Pencil beam scanning proton radiotherapy in the treatment of nasopharyngeal cancer

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INTRODUCTION
Radiotherapy plays a crucial role in the treatment of nasopharyngeal cancer. Patients with nasopharyngeal cancer have high curability rate also in very advanced local disease. But most of them suffer from late and very late effects of photon techniques like xerostomy, skin fibrosis, tube dependency, hearing loss et al. Patients with nasopharyngeal cancer are candidates for proton radiotherapy due to extensive and comprehensive target volumes and necessity of sparing healthy tissues, reducing total dose for organs at risk and reducing toxicity.

METHOD
Between January 2013 to June 2018 we treated 40 patients with nasopharyngeal cancer (NPC) with IMPT (proton radiotherapy with modulated intensity). Median of age was 47 years. Majority of patients had locally advanced tumors (stage 2 – 8 pts. (20%); stage 3 – 18 pts. (45%); stage 4A – 10 pts. (25%); stage 4B – 4 pts. (10%).

Patients were treated using standard five point immobilization devices (thermoplastic masks) at supine position. Computer tomography was used for treatment planning (scans 2.5 mm) and image registrations with planning MRI and PET FDG scans were performed before contouring. Contouring of target volumes was performed using the same recommendations as for photon radiotherapy.

Patients were irradiated in 3 phases: 50 GyE in 25 fractions for primary tumor and bilateral neck lymph nodes areas (Ib-V), 20 GyE in 10 fractions for primary tumor and involved lymph node neck areas and finally in selected cases - boost 4 GyE in 2 fractions for residual nasopharyngeal tumor. Median of total dose was 74 GyE (70-78 GyE) in 37 fractions (35–39). Concomitant chemotherapy (cDDP 40 mg/m2 weekly) was applied in 34 pts. (85%).

Robustness of treatment plans was evaluated.

All patients were treated using daily image guidance with kV-kV, with correction of position. Check-ups, using computed tomography, were performed once a week. New plans were prepared when dose distribution changed due to tumor regression, changes in cavity contents or changes in patient contours.

RESULTS
Median time of follow up was 24 months. All patients were treated without interruptions. Admission to hospital was necessary in only one case and was mainly due to nausea following chemotherapy. 2-years overall survival, disease free survival and locoregional control are 80%, 75% and 84%, respectively.

Toxicity was evaluated using the RTOG scale. Acute toxicity was generally mild despite extensive target volumes and application of concurrent chemotherapy, with skin toxicity (5 pts. Gr. 3 – 12.5%) and dysphagia as most frequent acute side effects. PEG was necessary in 4 pts. (10%). Serious late toxicity (Gr 3, RTOG) was observed in 1 pt. (2.5%) (dysphagia in patient with pre-existing disease of collagenous tissue).

Acute toxicity (RTOG scale):

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>skin toxicity</td>
<td>0 (0%)</td>
<td>7 (17.5%)</td>
<td>28 (70%)</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>mucositis</td>
<td>2 (5%)</td>
<td>8 (20%)</td>
<td>27 (67.5%)</td>
<td>3 (7.5%)</td>
</tr>
<tr>
<td>xerostomy</td>
<td>5 (12.5%)</td>
<td>29 (72.5%)</td>
<td>6 (15%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>dysphagia</td>
<td>8 (20%)</td>
<td>11 (27.5%)</td>
<td>17 (42.5%)</td>
<td>4 (2.5%)</td>
</tr>
</tbody>
</table>

CONCLUSION
- IMPT for nasopharyngeal cancer patients is feasible with mild acute toxicity.
- Treatment outcome is promising despite the high percentage of very advanced disease in this group.
- Adaptive approach seems to be necessary.