Effectiveness and Safety of Spot Scanning Proton Radiation Therapy for Skull Base Tumors: First Long Term Report of the PSI Experience

Carmen Ares, Antony J Lomax, Eugen B Hug, Alessandra Bolsi, Beate Timmermann, Hans Peter Rutz, Adolf Coray, Eros S Pedroni, Gudrun Goitein
Purpose

To evaluate the **effectiveness** and **safety** of **spot scanning** proton radiation therapy in chordomas and chondrosarcomas of the skull base.
Introduction

Skull Base Chordomas and Chondrosarcomas:
PSI Experience 1998 - 2005

During the period 1998 – 2005 in addition to eye treatments, chordomas and chondrosarcomas constituted the majority of our patients
Skull base tumors: PSI experience

Material and Methods

• N = 64 patients (Oct-98 Nov-05)
  – Chordoma 42 (65%)
  – Chondrosarcoma 22 (34%)

• Mean age 44.5 years

• Mean follow-up 38 months (14 - 92 months)
Material and Methods

Skull base tumors: PSI experience

• Prescription dose (mean)
  (at 2 Gy (RBE) per fraction, 4 fractions per week)

  – Chordoma (Ch) 74 Gy (RBE) (range 68 - 74)
  – Chondrosarcoma (ChSa) 68 Gy (RBE) (range 64 - 74)

• 5 patients mixed photons/protons (4 Ch, 1 ChSa)

• mean GTV volume
  – Ch 27 cc
  – ChSa 23 cc
## Skull base tumors: PSI experience

### Dose constraints for organs at risk

<table>
<thead>
<tr>
<th>OAR</th>
<th>Dmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brainstem surface</td>
<td>64 Gy (RBE)</td>
</tr>
<tr>
<td>Brainstem center</td>
<td>53 Gy (RBE)</td>
</tr>
<tr>
<td>Optic Chiasm</td>
<td>60 Gy (RBE)</td>
</tr>
<tr>
<td>Optic Nerves</td>
<td>60 Gy (RBE)</td>
</tr>
</tbody>
</table>
Skull base tumors: PSI experience

Local control definition

• Local control defined as
  - radiological control by MRI ± CT

• Local failure defined as
  - radiological tumor progression or
  - clinical symptomatic progression confirmed radiologically
### Failures and deaths

<table>
<thead>
<tr>
<th></th>
<th>Chordoma (n = 42)</th>
<th>Chondrosarcoma (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Local failure</strong></td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>local progression</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>NED</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Brainstem compression</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1*</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Abutment</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* patient with surgical pathway failure

P = 0.0077
Skull base tumors: PSI experience

Example of chondrosarcoma with subsequent local relapse

Pre-Proton-RT

Brainstem compression

GTV

V95 → 48%
Skull base tumors: PSI experience

Local control

Actuarial Local Control

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>3 years</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chordomas</td>
<td>87 %</td>
<td>81 %</td>
</tr>
<tr>
<td>Chondrosarcomas</td>
<td>94 %</td>
<td>94 %</td>
</tr>
</tbody>
</table>

P=0.08

Chordoma, N=42
Chondrosarcoma, N=22

P=0.25

P=0.23

Overall Survival

Time to local failure

Time to change of white matter

Time to event

Carmen Ares, Center for Proton Radiation Therapy

PTCOG - May 22, 2008
Skull base tumors: PSI experience

Disease Specific Survival

Disease Specific Survival

Disease Specific Survival

3 years     5 years

Chordomas     90%      81%

Chondrosarcomas     100 %    100 %
Skull base tumors: PSI experience

Prognostic factor for LC in chordoma:

Residual tumor volume

![Graph showing Prognostic factor for LC in chordoma: Residual tumor volume with GTV<25 and GTV>25.]
## Skull Base Chordomas: Comparison of Literature

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Radiation</th>
<th>Mean dose</th>
<th>LC 3-yr</th>
<th>LC 5-yr</th>
<th>LC 10-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Munzenrider, 1999</td>
<td>290</td>
<td>PT, RT</td>
<td>76</td>
<td>73</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Terahara, 1999</td>
<td>115</td>
<td>PT, RT</td>
<td>69</td>
<td>59</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Hug, 1999</td>
<td>58</td>
<td>PT, RT</td>
<td>71</td>
<td>67</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Noel, 2003</td>
<td>67</td>
<td>PT, RT</td>
<td>67</td>
<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schulz-Ertner, 2007</td>
<td>96</td>
<td>Carbon, RT</td>
<td>60*</td>
<td>81</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Igaki, 2004</td>
<td>13</td>
<td>PT, RT</td>
<td>72</td>
<td>67</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Weber, (PSI) 2005</td>
<td>18</td>
<td>PT</td>
<td>74</td>
<td>87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ares, (PSI) 2007**</td>
<td>42</td>
<td>PT</td>
<td>74</td>
<td>87</td>
<td>81</td>
<td></td>
</tr>
</tbody>
</table>

*at 3.0 CGE per fraction
** to be published
## Skull Base Chondrosarcomas: Comparison of Literature

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Radiation</th>
<th>Mean dose</th>
<th>LC 3-yr</th>
<th>LC 5-yr</th>
<th>LC 10-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Munzenrider, 1999</td>
<td>229</td>
<td>PT, RT</td>
<td>72</td>
<td>98</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Hug, 1999</td>
<td>25</td>
<td>PT, RT</td>
<td>71</td>
<td>92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johson, 2002</td>
<td>58</td>
<td>PT, RT</td>
<td>71</td>
<td>91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noel, 2004</td>
<td>26</td>
<td>PT, RT</td>
<td></td>
<td></td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Schulz-Ertner, 2007</td>
<td>54</td>
<td>Carbon, RT</td>
<td>60*</td>
<td>96</td>
<td>89 @4y</td>
<td></td>
</tr>
<tr>
<td>Weber, (PSI) 2005</td>
<td>11</td>
<td>PT</td>
<td>68</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ares, (PSI) 2007**</td>
<td>22</td>
<td>PT</td>
<td>68</td>
<td>94</td>
<td>94</td>
<td></td>
</tr>
</tbody>
</table>

*at 3.0 CGE per fraction
** to be published
Skull base tumors: PSI experience

Radiation induced late toxicity (CTCAE v3.0)

- Asymptomatic MRI white matter changes: 5 patients
  (= G1 neurologic toxicity)

- High grade late toxicity (all Ch): 4 patients
  - optic pathway G 4 → 1 patient (unilateral blindness)
    G 3 → 1 patient (unilateral visual deficit, steroid dependent)
  - neurologic G 3 → 2 patients (symptomatic brain necrosis)

- Any patient presented brainstem toxicity
Skull base tumors: PSI experience

Radiation induced toxicity (CTCAE v3.0)

• Actuarial 5-year freedom of high grade late toxicity 94%

  – Due to the small number of events no risk factors predictive of high grade toxicity were identified
Skull base tumors: PSI experience

Radiation induced toxicity (CTCAE v3.0)

• High grade late toxicity (≥ grade 3)
  • Grade 3 unilateral optic nerve neuropathy
    – developed 20 months after treatment
  • Grade 4 unilateral optic nerve neuropathy
    – 12 months after treatment
    (preexistent unilateral visual field deficits due to tumor involvement around the optic nerve)
  • 2 cases of Grade 3 temporal lobe brain necrosis
    – at 12 and 19 months after treatment
G1 - Neurologic toxicity example

Pre-PT
10/05
T1Gd
05/07
T1Gd
08/07
G3 - Brain necrosis example

PT 08/05

T1Gd 26.02.07

Flair 26.02.07

T1Gd 26.09.07

T2 26.09.07
Conclusions - 1

• Toxicity rates similar to passive scattering based proton-radiotherapy series, with comparable target definition, dose prescription and normal organ tolerance levels.

• As the majority of late toxicities are commonly detected during the 2 first years after RT, our data demonstrate the safety and efficacy of Spot-Scanning based Proton-Radiotherapy technology delivery for skull base tumors.
Skull base tumors: PSI experience

Conclusions - 2

• Established *outcome data for a cohort of patients* treated homogeneously, that will be the *basis for introducing new technologies* and *develop new treatment algorithms*.
Thank you for your attention