	no
Cerebrale	6870	40'	120' 180' (fusion)	120' 180'	20'	30'
Craniospinale	7770	60'	180' 240' (fusion)	480' 600'	30'	45'

EDITORIAL Int. J. Radiation Oncology Biol. Phys., Vol. 78, No. 2, pp. 321–322, 2010

HOW SAFE IS SAFE? RISK IN RADIOTHERAPY

ERIC C. FORD, PH.D., AND STEPHANIE TEREZAKIS, M.D.

Departments of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University, Baltimore, MD

- ✓ *"Receiving radiotherapy could be compared to taking an airplane flight.*
- ✓ *It can be an uncomfortable and scary process for some people, but it is often necessary to get from point A to point B".*

The New York Times
January 24, 2010

Radiation Offers New Cures, and Ways to Do Harm

Grazie

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