Proton therapy boost in locally advanced head and neck cancer: toxicity and clinical outcome

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PURPOSE
Evaluation of feasibility, acute toxicity and early clinical outcome in patients (pts) with locally advanced head and neck cancer (LAHNC) treated with sequential mixed beam (MB) approach: intensity modulated radiation therapy (IMRT) followed by proton therapy (PT) boost on high risk areas.

Methods
Between July 2012 to January 2018, 41 pts (29 male, 12 female), median age 51 years (range, 18-74), with histologically proven LAHNC (stage III and IV) were treated using a MB approach: IMRT of the neck and macroscopic disease, followed by PT boost on the pre-treatment macroscopic disease. Tumor sites were: nasopharynx 28 pts (69%), oropharynx 5 pts (12%), larynx 1 patient (2%), sinusal 4 pts (10%) and oral cavity 3 pts (7%). The histology was: squamous cell carcinoma for 11 pts (28%), neuroendocrine tumor for 2 pts (5%); nasopharynx tumor -classified according to the World Health Organization (WHO) classification (2005)-: I type 4 pts (10%), II type 19 pts (47%) and III type 4 pts (10%). IMRT prescription dose was 54-60 Gy (elective irradiation of the neck and macroscopic disease), PT prescription dose was 10-20 Gy Relative Biological Effectiveness (RBE), for a total dose up to 70-74 Gy RBE. Local control (LC) and toxicity profile (according to Common Terminology Criteria Adverse Events -CTCAE V4.03- scale) were evaluated.

Results
Twenty-three pts (56%) received platinum based induction chemotherapy, 39 pts (95%) received concurrent chemoradiation therapy. The median follow-up was 12 months, (range, 4-57). Treatment was well tolerated, 11 (27%) pts developed grade 3 acute radiation-related toxicity: 2 pts (5%) mucositis, 1 patient (2%) skin reaction and 5 pts (12%) dysphagia. No pts had high grade (grade 3-4) late toxicity. Grade 2 late toxicity was xerostomia found in 12 (29%) pts. Two pts (5%) developed G1 brain radionecrosis at 14 and 16 months after the end of the treatment respectively, in both cases it resolved at last follow-up. LC was 83%. Four pts had local recurrence at 12, 11, 8 and 8 months after treatment respectively. Three pts developed distant metastases at 6, 18 and 25 months after the end of the treatment. Three pts died for tumor specific-causes.

Conclusions
For pts with LAHNC a MB approach is feasible. Our results show good short-term outcome and limited radiation-related side effects. Preliminary results are encouraging. A longer follow-up and larger patient accrual are required.

Fig1: Example of a sequential MB approach for a patient with a diagnosis of locally advanced nasopharyngeal cancer (cT4N2).
1a. IMRT plan dose distribution
1b. Cumulative dose distribution (IMRT and PT boost)
1c. DVH of the summed final plan (solid lines) vs IMRT plan (dashed lines) for target and OARs volumes

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