Supplementary Methods

The design of intensity-modulated radiation therapy 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 computed tomography (CT) simulator for treatment planning. All patients were scanned with serial 3-mm slices from the vertex through the clavicles. Inverse intensity-modulated radiation therapy (IMRT) planning was performed using Corvus system ver. 3.0 (Peacock, Nomos, Deer Park, IL), and a MiMi multileaf collimator (Nomos, Sewickly, PA) was used for planning and treatment.

The primary and nodal gross tumor volumes (GTV_{nx} and GTV_{nd}) based on magnetic resonance imaging (MRI) were delineated by the same radiologist and oncologist. These images were fused into the planning computed tomography. GTV_{nx} and GTV_{nd} included all gross diseases visualized on MRI. The high-risk clinical tumor volume (CTV-1) included GTV plus 5-10 mm margin and encompassed the entire nasopharyngeal mucosa plus 5 mm submucosal 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 spheniod 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 (CTV_{nd}) included level II, III, IV, V, which were outlined according to the recommendation by the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer CTV delineation protocol for head and neck malignancies. For all patients, including those with negative neck, were treated with bilateral neck irradiation. For patients without node involvement (N0), radiation therapy encompassed the upper neck only (level II, III and Va). For patients with node positive disease, the whole neck was involved, including supraclavicular area (level II, III, IV, V). 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 organs at risk 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 (PTV_{nx}), 60 Gy to PTV1, 54 Gy to PTV2, and 60-70 Gy to PTV of the GTVnd (PTV_{nd}) 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.