reRadiotherapy in Head and Neck Cancers

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Need for Re-Treatment

- Cumulative estimated five year incidence of loco regional relapse is 29-31% in high risk patients.
  
  Bernier J, Cooper JS, Pajak TF et al.  

- Risk of second cancers which is about 5% per year, the incidence being between 16-30%.
  
  Haughey BH et al.  

- Longer survival: Probability of developing
  - Second Primary Tumors
  - Loco-regional recurrences
Re-treatment: Should Resi/ recc disease be treated?

Median survival (A) and 5-year overall survival (B) outcomes by treatment modality. *Largely palliative population.

Prognostic Factors (Prior to Re-RT)

Prognostic Factors for Survival After Salvage Reirradiation of Head and Neck Cancer

Tawee Tanweeyanon, Tapan Padhya, Judith McCaffrey, Weiwei Zhu, David Boulware, Ronald DeConti, and Andrea Trotti

Purpose
Patients who develop recurrent or new primary head and neck cancer in a previously irradiated site have poor prognosis. Reirradiation is a treatment option, although it is associated with substantial toxicities. We investigated potential prognostic factors, including comorbidity and pre-existing organ dysfunction, for survival after reirradiation.

Methods
Institutional electronic records of patients treated with reirradiation between January 1998 and 2008 were reviewed. Comorbidity was assessed by Charlson index and Adult Comorbidity Evaluation-27 (ACE-27) grading. Organ dysfunction was defined as feeding tube dependency, functioning tracheostomy, or soft tissue defect.

Results
There were 103 patients, including 46 patients who underwent salvage surgery before reirradiation. Median progression-free and overall survivals were 12.1 months (95% CI, 9.7 to 16.6) and 19.3 months (95% CI, 13.9 to 29.9), respectively. Significant comorbidity was present in 36% of patients by Charlson index and 24% by ACE-27. Baseline organ dysfunction was present in 37% of patients. Median overall survivals were 5.5 months among those with both organ dysfunction and comorbidity per Charlson index, and 4.9 months per ACE-27, compared with 59.6 and 44.2 months, respectively, among the patients with neither organ dysfunction nor comorbidity (P < .001 and < .001). Other independent prognostic factors were interval from previous radiation, recurrent tumor stage, tumor bulk at reirradiation, and reirradiation dose. A nomogram to predict the probability of death within 24 months after reirradiation was developed (concordance index = 0.75).
Prognostic Factors (Prior to Re-RT)

Nomogram: Prediction of death within 24 months after re-irradiation based on retrospective analysis.

- **Co-morbid disease** based on the Charlson index
- **Organ dysfunction** prior to re-irradiation
- Median OS among patients with none was 59.6 months vs 5.5 months with no survivors beyond 2 years of follow up in pts with both risk factors. (p:0.001)
- **Isolated neck recurrence** did better
- **Tumour bulk** > 60 cm³ have a poorer prognosis
- **Time interval** between completion of previous therapy and initiation of re-irradiation.

*Tanvetyanon et al, J Clin Oncol, 2009 Apr 20;27(12):1983-91*
Fig 2. Nomogram predicting probability of death within 24 months after re-irradiation. Comorbidity, any comorbid disease based on Charlson index (congestive heart failure, history of myocardial infarction, peripheral vascular disease, cerebrovascular disease, dementia, hemiplegia, chronic obstructive pulmonary disease, connective tissue disease, moderate or severe renal insufficiency, diabetes, ulcer disease, liver disease, leukemia, lymphoma, active solid tumor, or AIDS); Organ dysfunction, feeding tube dependency, functioning tracheostomy, or soft tissue defect (fistula, uncovered wound, osteonecrosis); isolated neck recurrence, tumor present in the neck without measurable mucosal tumor at salvage surgery (if applicable) or re-irradiation; Tumor bulk, sum of the maximal unidimensional diameter of tumor at the neck plus mucosal lesion at the time of re-irradiation; Time interval, interval between completion of previous radiation and initiation of re-irradiation. To read the nomogram, obtain the value of each variable and draw a straight line up until this intersects the line labeled as “points”. That value at the point of intersection denotes the number of points incurred. By repeating this process for each factor, a points score for each variable is obtained and accumulated. Finally, locate the value of the total points on the horizontal line labeled as “total points” and draw a straight line down, the estimated probability of survival at 24 months is indicated, ranging from 0 to 1.0.
Re-irradiation: Issues

- Patient selection
- Combined treatments, time interval
- Target volumes
  - Elective volumes
- OAR doses: Spinal cord
- Toxicities
- Fractionation:
  - Conventional or altered
  - Lower late sequelae?
  - Dose escalation?
- Technique
- Dose
Patient Selection: Things we need to know

- Adequate restaging:
  - Appropriate imaging & clinical information
- Multidisciplinary evaluation
- Radiotherapy details:
  - Time interval
  - Previously received dose/ no of fractions/ overall treatment time
  - Fractionation
    - BED, EQD2.
    - Hyperfractionation, Accelerated fractionation, Hypofractionation
  - Sequelae of previous treatment, in particular RT
  - Volume and dose details of OARs at 1st RT
  - Technique of RT
- Age, Presence of co-morbidity, life expectancy of the patient
ACR Appropriateness Criteria

• Careful restaging imaging
• Detailed history and assessment of life expectancy, access to the prior radiotherapy details, and evaluation of:
  – Comorbidities.
  – Performance status
  – Speech and swallowing function.
  – Sequelae of previous treatment (eg, fibrosis, carotid stenosis, osteoradionecrosis, or other severe toxicity).
• Local control higher: At least 60 Gy.
• Addition of chemotherapy: To estimate the benefit individually.
• Multidisciplinary approach with skilled oncology team.
• Advanced radiation techniques to be used.

To make life simpler

Selection of patients for re-treatment:
- Assessment of: results of diagnostic tests
- Comorbidity (Charlson comorbidity index, ACE-27)
- Toxicity of previous therapies
- Time interval from previous treatment

Sustainable treatment or best supportive care

Yes, operable + good health status
Salvage surgery

Yes, inoperable
Reirradiation
- Chemotherapy/biotherapy
  - Radiotherapy dose ≥60 Gy
  - New radiotherapy techniques

Adjuvant

High-risk factors:
- Non-radical surgery and/or
- Extracapsular extension

Adjuvant treatments

• Results best with combined modality management

• Chemo – Radiation
  – Definite - More acute toxicity
  – Uncertain – more late toxicity?
    affects normal tissue recovery?

• Surgery + PORT/CT-RT
  – Multimodality treatment more complications
  – Tissue planes are obscured by iatrogenic fibrosis
  – Compromises vascularity, may expose bone or neural tissues
  – Major issue for late tissue toxicity repair
<table>
<thead>
<tr>
<th>Type of Modality</th>
<th>Durable Complete Response Rate (at 2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (with R-0 Resection)</td>
<td>15 %</td>
</tr>
<tr>
<td>Surgery (R1/R2 resection)</td>
<td>Very poor</td>
</tr>
<tr>
<td>Surgery-&gt;RT/CTRT</td>
<td>20%</td>
</tr>
<tr>
<td>RT</td>
<td>RT / CTRT</td>
</tr>
<tr>
<td>CT</td>
<td>CT / Targeted therapy</td>
</tr>
<tr>
<td>BSC</td>
<td>Best Supportive Care</td>
</tr>
</tbody>
</table>

Annals of Oncology: 21 (Suppl 7) vii252-261, 2010
Stage wise: Results

Survival, quality of life, and complication outcomes by recurrent stage.¹

• Trial not powered to detect difference in OS

• Important note: More than half had adverse risk factors. Salvage CTRT was given in 25% of WS arm

• However identification of high risk group was crucial for optimising results & reducing toxicity

Target Volumes

- Late radiation-induced morbidity ↑ with CTRT and will increase with larger volumes irradiated.  
  
  *Langlois et al. 1985*

- Elective nodal irradiation:
  - Questionable in view of late sequelae
  - Primary in-field recurrences
  - Uncertainty with SPT

- Unpredictable pattern of recurrences with altered lymphatic pathways.

- Influence outcome of reRT: Disease control & morbidity
Target Volumes

- Retrospective Study
- N: 106
- Definitive Re-RT (3DCRT/IMRT) with/without CTRT
- Conv/HyperFr/Acc RT
- Target :
  - GTV with 0.5 cm margin
  - no prophylactic LN/Submucosal RT.
- Median Dose: 68 Gy
- 2 year Survival: 40%. LRC: 23%.
- All LRF within GTV except for 2 patients (4%)
- 29% ≥ Gr 3 Toxicities

## Target Volumes

<table>
<thead>
<tr>
<th>Series</th>
<th>N</th>
<th>Targets+Margins (cm)</th>
<th>Median Re-RT Dose (Gy)</th>
<th>%Late severe toxicity</th>
<th>% 2yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spencer</td>
<td>79</td>
<td>GTV+Min 2</td>
<td>60</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>Salama</td>
<td>114</td>
<td>GTV+1+Nodes</td>
<td>64</td>
<td>18</td>
<td>22 (3yr)</td>
</tr>
<tr>
<td>Lee</td>
<td>105</td>
<td>GTV+(1-2)</td>
<td>59.4</td>
<td>11</td>
<td>37</td>
</tr>
<tr>
<td>De Crevoiser</td>
<td>169</td>
<td>GTV+(1.5-2)</td>
<td>65</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Langer</td>
<td>99</td>
<td>GTV+2+Nodes</td>
<td>65</td>
<td>38</td>
<td>25</td>
</tr>
<tr>
<td>Sachaefer</td>
<td>32</td>
<td>GTV+2</td>
<td>40-50</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Kramer</td>
<td>38</td>
<td>GTV+2</td>
<td>50-60</td>
<td>38</td>
<td>35</td>
</tr>
</tbody>
</table>

OAR Tolerances (Spinal Cord)

• Re-RT of the full cord cross-section at 2 Gy per day after prior conventionally fractionated RT: cord tolerance appears to increase at least 25% 6 months after the initial course of RT based on animal and human studies

• Maximum repair upto 50-35% at 2yrs, minimal repair thereafter

• For partial cord irradiation as part of spine radiosurgery, maximum cord dose of 13 Gy in a single fraction or 20 Gy in three fractions appears associated with a <1% risk of injury

• Cumulative dose to SC is kept below 50 Gy in most series.
OAR Tolerances (Spinal Cord)

- Nieder and coworkers, 2005
- Re RT of 40 patients from 8 different reports for cervical spine
- Recalculated BED by LQ model a/b=2 Gy for cervical spine
- Cumulative doses: 108 - 205 Gy (Median: 135 Gy)
- Myelopathy seen in 11 patients (median: 11 mths, range: 4-25 mths)
  - 1 course of RT of 102 Gy (9)
  - Retreated before 2 months (2)
- < 2 risk factors: no myelopathy even with higher BEDs
- The risk of myelopathy is probably associated with
  - cumulative BED
  - Greatest BED of all treatment series
  - Interval between 2 treatments
Table 1. Summary of published reports of cervical spinal cord myelopathy in patients receiving conventional radiotherapy (18)

<table>
<thead>
<tr>
<th>Institution</th>
<th>Dose (Gy)</th>
<th>Dose/fraction (Gy)</th>
<th>Cases of myelopathy/total number of patients</th>
<th>Probability of myelopathy*</th>
<th>2-Gy dose equivalent†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake Forest (19)</td>
<td>60</td>
<td>2</td>
<td>1/12</td>
<td>0.090</td>
<td>60.0</td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>1.63</td>
<td>0/24</td>
<td>0.000</td>
<td>56.6</td>
</tr>
<tr>
<td>Caen (5)</td>
<td>54</td>
<td>3</td>
<td>7/15</td>
<td>0.622</td>
<td>72.8</td>
</tr>
<tr>
<td>Brookhaven (20)</td>
<td>19</td>
<td>9.5</td>
<td>4/13</td>
<td>0.437</td>
<td>68.6</td>
</tr>
<tr>
<td>Florida (21)</td>
<td>47.5</td>
<td>1.9</td>
<td>0/211</td>
<td>0.000</td>
<td>45.0</td>
</tr>
<tr>
<td></td>
<td>52.5</td>
<td>1.9</td>
<td>0/22</td>
<td>0.000</td>
<td>49.8</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>2</td>
<td>2/19</td>
<td>0.118</td>
<td>60.0</td>
</tr>
<tr>
<td>Yugoslavia (22)</td>
<td>65</td>
<td>1.63</td>
<td>0/19</td>
<td>0.000</td>
<td>56.6</td>
</tr>
</tbody>
</table>
Carotid Blow Out Syndrome

- Conventional RT schedule: 2.6%
- Interval from start of re-RT: 7.5 months (0-56 months) of which 76% are fatal
- No impact of previous salvage surgery or concurrent CT
- Standard fractionation., hyperfract. < accelerated hyperfract (1.3 vs 4.5 p=0.02)
- Hypofractionated schedule: 10-15%

Risk of developing CBS

Yamazaki et al, Radiother Oncol. 2013 Jun;107(3):305-9
Toxicities

• Dysphagia: Exceed tolerance to DARS
  Disease progression

• Trismus: (15-37%): Pterygoid musculature fibrosis

• Soft tissue necrosis (20-40%): Function of technique, dose, other treatment

• Osteoradionecrosis (8-11%): with cum dose of 130-135 Gy

• Temporal lobe necrosis: Variable incidence depending on the site of primary, dose received, technique
## Fractionation

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>RT</th>
<th>Chemo</th>
<th>Results</th>
<th>Severe Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dawson (2001)</td>
<td>40</td>
<td>1.8-2.0 Gy/fr (or 1.2 Gy BID)</td>
<td>33%</td>
<td>2 yr LRC 29%</td>
<td>Acute 10%</td>
</tr>
<tr>
<td>Michigan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee (2007)</td>
<td>105</td>
<td>1.8-2.0 Gy/fr (or 1.2 Gy BID)</td>
<td>33%</td>
<td>2 yr LRC 42%</td>
<td>Acute Gr3+ 23%</td>
</tr>
<tr>
<td>MSKCC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulman (2009)</td>
<td>74</td>
<td>2 Gy/Fr</td>
<td></td>
<td>2 yr LRC 64%</td>
<td>Late: 20% severe</td>
</tr>
<tr>
<td>MDACC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Popovtzer (2009)</td>
<td>66</td>
<td>1.8-2.0 Gy/fr (or 1.25 Gy BID)</td>
<td>33%</td>
<td>2 yr LRC 27%</td>
<td>Acute 10%</td>
</tr>
<tr>
<td>Michigan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duprez (2009)</td>
<td>84</td>
<td>2.0-2.5 Gy/Fr</td>
<td>20%</td>
<td>2 yr LRC 48%</td>
<td>Acute: 30% Gr3+</td>
</tr>
<tr>
<td>Ghent</td>
<td></td>
<td>Median 69Gy IMRT</td>
<td></td>
<td>5 yr LRC 40%</td>
<td>Late: 13% Gr3+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 yr OS 35%</td>
<td>No deaths</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5 yr OS 20%</td>
<td></td>
</tr>
</tbody>
</table>

Various fractionation regimens used:
- Split course
- Continuous
- Once daily vs hyperfractionation
- Hyperfractionation with breaks (RTOG studies)

Conventional and hyperfractionated schedules preferred

No definite advantage of one over the other.
Techniques

- In a recent Canadian Survey on Re-RT,
  - Most desirable for Re-RT: Brachytherapy
  - Highly conformal external irradiation techniques


- With the availability of advanced imaging like PET, MRI & option of image guided delivery of treatment, hypofractionation also a feasible modality.
Conformal RT Techniques

- Possible to deliver higher, clinically meaningful doses
- Superior OAR sparing
- Image guidance, reduce margins
- Acceptable toxicity
- Reasonable disease control

Choice:
- Patient and tumor characteristics
- Expertise of the treating team
- Infrastructure available
• Retrospective Review
• Single Institution Study
• Period: July 1996 – September 2005
• N = 105
• Median follow-up: 35 months
• Median Prior RT dose: 62 Gy (28 – 78 Gy)
• Median Re-RT dose: 59.4 Gy (30 – 70 Gy)
• In Re-RT, Concurrent chemotherapy used: 43%
  Sx prior to ReRT: 36%
<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>Unadjusted HR (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>105</td>
<td>1.01 (0.98–1.03)</td>
</tr>
<tr>
<td>Re-RT location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary only</td>
<td>63</td>
<td>Reference</td>
</tr>
<tr>
<td>Other</td>
<td>42</td>
<td>1.08 (0.63–1.83)</td>
</tr>
<tr>
<td>Aggressiveness of disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First recurrence followed by re-RT</td>
<td>60</td>
<td>Reference</td>
</tr>
<tr>
<td>Multiple recurrences prior to re-RT</td>
<td>45</td>
<td>1.51 (0.89–2.55)</td>
</tr>
<tr>
<td>Surgery (compared to no surgery)</td>
<td>36</td>
<td>0.61 (0.34–1.08)</td>
</tr>
<tr>
<td>Chemotherapy (compared to no chemotherapy)</td>
<td>75</td>
<td>2.03 (1.07–3.86)</td>
</tr>
<tr>
<td>RT technique</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-IMRT</td>
<td>31</td>
<td>Reference</td>
</tr>
<tr>
<td>IMRT</td>
<td>74</td>
<td>0.36 (0.21–0.61)</td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50 Gy</td>
<td>21</td>
<td>Reference</td>
</tr>
<tr>
<td>≥50 Gy</td>
<td>84</td>
<td>0.36 (0.20–0.65)</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>21</td>
<td>Reference</td>
</tr>
<tr>
<td>Pharynx</td>
<td>30</td>
<td>2.20 (0.9–4.91)</td>
</tr>
<tr>
<td>Other</td>
<td>54</td>
<td>1.44 (0.71–2.94)</td>
</tr>
</tbody>
</table>
Fig. 4. Kaplan-Meier estimate of 2-year locoregional progression-free probabilities for patients with and without surgical resection before re-irradiation.
Fig. 3. Kaplan-Meier estimate of 2-year locoregional progression-free probabilities for intensity-modulated radiation therapy (IMRT) vs. nonintensity-modulated radiation therapy patients.
Outcomes

• Sx+Post-op Re-RT > Re-RT + CT > Re-RT
• Acute RT toxicity:
  - 23%: Acute Grade-3 toxicities (Skin, Mucosa)
  - 11%: severe Grade-3/4 complications (trismus, stricture, dysphagia, cranial neuropathy, temporal lobe necrosis, hearing loss, blindness)
## ReRT Technique

<table>
<thead>
<tr>
<th>Author</th>
<th>RT Technique Re-RT dose</th>
<th>Pre-RT dose</th>
<th>N FU duration</th>
<th>Results PFS/OS</th>
<th>Toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wang et al IJROBP 1987</td>
<td>Conventional 50 Gy</td>
<td></td>
<td>51 (rT1/T2)</td>
<td>LRC 50% @5years</td>
<td>NA</td>
</tr>
<tr>
<td>Nancy LEE et al IJROBP 2007</td>
<td>Conv:30% IMRT:70%</td>
<td>105</td>
<td></td>
<td>LRC 20% LRC 52%@ 2 years</td>
<td>23% G-3 12% G-4</td>
</tr>
<tr>
<td>Sulman et al IJROBP 2009</td>
<td>IMRT 60Gy</td>
<td>78</td>
<td></td>
<td>LRC 64%, OS 58%</td>
<td>20% G3/4</td>
</tr>
<tr>
<td>Kwang et al IJROBP 2008</td>
<td>FSRT, Cyberknife RS 30Gy/3-5fx/3-5days</td>
<td>N=36, Sites =44</td>
<td>80% LRC @ 17months</td>
<td>13/44 : acute G3/4 3/44:Late G3</td>
<td></td>
</tr>
</tbody>
</table>
# RTOG 96-10 vs 99-11

<table>
<thead>
<tr>
<th>Parameters</th>
<th>RTOG-9610 (Spencer et al.)</th>
<th>RTOG-9911 (Langer et al.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ReRT dose schedule</td>
<td>1.5Gy, bid to 60 Gy</td>
<td>1.5Gy, bid to 60 Gy</td>
</tr>
<tr>
<td>Target volume</td>
<td>Tumor + 2 cm</td>
<td>Tumor + 2 cm</td>
</tr>
<tr>
<td>RT technique</td>
<td>2D/ 3D</td>
<td>3D/ IMRT</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>5FU, HU</td>
<td>Cisplat, Pacli</td>
</tr>
<tr>
<td>OS (2yrs)</td>
<td>15.2%</td>
<td>26%</td>
</tr>
<tr>
<td>Ac Toxicity: Gr3 Gr4</td>
<td>38% 17.7%</td>
<td>50% 28%</td>
</tr>
<tr>
<td>Late Toxicity</td>
<td>9.4%</td>
<td>34%</td>
</tr>
</tbody>
</table>
RTOG 96-10 vs 99-11

Kaplan-Meier estimates of overall survival for Radiation Therapy Oncology Group protocols 9911 and 9610.

<table>
<thead>
<tr>
<th></th>
<th>1 year (%)</th>
<th>95% CI</th>
<th>2 year (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>9911</td>
<td>50.2</td>
<td>40.0 to 59.6</td>
<td>25.9</td>
<td>17.3 to 35.3</td>
</tr>
<tr>
<td>9610</td>
<td>47.1</td>
<td>30.9 to 52.5</td>
<td>16.9</td>
<td>08.5 to 25.3</td>
</tr>
</tbody>
</table>

P = .044
Particle beam radiotherapy

Re-irradiation with scanned charged particle beams in recurrent tumours of the head and neck: Acute toxicity and feasibility

Alexandra D. Jensen\textsuperscript{a,*}, Anna Nikoghosyan\textsuperscript{a}, Malte Ellerbrock\textsuperscript{b}, Swantje Ecker\textsuperscript{b}, Jürgen Debus\textsuperscript{a}, Marc W. Münter\textsuperscript{a}

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ARTICLE INFO

Article history:
Received 30 October 2010
Received in revised form 21 March 2011
Accepted 3 May 2011
Available online 2 June 2011

Keywords:
Re-irradiation
Head and neck cancer
Carbon ion therapy
Toxicity

ABSTRACT

\textit{Background:} Treatment of surgically unresectable recurrence in the head and neck region remains a therapeutic problem with the only curative option being a second course of radiation with a tumouricidal dose. We report initial toxicity and efficacy of charged particle therapy in this situation.

\textit{Methods:} Treatment-related side-effects of patients treated with charged particle beams for recurrent tumours of the head and neck were prospectively collected and patient data was retrospectively analysed with regard to toxicity and efficacy of the treatment according to CTCAE v. 4.03 and RECIST.

\textit{Results:} Treatment was tolerated well without any severe acute toxicity. In non-chordoma/chondrosarcoma patients, overall response rate was 53.3\% at 8 weeks post RT. 4/5 chordoma/chondrosarcoma patients showed no signs of further tumour progression.

\textit{Conclusion:} Initial experience of re-irradiation with scanned particle beams in recurrent tumours of the head and neck seems feasible and encouraging. Further follow-up is needed to investigate potential late effects.

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### Tumour site

<table>
<thead>
<tr>
<th>Tumour site</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base of skull</td>
<td>8 pts</td>
</tr>
<tr>
<td>Paranasal sinus</td>
<td>3 pts</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>2 pts</td>
</tr>
<tr>
<td>Posterior fossa</td>
<td>1 pt</td>
</tr>
<tr>
<td>External auditory canal</td>
<td>1 pt</td>
</tr>
</tbody>
</table>

### Histologies

<table>
<thead>
<tr>
<th>Malignant salivary gland tumours</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>6 pts</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>1 pt</td>
</tr>
<tr>
<td>Acinic cell carcinoma</td>
<td>1 pt</td>
</tr>
<tr>
<td>Chordoma</td>
<td>4 pts</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>2 pts</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>2 pts</td>
</tr>
</tbody>
</table>

| Age at 2nd RT                   | 51 a (median) [32–71a] |
| Follow-up                       | 4 months (median) [1.33–11.1] |

### Radiotherapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median</th>
<th>[min–max]</th>
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<tbody>
<tr>
<td>Interval between RT</td>
<td>73.03 months</td>
<td>[12.2–349.6]</td>
</tr>
<tr>
<td>Prior RT dose</td>
<td>67 GyE</td>
<td>[38–72]</td>
</tr>
<tr>
<td>Re-RT dose</td>
<td>44.8 GyE</td>
<td>[36–72.7]</td>
</tr>
<tr>
<td>Cumulative dose</td>
<td>111.8 GyE</td>
<td>[91.2–132.7]</td>
</tr>
<tr>
<td>Treatment characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTV1 (boost) volume</td>
<td>61.1 ml</td>
<td>[9.2–284.1]</td>
</tr>
</tbody>
</table>

### Response 8 weeks post RT.

<table>
<thead>
<tr>
<th>Early response according to RECIST</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>CR</td>
<td>1 pt</td>
</tr>
<tr>
<td>PR</td>
<td>5 pts</td>
</tr>
<tr>
<td>SD</td>
<td>8 pts</td>
</tr>
<tr>
<td>PD</td>
<td>1 pts</td>
</tr>
<tr>
<td>Not applicable</td>
<td>1 pt</td>
</tr>
</tbody>
</table>

### Acute toxicity.

<table>
<thead>
<tr>
<th>Acute toxicity CTC v. 4</th>
<th>I</th>
<th>II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>2 pts</td>
<td>1 pt</td>
</tr>
<tr>
<td>Mucositis</td>
<td>3 pts</td>
<td>3 pts</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>0</td>
<td>1 pt</td>
</tr>
<tr>
<td>Xerostomia</td>
<td>1 pt</td>
<td></td>
</tr>
<tr>
<td>Alterations of taste</td>
<td></td>
<td>1 pt</td>
</tr>
</tbody>
</table>
ReRT Doses

Pomp et al (1988)
- showed benefit of > 50 Gy in tumor control rates

- N: 124 patients
- Re-RT alone or in combination with induction or concomitant chemotherapy
- Response rate: > 40 Gy vs < 40 Gy (91% vs. 33%; P: 0.001)

Tanvetyanon et al (2009)
- dose > 50 Gy had a significantly better OS < 50 Gy (P: 0.002)

- Dose < Vs > 58 Gy - 2 yr OS was 8% vs 35%
**Prognostic Factors**

- **Time interval** between the development of recurrence & Re-RT:
  - Median survival for those treated >12 months vs < 12 months of 9.8 vs 5.8 months, p =0.036
  

- **Volume of tissue** requiring reirradiation:
  - A reflection of the disease volume
  - 2 yr OS of Vol < 650cc : 25% VS Vol > 650cc: 18%
  

- **Subsite:**
  - Nasopharyngeal and Laryngeal Sites have better prognosis.
  
  *Yu et al, Head Neck. 2005 May;27(5):397-405*  
  *Lee et al, Int j radiat oncol biol phys 2007;68:731-740*
Problems....(Interpreting Prognostic factors)

- Mostly retrospective studies:
  - different eligibility criteria across the studies

- Heterogeneity in reporting outcomes:
  - Local relapse, regional relapse, or second primary tumors might be included

- Inadequate numbers to detect clinically relevant prognostic factors

- Different treatment regimens: spanning long time periods
  - Evolution in RT techniques
  - Better imaging

- No NTCP models available in Re-RT setting to predict the side effects.
  - Accountability for Dose, time and volume of re-irradiated tissue
Conclusions

- Patient selection is the cornerstone to successful outcome
- Ascertain details of previous RT
- Optimal treatment of localized recc: Combined modality whenever feasible

Issues with ReRT:
- Longer time intervals: Superior outcomes
- Target volumes: No Elective volumes, use of functional imaging
- OAR doses: To be respected, as low as achievable
- Fractionation: Conventional or altered
- Technique: Conformal
- Dose: 50 – 60Gy

- Attention to supportive care & QOL issues
- Diligent documentation & reporting
THANK YOU