Treatment of T4 nasopharyngeal carcinoma (NPC) is challenging due to the close proximity of the tumor to the central nervous system. We evaluated our disease control and toxicity outcomes for patients with T4 NPC treated with intensity-modulated radiation therapy (IMRT) and chemotherapy.

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**Background:** Treatment of T4 nasopharyngeal carcinoma (NPC) is challenging due to the close proximity of the tumor to the central nervous system. We evaluated our disease control and toxicity outcomes for patients with T4 NPC treated with intensity-modulated radiation therapy (IMRT) and chemotherapy.

**Methods:** The medical records of 66 patients with T4 NPC treated from 2002–2012 with IMRT were reviewed. Endpoints included tumor control and toxicity, as assessed by Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). Preliminary prospective patient-reported quality-of-life outcomes were obtained from survivors who completed the MD Anderson Symptoms Inventory and Brief Fatigue Inventory (BFI). For both scoring systems, a score of 0 represents absence of the symptom, while a score of 10 is most severe.

**Results:** Median follow-up was 38 months. On institutional pathology review, 13 patients were identified as having World Health Organization (WHO) I NPC, 6 patients were WHO II, and 46 patients were WHO III. WHO classification was unavailable for one patient. Fifteen patients were N0, 10 had N1 disease, 27 patients had N2 disease, and 14 had N3 disease. Epstein-Barr virus (EBV) status was available for 28 patients, 17 of whom were positive. Sixty-five patients received chemotherapy—2% induction, 26% concurrent, and 71% both. Actuarial 5-year rates of locoregional control (LRC), distant metastasis-free survival (DMFS), progression-free survival (PFS), and overall survival (OS) were 80%, 82%, 57%, and 69%, respectively. There was a trend toward improved OS ($P = .056$) and LRC ($P = .050$) in patients with WHO III disease compared to patients with WHO I/II disease. Evidence of EBV infection was associated with improved OS ($P = .023$) and PFS ($P = .003$). Nodal involvement was associated with worse PFS ($P = .015$), while advanced nodal disease (N2/N3) was associated with worse DMFS ($P = .044$) compared with N0/N1 disease. PTV volume $> 400 \text{ cm}^3$ was associated with worse OS ($P = .024$), PFS ($P = .001$), and DMFS ($P = .024$).

Ototoxicity was the most common toxicity ($n = 42$), with 19 patients experiencing grade 3 symptoms. Twenty-nine patients experienced xerostomia, and 16 patients had ophthalmologic toxicity. Actuarial non–feeding tube grade 3 toxicity rate at 5 years was 49% overall and 33% excluding ototoxicity. No grade 4 or 5 toxicity was observed. There was no late feeding tube dependence, although two patients developed esophageal strictures requiring surgical dilatation. Nine patients (14%) presented with radiographic evidence of temporal lobe necrosis, two of whom experienced significant cognitive impairment, including severe short-term memory deficit and personality change. Mean dose to the temporal lobe was 5,599 cGy (range: 1,500–7,903 cGy). Preliminary patient-reported outcomes data from 7 patients (of 46 living) revealed dry mouth to be the most significant symptom (average score 5.6), followed by memory difficulties (average score 5.3). Average fatigue score at the time of BFI completion was 4.4, with an average score for worst fatigue in the previous 24 hours of 5.

**Conclusions:** We report acceptable disease control outcomes for a homogenous population of T4 nasopharynx cancer patients treated with IMRT and chemotherapy. Survival and locoregional disease control rates have improved, consistent with the use of chemotherapy and advances in radiotherapy; however, late treatment toxicity remains a concern in this challenging patient cohort.