

Appendix materials

The design of IMRT plan:

All patients were immobilized in the supine position with a head, neck, and shoulder thermoplastic mask. Two sets of images, with and without contrast, were obtained from the CT simulator for treatment planning. All patients were scanned with serial 3-mm slices from the vertex through the clavicles. Inverse IMRT planning was performed using Corvus system, version 3.0 (Peacock, Nomos, DeerPark, IL), and a MiMi multileaf collimator (Nomos, Sewickly, PA) was used for planning and treatment.

The primary and nodal gross tumor volumes (GTV-P and GTV-N) included all gross diseases visualized on CT and/or MRI. The high-risk clinical tumor volume (CTV-1) included GTV plus 5-10 mm margin and encompassed the entire nasopharyngeal mucosa plus 5mm sub mucosal volume. CTV-2 was designed for potentially involved regions included the nasopharyngeal cavity (limited only to the posterior part of nasal cavity),maxillary sinus (limited to 5-mm anterior to the posterior nasal aperture and maxillary mucosa), pterygopalatine fossa, posterior ethmoid sinus, parapharyngeal space, skull base, anterior third of clivus and cervical vertebra, inferior sphenoid sinus and cavernous sinus,and included the retropharyngeal lymph nodal regions from the base of skull to cranial edge of the second cervical vertebra. The CTV of the neck nodal regions (CTVnd) included level II, III, IV, V, which were outlined according to the recommendation by the RTOG/EORTC CTV delineation

protocol for head and neck malignancies. The planning target volume (PTV) was created based on each volume with an additional 3-mm margin, allowing for setup variability. Critical normal structures including the brainstem, spinal cord, parotid glands, optic nerves, chiasm, lens, eyeballs, temporal lobes, temporomandibular joints, mandible, hypophysis were contoured and set as OARs during optimization.

The dose–volume histograms of the treatment targets and critical normal structures were evaluated. Prescribed dose was 68-70 Gy to the PTV of GTVnx (PTVnx), 60 Gy to PTV1, 54 Gy to PTV2, and 60–70Gy to PTV of the GTVnd (PTVnd) in 30-33 fractions. For GTV and CTV, the target volumes receiving 95% of the prescribed dose were used to reflect the target coverage, and the maximal, minimal, and mean doses delivered to the target volumes were also calculated. For critical organs with functional subunits organized in series, such as the brain stem, optic chiasm, and optic nerves, dose to 5% of the volumes was examined. For critical organs with functional subunits organized in parallel, dose delivered to 33% of the volumes was evaluated. The dose distribution was also examined slice by slice on the CT image.