TITLE
The Risk without Adaptive Replanning for HPV-Associated N2b Oropharyngeal Squamous Cell Carcinoma in Response to Anatomic Change during Radiotherapy

HYPOTHESIS:
The hypothesis is that anatomic change in patients with HPV-associated N2b oropharyngeal squamous cell carcinoma undergoing curative chemoradiation can cause clinically significant dosimetric variations requiring adaptive replanning.

BACKGROUND/AIMS:
Replanning for head and neck cancer due to weight loss or tumor response takes substantial time, effort, and resources. There is no consensus on if, when, or how replanning should be done. Most published studies are limited by heterogeneity of the study population, variation in timing of replanning, and lack of clinically important dosimetric endpoints. The present study prospectively evaluated dosimetric changes at a uniform timepoint in a uniform patient population.

METHODS:
The prospective program enrolled 10 consecutive patients with biopsy-proven p16-positive oropharyngeal squamous cell carcinoma (OPX SCC) of clinical stage T1-3 and N2b who underwent primary radiotherapy and concurrent weekly chemotherapy between May and Dec 2016. All patients underwent repeat CT simulation on treatment day 21. Normal and target structures were contoured by the first author on both initial and second simulation CT. The target volumes and normal tissue constraints were defined per recent RTOG protocols. High-risk and standard-risk planning target volumes (PTV) were given 70Gy and 56Gy in 35 treatment days, respectively, using simultaneously integrated boost intensity-modulated radiotherapy (IMRT).

We evaluated the effect of changes in anatomy without replanning by deformable registration of the initial dose map to the day 21 scan, which was scaled proportionally to its actual respective days of use. A combined dose map was then created with accumulated dose accounting for the anatomy change in the last 14 days of a 35-day treatment program. The impact of tumor response and weight change was analyzed in multivariate linear regression models.

RESULTS & CONCLUSIONS
No replanning resulted in underdose of both high-risk and standard-risk target volumes: PTV70 coverage reduced by 16.6 ± 8.4% and PTV56 reduced by 10.6 ± 4.9%. Failure to meet the main coverage requirement (D95% = prescription dose) occurred in 90% of patients. Failure to meet PTV coverage goals was associated with volume shrinkage of adenopathy (p < 0.001), but not weight loss.

No replanning led to ≤1% change in mean dose of the contralateral parotid and <3% change in maximum dose to the spinal cord and brainstem. Overall, no normal tissues (spinal cord, brainstem, both parotids, larynx, pharyngeal constrictors, oral cavity) had dosimetric change to a significant degree.

This is the first study of the adaptive replanning issue in a homogeneous study population with standardized evaluation parameters. Our findings were dramatically different from most prior publications. The primary risk without replanning was the underdosing of tumor targets, not an increased dose to normal structures. Our results suggest that most patients with HPV-associated oropharyngeal cancer who present with N2b adenopathy would benefit from replanning for at least the last 2 weeks of radiotherapy.