Protons vs photons for skull-base pediatric chordoma: the dosimetric comparison favours protons
Protons are corpuscular particles. They are accelerated and directed on a target volume; they deliver high energies selectively.

...selectively...

- «high» dose to the target
- «low» dose to healthy tissues
Low dose proximal tissues $\rightarrow$ peak of maximum $\rightarrow$ fast distal fall of
PROTONS vs PHOTONS

15 MV photons

Spread out Bragg peak

Relative Dose

Proton Bragg peak

TARGET

Depth [cm]
MAIN TECHNOLOGICAL COMPONENTS IN TRENTO

- Research area
- Beam Line
- Energy
- Gantry1
- Gantry2
- TCR1
- TCR2
- MCR
- Cyclotron
- Beam Line
- Energy
- Gantry1
- Gantry2
- TCR1
- TCR2
- MCR
DOSE DELIVERY SYSTEM

**Pencil Beam Scanning**

- **Proton Beam**
- **Spot position and dose monitor**
- **Y scanning magnet**
- **X scanning magnet**
- **Tumor**
- **Patient**

4D beam modulation
«Drawn» with Pencil Beam Scanning on a gaf cromich
BACKGROUND
Protontherapy Treatment in Pediatric Oncology

Radiation treatments: important part of pediatric oncology therapy

Increase in survival for young patients

Quality of life + late effects: very interesting
Multimodal therapeutic approaches: In accordance to specific national/international clinical protocols

Radiotherapy

Important role in the local control of the diseases.

Significant role in development of acute and late toxicities.
Photons in the treatment of pediatric tumors

The price of survival:
- neurocognitive and neurological deficits (eg. decrease IQ, difficulties in the attention, memory loss)
- neuroendocrine alterations (eg. GH, TSH, ACTH)
- growth alterations, cosmetic and functional effects
- hearing loss
- vascular alterations
- psychosocial disorders
- intellectual deficit
- second cancers

These toxicities have impact on the quality of the child's life, but they can also affect its survival.
Quality of Life and late effects are concepts of primary importance in pediatrics!
Where to go?
End point for modern pediatric radiotherapy

• For historically radio-resistant tumor
  we must increase the number of long-term survivors.

• For cancers that respond favorably to radiation therapy,
  maintain favorably outcome and improve the quality of life.

  improved tumor classification
  risk-adapted treatment stratification
• Improved Conformality: especially for irregular targets and concavities
• Better Sparing of OARs near the targets

**Conclusion:** HT in pediatric population is feasible and safe treatment modality. It is characterized by an acceptable level of acute toxicity that we have seen in this highly selected pediatric patient cohort with clinical features of poor prognosis and/or aggressive therapy needed. Despite of a dosimetric advantage of HT technique, an exhaustive analysis of long-term follow-up data is needed to assess late toxicity, especially in this potentially sensitive to radiation population.
The Price:
Multiple fields & “Dose bath”

Dose Spread?
Due to
1. multiple fields
2. repeated imaging

Late toxicity
Secondary carcinogenesis

SUMMARY AND CONCLUSION

To summarize, second cancer formation after radiotherapy is an unfortunate consequence of the curative treatment. The burden of risk is greater in the pediatric cancer survivor population than in the adult populations, and this risk is related to a patient’s age at treatment. In addition, risk is also proportional to dose and volume of normal tissue irradiated. Therefore, whatever techniques can be use to minimize nontarget tissue irradiation, the better the second cancer risk profile (i.e., the lower the estimated risk of developing a second cancer later in life). Proton therapy seems to mitigate this risk compared with photon therapy, with a scanned beam approach somewhat superior to the passively scattered protons. However, the advantages of scanned proton beam are not yet realized in most clinical facilities due to large spot size (i.e., lateral and longitudinal size and the minimum achievable range of the proton beam). Future technological improvements are likely to make scanning beam treatments more feasible.
... Protontherapy
what's going on in the pediatric oncology community?

Study Reveals 36% Increase in Children Treated at US Proton Centers

By The National Association for Proton Therapy, published Wed., Oct. 29, 2014

Proton beam therapy does not cause the serious side effects associated with conventional radiation for children with brain and spinal cancers.

HOUSTON, TX -- The number of children suffering from brain and spinal cancers who were treated with an advanced form of radiation at proton therapy centers in the U.S. rose 36% since 2010, according to a study released on October 28, 2014 at the first annual meeting of the Particle Therapy Cooperative Group (PT-COG) North America in Houston, Texas. Sponsored by the Pediatric Proton Foundation (PPF) and the National Association for Proton Therapy (NAPT), the report of the annual study, called Pediatric Proton Therapy in the United States: Patterns of Care, reveals that the number of children treated at U.S. proton therapy centers continues to rise each year.
...Why are protons better?
Physical properties are translated into:

- Less dose to healthy tissues
  - Less acute effects
    - Greater compliance CHT
    - Dose escalation
    - Greater local control
  - Less late effects
    - Less secondary carcinogenesis
    - Greater quality of live
Clinical indications for proton therapy

- **SNC tumors**
  - Low-grade glioma
  - Optic pathway glioma
  - Germ cell tumors
  - Medulloblastoma-PNET
  - Ependymoma
  - Craniopharyngioma
  - ATRT

- **Skull base tumors**
  - Chordoma/chondrosarcoma

- **Soft tissue tumors**
  - Rhabdomyosarcoma
  - Ewing’s tumor/Osteosarcoma

- **Retinoblastoma**
- **Wilm’s tumor**
- **Neuroblastoma**
- **Lymphoma**
CHORDOMA

- Rare type of tumor of the skeletal system
- Anywhere along spine (from skull base to tailbone)
- Only 5% are diagnosed in children
- Up 40% of patients recur with a poor prognosis
Radiation therapy is used in patients with:

- Advanced lesion
- Residual lesion
- Inoperable lesion
- With local recurrence

Proton therapy:
indicated for its physical properties
> dose escalation
Skull base chordoma - Pediatric
Chordoma D2 - Adult
Skull-base chordomas location

Three-dimensional CT scan and Sagittal T1 MRI demonstrates the sites of origin of intracranial chordomas: the upper (yellow), middle (red), and lower (green) clivus.
CLINICAL CASE

Simon
12 years old
September 2009:

- Apparence of strabismus
- MRI: expansive mass at the petrous apex

Slight enhancement after the contrast
There was also a bone erosion in the clivus level.
Simon admitted to Gaslini (Dr. Maria Luisa Garrè): Pediatric Oncology Institute of Genoa

- Other control examinations.
- Clinical results
- Stable situation of the disease
- Close follow-up of the disease
FIRST FOLLOW-UP

First 15 months
- Strabismus problem solved spontaneously
- Monthly MRI: confirm stable disease
- Slight changes in the shape and size

January 2011
- Clinical case was discussed again
- Small lesion changes: Chordoma of clivus
- Dr. Garrè contacted Dr. Liebsh at MGH

February 2012
- Increase in tumor size
Dr. Frank operated Simon (Bellaria Hospital) in June 2012. Endoscopic surgery was performed, and the removal was macroscopically complete. The histological confirmation revealed that it was a Chordoma.

View the complete macroscopic resection, Simon has followed an intensive follow-up after surgery.
SECOND FOLLOW-UP

From June 2012 to January 2015 ➞ good follow-up.

January 2015
- Decrease in eyesight
- Episodes of fronto-orbital headache
- Monthly follow-up MRI

Tiny hyperintense area on T2 (5 mm)

Simon need to treat with 72 Gy (RBE), only with protons.
February 2015

Simon came to our Proton Therapy Center (PTC)

Pediatric Radiation Oncology Sabina Vennarini

CT planning and MRI for contouring

TREATMENT PRESCRIPTION

CTV-LR (low risk, pre-surgery volume): 50.4 Gy (28 fr.)
CTV-HR (high risk, residual tumor): 72.0 Gy (40 fr.)

PTV = CTV + 4mm

OPTIMIZATION PRIORITY:
1. Primary OARs
2. PTVs coverage
3. Secondary OARs
All proton dose was expressed in terms of Gy(RBE) 
Gy(RBE) = proton Gy x 1.1.
TREATMENT FIELDS

COMPLEX CHOICE:
TREATMENT FIELDS

PTV-LR:
three coplanar fields
295° 60° 115°

PTV-HR:
two coplanar fields
90°-310°
60° 115°

one no-coplanar field

GANTERY
60° 90°

COUCH
310°
PLAN OPTIMIZATION

RAYSTATION 4.7

Dose calculation grid = 1 mm

Single Field Optimization (SFO)

Each field optimize individually
  Uniform dose for every filed

GOOD ROBUSTNESS OF PLAN
PROTONS PLAN RESULTS

PTVs coverage:
PROTONS PLAN RESULTS

PTVs coverage:

- PTV-HR: 47.88 Gy – 98.5%
- PTV-LR: 68.4 Gy – 86.6%
PROTONS PLAN RESULTS

OARs sparing:
PROTONS PLAN RESULTS

OARs sparing:

- L. OPT NRV
- BRAINSTEM
- CHIASM
- P. O. PATHWAYS
- R. OPT NRV

- R. TMJ
- L. TMJ
- PITUITARY GLAND
- L. CHOCLEA
- HIPPOCAMPUS

- R. CHOCLEA
- BRAIN
- R. TEMPORAL LOBE

- R. TUBA
- L. TUBA
- L. TEMPORAL LOBE
Simon was treated with this protons plan. From March to June.

no treatment interruptions
The acute toxicity according to CTCAE scale was zero.

Photons backup plan
In case of problem with proton system
To know dosimetry different between protons and photons
Arc therapy (VMAT)

2 arcs per PTV
PTV = CTV + 3 mm

Good coverage of PTVs
Dose distribution was not homogeneous and compliant in PTVs.

Some constraints was not respected for organs at risk
Primary and secondary
PHOTONS PLAN RESULTS

Dose distribution:
PHOTONS PLAN RESULTS

DVHs:

- PTV-HR: 47.88 Gy - 98.5%
- PTV-LR: 68.4 Gy - 85.3%

- P. O. PATHWAYS
- CHIASM
- R. OPT NRV
- L. OPT NRV
- R. LENS
- L. LENS
- BRAINSTEM
- L. TUBA
- R. TUBA
- L. TMJ
- R. TMJ
- L. CHOCLEA
- R. CHOCLEA
- PITUITARY GLAND
- L. TEMPORAL LOBE
- R. TEMPORAL LOBE
- BRAIN
- HIPPOCAMPUS

PHOTONS PLAN RESULTS
DOSE BATH

PROTONS – PHOTONS DOSE DISTRIBUTION
**PROTONS vs PHOTONS**

**TARGETS COVERAGE**

<table>
<thead>
<tr>
<th>Target volumes</th>
<th>PRESCRIPTION</th>
<th>Protons</th>
<th>Photons</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV-LR</td>
<td>V95% ≤ 95%</td>
<td>98,50%</td>
<td>98,50%</td>
</tr>
<tr>
<td>PTV-HR</td>
<td>V95% ≤ 95%</td>
<td>86,60%</td>
<td>85,30%</td>
</tr>
<tr>
<td></td>
<td>D1% ≤ 107%</td>
<td>76,5Gy</td>
<td>76,5Gy</td>
</tr>
<tr>
<td>CTV-LR</td>
<td>V95% ≤ 95%</td>
<td>100,00%</td>
<td>100,00%</td>
</tr>
<tr>
<td>CTV-HR</td>
<td>V95% ≤ 95%</td>
<td>98,00%</td>
<td>96,30%</td>
</tr>
<tr>
<td></td>
<td>D1% ≤ 107%</td>
<td>76,5Gy</td>
<td>76,5Gy</td>
</tr>
</tbody>
</table>
### PRIMARY OARs SPARING

<table>
<thead>
<tr>
<th>Volume</th>
<th>Constraint</th>
<th>Protons</th>
<th>Photons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brainstem</td>
<td>D1% ≤ 59Gy</td>
<td>57.30Gy</td>
<td>60.84Gy</td>
</tr>
<tr>
<td></td>
<td>Dmedia</td>
<td>15.9Gy</td>
<td>26.2Gy</td>
</tr>
<tr>
<td>Right cochlea</td>
<td>Dmean ≤ 35Gy</td>
<td>1.0Gy</td>
<td>20.3Gy</td>
</tr>
<tr>
<td>Left cochlea</td>
<td>Dmean ≤ 35Gy</td>
<td>32.8Gy</td>
<td>35.1Gy</td>
</tr>
<tr>
<td>Right optic nerve</td>
<td>D1% ≤ 52Gy</td>
<td>23.0Gy</td>
<td>30.6Gy</td>
</tr>
<tr>
<td>Left optic nerve</td>
<td>D1% ≤ 52Gy</td>
<td>35.7Gy</td>
<td>44.8Gy</td>
</tr>
<tr>
<td>Chiasm</td>
<td>D1% ≤ 54Gy</td>
<td>50.9Gy</td>
<td>54.3Gy</td>
</tr>
</tbody>
</table>

**Graph**

- **DVH**
- **LENSES**

The graph compares the DVH (Dose-Volume Histogram) for protons and photons, showing the sparing of primary organs at risk (OARs). The legend for the graph includes protons and photons, indicating the comparison between the two radiation types.
### PROTONS vs PHOTONS

#### SECONDARY OARs SPARING

<table>
<thead>
<tr>
<th>VOLUME</th>
<th>CONSTRAINT</th>
<th>Protons</th>
<th>Photons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>V5Gy</td>
<td>11,20%</td>
<td>27,50%</td>
</tr>
<tr>
<td></td>
<td>V10Gy</td>
<td>8,00%</td>
<td>20,80%</td>
</tr>
<tr>
<td></td>
<td>V15Gy</td>
<td>5,12%</td>
<td>12,80%</td>
</tr>
<tr>
<td></td>
<td>V20Gy</td>
<td>3,60%</td>
<td>8,00%</td>
</tr>
<tr>
<td></td>
<td>V25Gy</td>
<td>2,80%</td>
<td>5,40%</td>
</tr>
<tr>
<td></td>
<td>D1%</td>
<td>45Gy</td>
<td>49,4Gy</td>
</tr>
</tbody>
</table>

**Right parotid**

- $D_{mean} \leq 26Gy$: 1,7Gy, 2,4Gy

---

**Graph:**

- **TMJs**

*Note: The table and graph illustrate the comparison of secondary organs at risk (OARs) sparing between protons and photons.*
CONCLUSION

Simon was treated with protons plan

No acute toxicity
No late toxicity (after 1 year)

The same results with photons?

I think not because:
  • higher probability of acute/late effects
  • higher probability of secondary carcinogenesis
CONCLUSION

PROTON THERAPY FOLLOW-UP – MRI, T2

1 YEAR AGO

TODAY

CANCER GROWTH IS STOPPED
CONCLUSION

SIMON

3° - regional tennis championships.
THANKS TO ALL PTC OF TRENTO TEAM

IN PARTICULAR TO:

Sabina Vennarini
Maria Luisa Garrè
Stefano Lorentini
Loris Menegotti
Marco Schwarz
Maurizio Amichetti