Prospectively-collected, tooth-specific dosimetry correlated with adverse dental outcomes

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Objectives. To correlate radiation dose to specific tooth-bearing portions of bone with adverse dental outcomes.
Study Design. Eighty-nine patients treated with intensity-modulated radiation therapy with or without chemotherapy had radiation dose to specific tooth-bearing portions of the mandible and the maxilla. Data were collected prospectively during treatment planning, which resulted in 2490 data points. These patients underwent a comprehensive dental intake evaluation that included measurement of pocket depths and were then followed up with serial dental evaluations for a median of 2.5 years (range 0.2−6.9 years).
Results. At the patient level, the 3-year risks of osteoradionecrosis (ORN) and periodontal disease were 2.5% and 36.6%, respectively. For any individual tooth, the risks of ORN and periodontal disease were 0.1% and 5.1%, respectively, at 3 years. Radiation dose to individual tooth−bearing portions of bone was correlated with ORN development ($P = .0165$). Periodontal disease also demonstrated a significant, but more gradual, dose response ($P = .0395$).
Conclusions. Adverse dental outcomes directly correlate with increased tooth-specific doses. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:158-163)

Radiation therapy for head and neck cancer is a well-established risk factor for adverse dental outcomes.[1,2] Osteoradionecrosis (ORN) has been associated with radiation dose,[3-5] volume of mandible radiated,[6,7] and various patient factors.[8] Analyses attempting to correlate dosimetric factors with ORN have shown an association, but the methods employed so far have been relatively crude, often focusing on prescription dose as a surrogate or on maximum or mean doses to the mandible.[3,6,9] There is even less data linking radiation treatments with development of subsequent periodontal disease.[10]

A study from Memorial Sloan Kettering Hospital in 2012 investigated radiation dose delivered with intensity modulated radiation therapy (IMRT) to the tooth-bearing regions of the mandible in a small cohort of patients.[11] The study concluded that there was a need for dosimetric analysis to correlate radiation dose to clinical dental outcomes. This paper investigates that proposed question.

Our hospital-based radiation oncology clinic is relatively unique in that a dental hygienist has been employed in the department for nearly 20 years. Approximately 8 years ago, we began prospectively collecting data on radiation dose to a specific segment of the mandible or the maxilla anchoring each tooth (or socket for some patients with dental extractions), and we have monitored our patients in a comprehensive manner to assess for subsequent dental complications. We present the first report of prospectively collected, tooth-specific dosimetry correlated with long-term adverse dental outcomes.

MATERIALS AND METHODS

In this study, which was approved by the Internal Review Board, we performed a retrospective analysis of dental outcomes in 89 patients treated with IMRT to a median dose of 7000 cGy (5800−7200 cGy) with or without chemotherapy between 2008 and 2014. The study was conducted in accordance with the ethical standards of the Helsinki Declaration for human subjects. The specifics of our IMRT prescription process have been previously reported.[12] Patients were excluded from the study if they did not have prospectively collected dosimetry to specific tooth-bearing portions of the mandible or the maxilla (referred to as "tooth-specific dosimetry" below); otherwise, the study population consisted of an unselected cohort of consecutive patients treated for head and neck cancer in the region of the maxilla and the mandible.

Tooth-specific dosimetry was collected prospectively via collaboration between the dental hygienist and the dosimetrist. IMRT plans were reviewed by using the cursor to estimate point doses in the treatment planning system along the tooth-bearing portions of the maxilla

Statement of Clinical Relevance

In oral oncology, there is a need to directly correlate radiation dose to specific teeth with osteoradionecrosis and periodontal disease so that patients can be counseled on risk and treatment needs.

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and the mandible. Data on the maximum dose at each bone−tooth interface was entered into a prospective database. Initially, data on radiation dose was collected for all remaining teeth and the mandibular or maxillary regions where a tooth would have been if prior extractions had been performed. This was a relatively laborious process and with subsequent staffing limitations, a change was made to collect dose information only for in situ or remaining teeth for patients treated in recent years. In total, the process resulted in 2490 specific dosimetric data points for the 89 patients.

Patients were assessed clinically by the radiation oncologist, and a comprehensive initial dental evaluation was concurrently coordinated by our dental hygienist. Panoramic radiography was ordered as standard practice, and any patient with questionable dentition was referred to an oral surgeon for evaluation and extractions, as needed. Extractions were only recommended for those teeth deemed to have a poor long-term prognosis; healthy teeth were not routinely extracted before radiation.

The initial comprehensive dental evaluation included assessment of pocket depth measurements for periodontal disease, subjective binary assessment of overall dental condition, review of dental imaging, documentation of existing fillings and crowns, assessment for dental caries, and fabrication of shields for patients with metallic fillings. Patients with oral cavity lesions had custom bite-blocks created to expand the intraoral incisor separation in an attempt to minimize dose to the maxilla and the palate. Extensive counseling was provided, with a focus on the importance of ongoing dental health maintenance and lifelong fluoride use.

The dental hygienist monitored each patient with weekly visits during radiation and offered assistance with monitoring for mucositis, xerostomia, and oral candidiasis. After treatment, the hygienist was an instrumental part of a comprehensive package of follow-up care, offering longitudinal dental follow-up for patients when they were seen by the radiation oncologist. We followed a standard follow-up protocol of seeing the patient after radiation at 2 weeks, 6 weeks, and 12 weeks and performed repeat imaging. After this, patients were offered follow-up every other month for the first 2 years, every third month for the third year, and twice a year for years 4 and 5. Follow-up often alternated with the patient's otolaryngologist appointment at an alternative site.

Subsequent follow-up dental examinations consisted of the following: longitudinal assessment of pocket depth, assessment for caries, extractions, and assessment for development of ORN and/or other dental complications. When ORN occurred, the location of the lesion was correlated with the closest adjacent tooth or tooth socket. ORN was graded according to the Common Terminology Criteria for Adverse Events, version 4 (CTCAE v.4). Teeth were coded as developing periodontal disease if they had both an increase in pocket depth and a final pocket measurement greater than 6 mm.

The median follow-up for all patients was 2.5 years (range 0.2−6.9 years). Approximately 50% of the patients were compliant with longitudinal dental follow-up examinations with the dental hygienist and thus had serial measurements of pocket depth to assess for development of periodontal disease. The remaining patients were followed up by physicians only and were queried and examined for interval dental extractions or development of ORN; these patients were excluded from the periodontal analysis.

Univariate analysis was performed to assess for correlation between ORN or periodontal disease and the following risk factors: age, gender, baseline dental condition, surgery followed by radiation therapy (RT) versus definitive radiation therapy, panoramic radiography (performed at baseline vs not performed), tumor (T) stage, chemotherapy, alcohol use (current), tobacco use (>15 pack-year history), and the presence of diabetes, heart disease (i.e., coronary artery disease, myocardial infarction, congestive heart failure), hypertension, pulmonary disease (i.e., chronic obstructive pulmonary disease or emphysema) as self-reported by the patients in their medical history.

JMP software was utilized for statistical analysis (SAS Institute, Cary, NC). Logistic regression provided estimated rates of ORN, tooth extraction, and periodontal disease as a function of dose. In complement, the time-dependent rate of each of these events was assessed with the Kaplan-Meier product-limit method. Kaplan-Meier curves were truncated at 3 years to maintain validity in light of our median follow-up of 2.5 years. The level of statistical significance between the strata of selected prognostic factors was assessed with log-rank statistics.

RESULTS

The median dose to the mandibular or maxillary tooth-bearing portions of bone was 3100 cGy (range 206−7200 cGy). Two hundred forty-three teeth received greater than 5000 cGy and 79 received greater than 6000 cGy. Figure 1 represents a histogram of radiation dose to tooth-bearing sites.

Four hundred twenty-nine teeth were extracted from 59 patients before radiation. Subsequently, an additional 56 teeth in nine patients were extracted after radiation. Postradiation dental extractions were performed in 7.3% of patients at 3 years. The risk of an individual tooth requiring extraction after radiation was 0.9% at 3 years. There was no dose response for any-cause post-RT dental extractions ($P = .2910$).