



Radiation Exposure Alters Airway Deformability and Bony Structure Displacement During Laryngoscopy

Christiaan A. Rees, PhD ; Xiaotian Wu, PhD; Eric A. Eisen, MD; David A. Pastel, MD;
 Ryan J. Halter, PhD; Joseph A. Paydarfar, MD 

Background: Prior therapeutic radiation exposure in the setting of head and neck malignancies is associated with difficult airway instrumentation. We sought to characterize the anatomic changes that produce this phenotype.

Study Design: Retrospective review.

Methods: Five individuals with prior radiation therapy to the upper aerodigestive tract (previously irradiated) and 10 with no prior history of therapeutic radiation exposure (nonirradiated) were enrolled. Computed tomography images obtained before and during laryngoscope insertion ("uninstrumented" and "instrumented", respectively) were used to reconstruct three-dimensional representations of the pharyngeal airway, hyoid, and mandible.

Results: In the instrumented state, pharyngeal airway volumes were significantly greater in nonirradiated subjects relative to previously irradiated subjects ($P = .01$), and overall translation of both the hyoid and mandible was also greater in nonirradiated subjects ($P = .01$ and $.04$, respectively).

Conclusion: Individuals with prior therapeutic radiation exposure to the upper aerodigestive tract differ from nonirradiated subjects with respect to airway deformation and bony structure translation during laryngoscopy.

Key Words: Airway, cancer, deformation, modeling, radiation therapy.

Level of Evidence: 4

INTRODUCTION

Variations in head and neck anatomy can have major implications regarding airway management. The difficult airway can present potentially life-threatening situations during intubation,¹ and impact adequate exposure and margin control during operative laryngoscopy.² Because of this, several anatomically based screening tools exist to help predict the difficulty of airway exposure prior to direct or operative laryngoscopy, including the well-established Mallampati class score, which is a visual assessment of the distance between the tongue base and palate.^{3,4} Aside from anatomy, other variables associated with airway management difficulty include a history of sleep apnea,^{5,6} alterations in upper airway tissue in the setting of head and neck cancer,⁷

and prior radiation therapy to the neck.^{5,6} Although these variables are associated with a lower probability of clinical success, the extent to which any one of these directly contributes to airway patency and/or tissue deformability during laryngoscopy has proven challenging to quantify.

In recent years, a number of studies have sought to measure structures of the upper airway using three-dimensional models derived from computed tomography (CT) or magnetic resonance imaging (MRI), and some have used this approach to assess airway anatomy in various clinical scenarios. For example, Ohya et al combined CT angiography with three-dimensional modeling to assess carotid artery deformation associated with head and neck movement.⁸ Welch et al evaluated changes in upper airway volume in obese patients after weight loss using MRI combined with computational modeling.⁹ Finally, Trudo et al used MRI in combination with three-dimensional modeling to identify differences in retropalatal and retroglottal airway volumes between asleep and awake states.¹⁰ Despite advances in the computational modeling tools available for image analysis, to the best of our knowledge, no prior studies have evaluated the effect of therapeutic radiation exposure on airway volume, tissue deformation, or bony structure displacement in the setting of operative laryngoscopy.

In this pilot study, we combine CT imaging of the head and neck with three-dimensional computational modeling to measure airway deformation during suspension laryngoscopy. Specifically, we focus on differences in: 1) airway deformability and 2) translational/rotational movement of the hyoid and mandible between nonirradiated and previously irradiated subjects. We hypothesized that, in the

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

From the Geisel School of Medicine at Dartmouth (C.A.R., D.A.P., R.J.H., J.A.P.), Hanover, New Hampshire, U.S.A.; Thayer School of Engineering at Dartmouth (X.W., R.J.H.), Hanover, New Hampshire, U.S.A.; Section of Otolaryngology (E.A.E., J.A.P.), Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, U.S.A.; Department of Radiology (D.A.P.), Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, U.S.A.

Editor's Note: This Manuscript was accepted for publication on August 20, 2019.

Meeting information: A subset of this data was presented as a scientific poster at The Triological Society Combined Sections Meeting, Coronado, CA, United States, January 24th–26th, 2019.

Conflict of Interest: The authors report no conflicts of interest.

Send correspondence to Joseph A. Paydarfar, MD, FACS, Division of Otolaryngology–Head and Neck Surgery, Dartmouth-Hitchcock Medical Center, 1 Medical Center Drive, Lebanon, NH 03756. E-mail: joseph.a.paydarfar@hitchcock.org

DOI: 10.1002/liv.2.311

setting of suspension laryngoscopy, study subjects with prior therapeutic radiation exposure to the head and neck would have reduced airway deformability and limited displacement of the mandible and hyoid relative to nonirradiated subjects, leading to reduced airway volume. The present study thus aims to improve our understanding of the mechanisms that contribute to increased technical difficulty associated with laryngoscopy in the setting of prior therapeutic radiation exposure.

MATERIALS AND METHODS

Subject Enrollment and Imaging Protocol

Subjects scheduled for laryngoscopy as part of routine care in the setting of suspected or confirmed head and neck malignancies were recruited for this pilot study, which was approved by Dartmouth College's Institutional Review Board (STUDY#: 00028153). All procedures were performed under general anesthesia, either via nasal intubation or through an existing tracheostomy. For each subject, two CT scans (Siemens SOMATOM Definition AS 64-Slice, 5.0 mm slice thickness acquisition, reconstructed to 1.0 mm slices with B31s medium smooth+ kernel) were acquired following the administration of intravenous contrast (iohexol, 300 mg/mL, 25 mL): one prior to laryngoscopy (the "uninstrumented" state) with the patient in repose, and the other during suspension laryngoscopy (the "instrumented" state). Both CT scans were performed after induction of general anesthesia. A custom CT-compatible polymer laryngoscope system (Fig. 1) was used to avoid CT imaging artifacts produced by standard metallic laryngoscopes.¹¹ The laryngoscope was inserted on the right side in 14 of 15 study subjects in an effort to minimize interindividual variability with respect to laryngoscope positioning. Left-sided laryngoscopy was performed in one study subject due to tumor location, and for this individual, both instrumented and uninstrumented CT images were inverted along the left-right axis to improve alignment with the remaining study subjects. As per standard clinical procedure, the laryngoscope was suspended with the tip of the blade located at the vallecula to achieve a grade 1 to 2 view for all patients.



Fig. 1. Computed tomography-compatible laryngoscope system in place for suspension laryngoscopy.

Image Analysis and Computation

Three-dimensional representations of the pharyngeal airway and bony/cartilaginous structures (ie, hard palate, hyoid, mandible, and thyroid cartilage) were obtained from CT imaging using the image segmentation tools included in the Mimics 15.01 software package (Materialise, Plymouth, MI). The "pharyngeal airway" was bounded *superiorly* by the choanae, *anteriorly* by a plane extending from the junction of the hard and soft palate to the inferior margin of the hyoid, *inferiorly* by a plane extending from the inferior margin of the hyoid to the inferior margin of the cricoid cartilage, and *posteriorly* by the posterior pharyngeal wall (Fig. 2). *Total pharyngeal airway volume* encompassed both the free air within this anatomically defined region, as well as the volume occupied by the endotracheal tube (including both the tube itself and the air space within the tube). Airway volumes were computed in Mimics from the segmented airway masks.

To identify specific areas within the pharyngeal airway that deformed differentially between nonirradiated and previously irradiated subjects, we aligned CT images acquired in the instrumented state across all 15 study subjects. The laryngoscope was registered to the same orientation and location across all CT scans, thereby minimizing both *rotational* and *translational* differences in laryngoscope position across study subjects. An example of this alignment approach is presented in Figure 3. Because there were no significant intergroup differences in total pharyngeal airway volume in the uninstrumented state, no alignment step was utilized in the analysis of uninstrumented CT images.

After three-dimensional airway volumes had been aligned across study subjects in the instrumented state (using the protocol outlined in the prior paragraph), two-dimensional slices were generated in the axial, coronal, and sagittal planes. The maximum cross-sectional airway areas in each of the three planes (axial, coronal, and sagittal) were aligned across subjects to minimize any residual

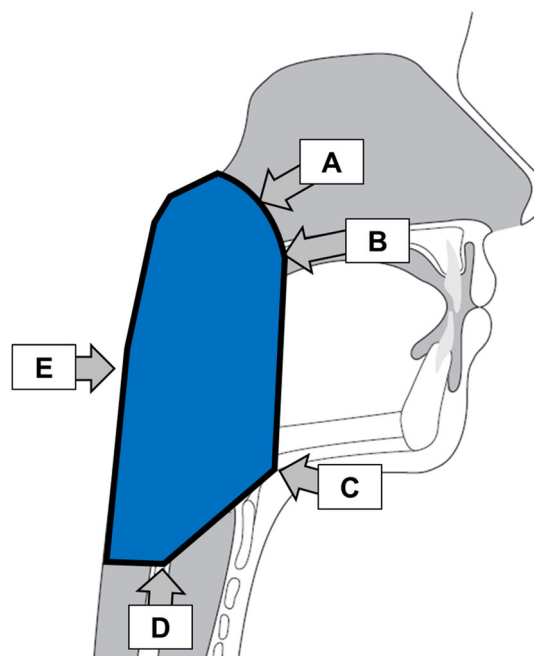


Fig. 2. Sagittal view depicting the boundaries of the pharyngeal airway (blue). The pharyngeal airway was bounded superiorly by the choanae (A), anteriorly by a plane extending from the junction of the hard and soft palate (B) to the inferior margin of the hyoid (C), inferiorly by a plane extending from the inferior margin of the hyoid (C) to the inferior margin of the cricoid cartilage (D), and posteriorly by the posterior pharyngeal wall (E).

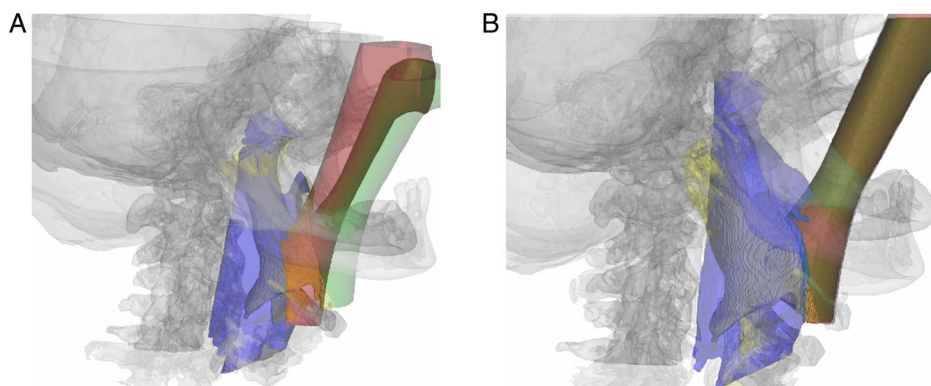


Fig. 3. Alignment of computed tomography images in the instrumented state involved registration of the laryngoscope to the same position across all 15 study subjects. (A) The “unaligned” state, with noticeable differences in laryngoscope position between subject 1 (red laryngoscope, blue airway), and subject 2 (green laryngoscope, yellow airway). (B) The “aligned” state, with overlapping laryngoscope position in subject 1 and subject 2.

differences in laryngoscope position, and a two-sided *t* test was used to identify two-dimensional slices whose airway area was significantly different between nonirradiated and previously irradiated subjects. Finally, the two-dimensional slices whose airway area was significantly different between groups were recombined in three dimensions (axial, coronal, and sagittal) to identify the specific region within the pharyngeal airway that deformed differentially between nonirradiated and previously irradiated subjects.

For the translational and rotational analysis of the mandible and hyoid, each patient’s skull was registered to a coordinate system defined by the frankfurt plane, midsagittal plane, and vertical porion plane coordinate.¹² Center displacements (T_x , T_y , T_z , and magnitude T) and rotations (A_x , A_y , A_z) of the mandible and hyoid bones from the “uninstrumented” and “instrumented” states were computed via iterative closest point (ICP) rigid registration.¹³

Statistical Analyses

All statistical analyses were performed using either R version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria) or MATLAB R2018a (Mathworks, Natick, MA). Statistical significance was evaluated using either a Mann–Whitney *U* test for continuous variables or a Pearson’s chi-squared test without Yates’ continuity correction for categorical variables, with $P = .05$ defined as the threshold for significance. Correlations between variables were evaluated using Pearson’s correlation coefficient.

RESULTS

Fifteen subjects undergoing suspension laryngoscopy for suspected malignancies of the head and neck were enrolled in this pilot study. Five had previously received therapeutic radiation for a head and neck malignancy (of which four received combination radiation therapy and chemotherapy), while the remaining 10 had neither a prior history of head and neck malignancies nor a history of previous therapeutic radiation exposure. The majority of study subjects were male (13/15, 87%), with an average age of 66 (range: 44–77) and average body mass index (BMI) of 26.5 (range: 18.0–39.9). For the comparison of nonirradiated and previously irradiated subjects, there were no significant intergroup differences with respect to age ($P = .86$), sex ($P = .28$), BMI ($P = .30$), Mallampati class ($P = .30$),

thyromental distance ($P = .71$), and neck range of motion ($P = .92$) (Table I). Airway grade was not significantly different between groups when tracheostomy subjects were excluded from the analysis ($P = .11$) but was significantly different when tracheostomy subjects were considered as a distinct category ($P = .02$). Primary tumor location varied considerably across the study population but did not differ noticeably between nonirradiated and previously irradiated subjects. Most lesions occurred in either the supraglottic larynx ($n = 5$), tongue base ($n = 2$), or glottis/vocal cord ($n = 2$). Lesions rarely occurred at other sites, including the oral tongue, posterior pharynx, and tonsil ($n = 1$ per site), while a small number of tumors ($n = 4$) demonstrated extension across adjacent anatomic sites (eg, the supraglottic larynx extending to the tongue base). One individual presented with two primary lesions, one of which was localized to the posterior pharynx and the other to the glottis. Among the five previously irradiated study subjects, four had primary tumors of the supraglottic larynx and one had a primary tonsillar tumor. Four patients were treated with intensity-modulated radiation therapy with 70 Gy of radiation applied to the primary lesion. The bilateral neck was also irradiated to between 54 and 56 Gy in all four patients. For the fifth patient, prior radiation records were unavailable; however, he did have radiation to the glottic larynx in the late 1990s, presumably using conformal methods.

Prior to laryngoscope insertion (ie, the “uninstrumented” state), there were no significant differences in pharyngeal airway volume between nonirradiated and previously irradiated subjects ($17.8 \pm 4.5 \text{ cm}^3$ vs. $14.7 \pm 5.7 \text{ cm}^3$, $P = .25$). Following laryngoscope placement (ie, the “instrumented” state), the airway volumes of nonirradiated subjects were significantly greater than those of previously irradiated subjects ($97.2 \pm 18.9 \text{ cm}^3$ vs. $60.0 \pm 16.3 \text{ cm}^3$, $P = .01$), and the change in pharyngeal airway volume (ie, instrumented volume minus uninstrumented volume) was also significantly greater in nonirradiated subjects relative to previously irradiated subjects ($79.5 \pm 17.3 \text{ cm}^3$ vs. $45.2 \pm 11.3 \text{ cm}^3$, $P = .01$) (Fig. 4). There was a strong positive correlation between instrumented airway volume and change in airway volume ($r = 0.99$, $P = 3.3 \times 10^{-11}$) across all subjects, but only a relatively modest, nonsignificant correlation

TABLE I.
Demographic and Anatomical Characteristics of Study Participants.

Subject	Age	Sex	BMI	Airway Grade	Mallam Class	TM Dist	Neck ROM	Tumor Site	Tumor Stage	Radiation Dose (Gy)
Nonirradiated										
1	72	M	28.2	1	1	NR	Full	Supraglottic larynx	T3 N1	—
2	64	M	25.1	1	2	>3 FB	Full	Glottis, Posterior pharynx [§]	T1 N0, T2 N0	—
3	67	M	32.6	1	2	>3 FB	Full	Vocal cord	T1 N0	—
4	53	F	26.2	1	2	>3 FB	Full	Tongue base	Benign	—
5	74	F	28.4	NR	NR	NR	NR	Supraglottic larynx	T4a N0	—
6	74	M	25.1	2	1	>3 FB	Full	Transglottic	T3 N2b	—
7	64	M	18.8	2	2	>3 FB	Limited	Unknown primary	Tx N3	—
8	64	M	39.9	2	2	>3 FB	Full	Tongue base	T2 N2a	—
9	44	M	24.5	1	2	>3 FB	Full	Oral tongue	T2 N2b	—
10	70	M	24.0	1	3	<3 FB	Limited	Supraglottic larynx	T2 N2c	—
Previously irradiated										
11	77	M	23.8	*	3	>3 FB	Full	Supraglottic larynx	T4a/b N2b	70 (54)
12	69	M	18.0	*	2	>3 FB	Full	Supraglottic larynx	T3 N0	70 (56)
13	67	M	31.7	*	2	>3 FB	Full	Supraglottic larynx to tongue base	T3 N2c	70 (56)
14	61	M	27.2	2	2	>3 FB	Limited	Supraglottic larynx	T1 N0	Unknown
15	64	M	23.6	2	3	<3 FB	Full	Tonsillar	T2 N2b	70
Comparison: Nonirradiated vs. previously irradiated										
P value	.86	.28	.30	.11 [†] .02	.30	.71	.92	—	—	—

*Not reported due to tracheostomy tube placement.

[†]P value calculation excludes tracheostomy patients.

[§]Two distinct primary tumors.

^{||}Value outside parentheses is total dose applied to primary tumor, while values inside parentheses indicate dose applied to the neck (if known).

BMI = body mass index (kg/m²); FB = finger breadths; Mallam class = Mallampati class; NA = not available; Neck ROM = neck range of motion; NR = not recorded; TM Dist = thyromental distance (measured in finger-breadths).

between uninstrumented airway volume and change in airway volume ($r = 0.46$, $P = .09$). Taken together, these results suggest that airway deformability (as defined by change in airway volume) is driven by instrumented rather than uninstrumented airway volume.

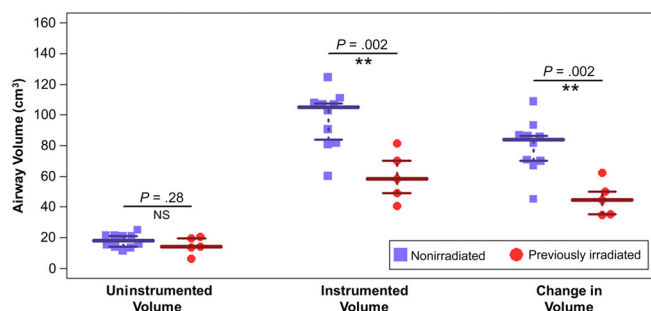


Fig. 4. Pharyngeal airway volumes for nonirradiated (blue) and previously irradiated (red) study subjects. Airway volumes are reported for the uninstrumented state (prior to laryngoscope introduction, left), instrumented state (during laryngoscope insertion, middle), and the change between instrumented and uninstrumented states (right). Wide horizontal bars represent the median of each group, while narrow horizontal bars represent the first and third quartiles. ** $P \leq .01$. NS = not statistically significant.

Having demonstrated that previously irradiated subjects had smaller overall pharyngeal airway volumes relative to nonirradiated subjects in the instrumented state, we next sought to define the specific region(s) within the pharyngeal airway that deformed differentially between these two groups. Specifically, sagittal, coronal, and axial airway slices were compared between groups, and a three-dimensional region (defined by the union of axial, coronal, and sagittal slices that were significantly different between groups) was identified that was significantly smaller in previously irradiated subjects relative to nonirradiated subjects. The region of differential deformation was $7.7 \text{ cm} \times 6.0 \text{ cm} \times 5.6 \text{ cm}$ (sagittal \times axial \times coronal) and was located approximately at the site of laryngoscope placement (Fig. 5). This suggests that differences in airway volume between nonirradiated and previously irradiated subjects in the instrumented state occur via local tissue deformation surrounding the laryngoscope itself.

In addition to differences in airway deformation, both the hyoid and mandible were differentially displaced between nonirradiated and previously irradiated subjects. The overall displacement was significantly different between nonirradiated and previously irradiated subjects for both the hyoid ($13.5 \pm 3.1 \text{ mm}$ vs. $9.0 \pm 1.8 \text{ mm}$, $P = .01$) and mandible ($12.5 \pm 3.3 \text{ mm}$ vs. $7.9 \pm 2.8 \text{ mm}$, $P = .04$) (Fig. 6).

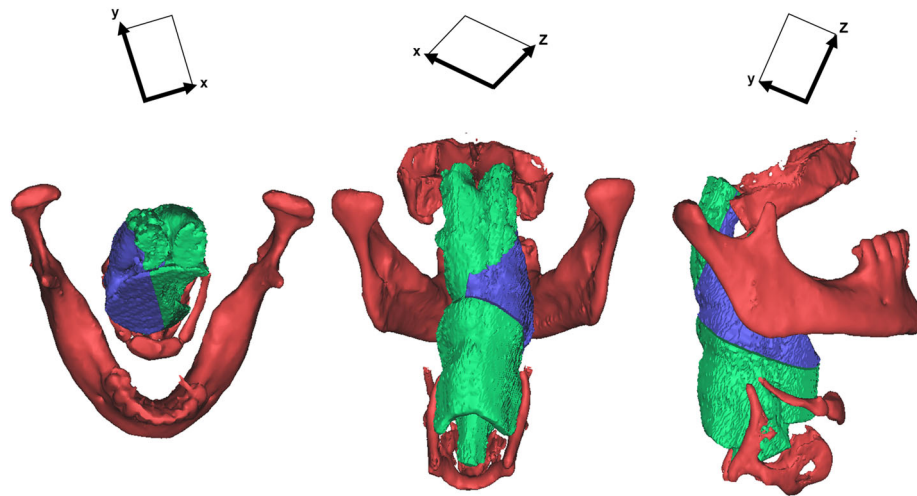


Fig. 5. Representative three-dimensional airway reconstruction depicted in axial (X-Y, left), coronal (X-Z, center), and sagittal (Y-Z, right) orientations. Blue indicates the region of the pharyngeal airway that differed significantly ($P < .05$) between nonirradiated and previously irradiated subjects in the instrumented state, defined as the union of the axial, coronal, and sagittal slices that were significantly different between groups. Green indicates the region of the pharyngeal airway that was not significantly different between nonirradiated and previously irradiated subjects. Bony and cartilaginous structures (the hard palate, hyoid, mandible, and thyroid cartilage) are presented in red.

Displacement of the hyoid and mandible in both anterior-posterior and superior-inferior directions was significantly different between nonirradiated and previously irradiated subjects, while no significant between-group differences were noted with respect to left-right displacement. Notably, airway deformation (ie, change in airway volume between the uninstrumented and instrumented states) was significantly correlated with the overall displacement of the mandible ($r = 0.68$, $P = .005$), as well as displacement in the anterior-

posterior ($r = -0.69$, $P = .004$), superior-inferior ($r = 0.55$, $P = .03$), and left-right ($r = -0.59$, $P = .02$) directions. Change in airway volume was also significantly correlated with the anterior-posterior displacement of the hyoid ($r = -0.61$, $P = .02$), but was not significantly correlated with the displacement of the hyoid in other directions. Of interest, only one of the five previously irradiated subjects reported trismus as a side effect of their radiation therapy, suggesting that the reduced mobility identified via CT imaging in

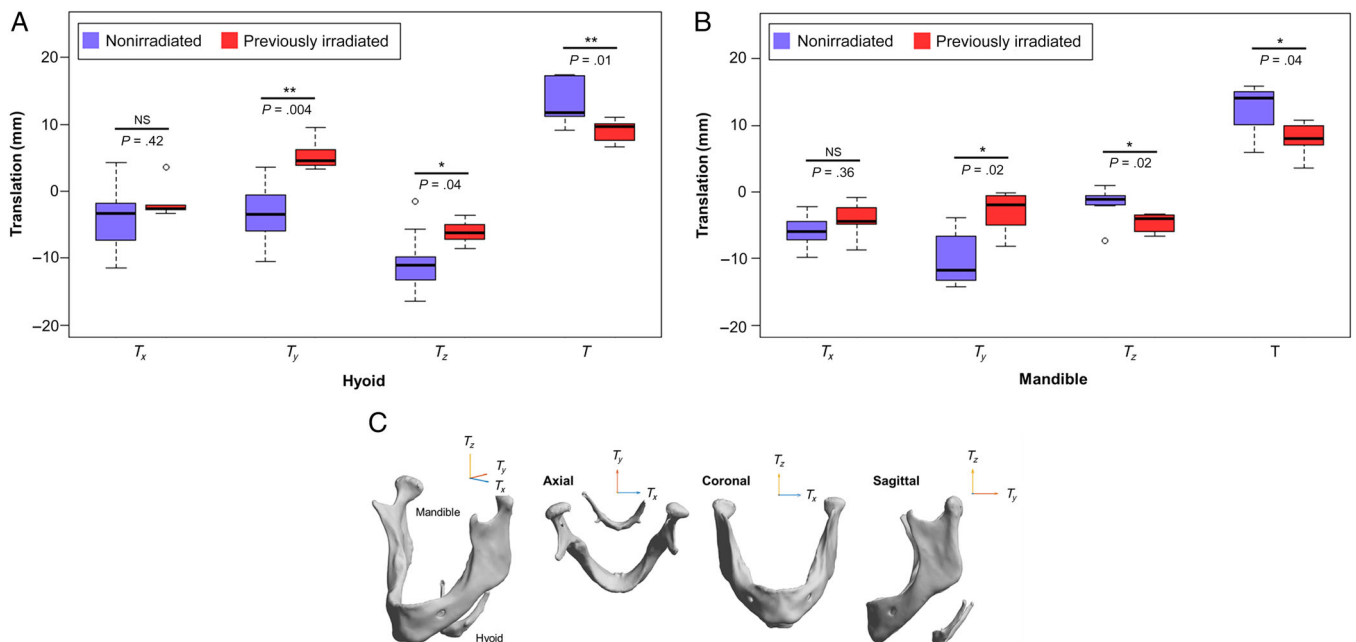


Fig. 6. Displacement of the hyoid (A) and mandible (B) in both nonirradiated (blue) and previously irradiated (red) subjects. T_x , T_y , and T_z correspond to displacement in the right-left, anterior-posterior, and superior-inferior directions, respectively (C), while T corresponds to the overall displacement magnitude ($= \sqrt{T_x^2 + T_y^2 + T_z^2}$). * $P < .05$; ** $P \leq .01$. NS = not statistically significant.

previously irradiated subjects may have been more due to fibrosis of the suprahyoid muscle attachments.

In contrast to the substantial differences observed between nonirradiated and previously irradiated subjects with respect to the *translational* displacement of both the hyoid and mandible, the difference in *rotational* movement of these structures between groups was less pronounced. Specifically, there were no significant differences between groups in the rotational movement of the hyoid about any of the three axes (axial, coronal, or sagittal) (Fig. 7). With respect to the mandible, rotational movement in the sagittal plane (about the A_x axis) was significantly different between nonirradiated and previously irradiated subjects (-0.08 ± 0.07 vs. 0.06 ± 0.05 rad, $P = .01$), while rotational movement in the coronal and axial planes (about the A_y and A_z axes, respectively) were not significantly different between groups.

Finally, evaluating the relationship between airway deformation and other clinical variables revealed a significant negative correlation between change in airway volume and subject age ($r = -0.63$, $P = .01$) (Fig. 8). Subgroup analysis revealed that this negative correlation persisted among nonirradiated subjects ($r = -0.75$, $P = .01$), while in previously irradiated subjects, the correlation was not significant despite a similar overall trend in the data ($r = -0.78$, $P = .12$). Subject age did not correlate with the translation or rotation of the mandible in any direction but was modestly correlated with the overall translation of the hyoid ($r = -0.55$, $P = .03$). We did not identify any additional

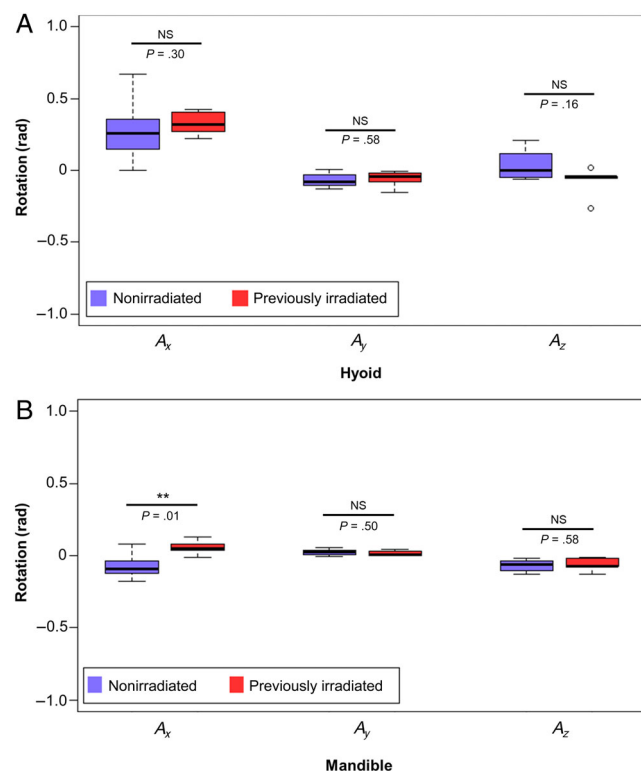


Fig. 7. Rotation of the hyoid (A) and mandible (B) in both nonirradiated (blue) and previously irradiated (red) subjects from their uninstrumented state. A_x , A_y , and A_z correspond to rotations in the sagittal, coronal, and axial planes, respectively. ** $P \leq .01$. NS = not statistically significant.

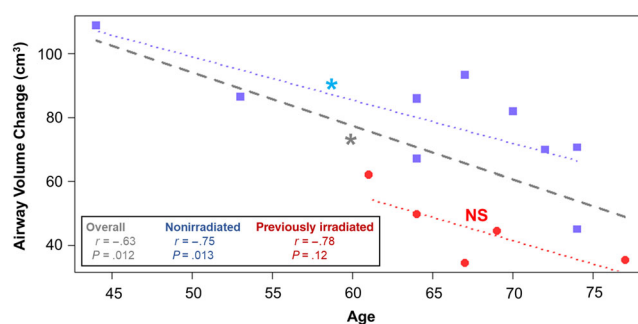


Fig. 8. Correlation between subject age and change in airway volume. Gray lines indicate the line of best fit for the entire study population, while the blue and red lines indicate the line of best fit for the nonirradiated and previously irradiated subjects, respectively. Pearson's correlation coefficient (r) and the P value associated with the correlation are provided for the overall study population as well as the subgroup analyses. * $P < .05$. NS = not statistically significant.

correlations between our clinical variables and either airway deformation or displacement/rotation of the mandible or hyoid.

DISCUSSION

The present study reveals substantial differences in pharyngeal airway deformability between previously irradiated and nonirradiated subjects in the context of clinically indicated suspension laryngoscopy. Specifically, previously irradiated subjects were found to have an approximately 40% reduction in pharyngeal airway volume following laryngoscope insertion relative to nonirradiated subjects (Fig. 4). The region of the airway that differed most substantially with respect to volume between these two groups was in direct approximation to the laryngoscope itself, with minor differences in airway volume observed more distal to the laryngoscope. The reduced pharyngeal airway volume observed in previously irradiated subjects relative to nonirradiated subjects in the instrumented state could not be accounted for by differences in other measured variables, including age, sex, BMI, Mallampati score, airway grade, thyromental distance, neck range of motion, and perhaps most importantly, undeformed airway volume. Taken together, these findings suggest that therapeutic radiation exposure alters the deformability of head and neck tissues, and this reduced deformability likely contributes to the difficulty associated with laryngoscopy in this patient population.

Radiation-induced fibrosis represents one likely explanation for the reduced tissue deformability observed among our cohort of previously irradiated subjects. This process can occur in numerous tissues throughout the body,^{14–16} but may be particularly problematic in the setting of malignancies of the head and neck due to the high overall doses of radiation administered, as well as the aggressive radiation schedules that are often utilized in the treatment of these cancers.¹⁶ This process is thought to involve the deposition of collagen in a disorganized fashion (mediated by the production of pro-fibrotic molecules such as tumor necrosis factor) accompanied by loss of tissue elasticity, and both of

these processes could reasonably be expected to contribute to the reduced airway deformability that we observe among our previously irradiated subjects. To the best of our knowledge, however, irradiated and nonirradiated tissues of the upper airway have never been compared with respect to their elasticity and/or deformability, although this could represent an important future direction for this work.

In addition to observing deformational differences of the nonrigid pharyngeal airway, we observed translational differences of both the hyoid and mandible between nonirradiated and previously irradiated subjects. Notably, there were no intergroup differences with respect to left-right displacement of either structure, while anterior-posterior and superior-inferior displacement of both structures was greater in nonirradiated subjects. In addition to differences in the displacement of the hyoid and mandible individually, it is clear that the overall geometry of the neck during laryngoscopy differs between groups. Specifically, nonirradiated subjects experienced a more dramatic elongation of the space between the mandible and hyoid (8.9 mm) relative to previously irradiated subjects (1.4 mm) in the superior-inferior direction.

Finally, our results demonstrate an age-dependent reduction in deformed airway volume in nonirradiated subjects only, although a nonsignificant trend is observed in previously irradiated subjects as well. In our comparison of previously irradiated and nonirradiated subjects, we observe significant correlations between airway deformability (as defined by deformed airway volume and change in airway volume) and translational motion of the hyoid and mandible, implying that the movement of the hyoid (anterior-posterior) and mandible (anterior-posterior, superior-inferior, and left-right) likely contributes to airway deformation or vice versa. In contrast, there is no significant correlation between patient age and movement of the hyoid or mandible in any of these orientations. We therefore hypothesize that differences in airway deformability as a function of age are independent of hyoid and mandible translation. This age-dependent decrease in airway volume may therefore represent tissue with increased flaccidity rather than decreased elasticity, as we hypothesize in the case of our previously irradiated subjects.

We believe that this work is the first to evaluate differences in airway deformation as a function of prior radiation exposure using CT imaging, thereby providing image-based evidence to support the clinical evidence that laryngoscopy is a particular challenge in patients with a history of head and neck radiation.⁶ This work also demonstrates the utility of advanced imaging tools (ie, three-dimensional renderings of airway volumes as well as bony structures such as the mandible and hyoid) to precisely measure the impact of specific clinical interventions on head and neck anatomy. Finally, the present body of work provides a foundation upon which further studies may build in terms of improving our understanding of the effect of radiation exposure on the deformability of upper airway tissues. For example, a repeat analysis involving the same cohort in the future could provide insight about the progression of tissue fibrosis over time.

There are several limitations to this study. We acknowledge that our patient population was relatively small, and that future studies should evaluate larger patient cohorts. In

addition, the differences we observed in airway deformability and bony structure displacement between nonirradiated and previously irradiated subjects could be accounted for by unmeasured clinical variables that were not included in our evaluation. These include prior exposures that might promote tissue fibrosis, including the use of alcohol or tobacco.^{17–20} Future studies should more precisely evaluate the effect of radiation therapy on head and neck tissue deformability by evaluating both pre- and postradiation therapy CT images from single individuals.

This pilot study demonstrates that individuals with a history of therapeutic radiation to the head and neck have substantially reduced airway deformability compared with nonirradiated subjects in the setting of operative laryngoscopy. Furthermore, displacement of both the hyoid and mandible were found to differ between groups, and nonirradiated subjects were noted to have substantially greater superior-inferior elongation of the space between the hyoid and mandible as compared with previously irradiated subjects. Importantly, the differences that we observe in airway deformation and bony structure displacement cannot be accounted for by any of the clinical variables that we evaluated, although it is possible that other unmeasured variables remain that may contribute to the differences observed. In conclusion, this study provides CT imaging-based evidence to support the clinical evidence that suspension laryngoscopy is a particular challenge in patients with a history of head and neck radiation.

ACKNOWLEDGMENTS

This study was supported by the Dartmouth SYNERGY Clinical and Translational Science Institute (UL1TR001096) from the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH). We thank Mr. Patricio R. Sarzosa at the Thayer School of Engineering at Dartmouth for his assistance in preparing the figures associated with this manuscript.

BIBLIOGRAPHY

- Peterson GN, Domino KB, Caplan RA, Posner KL, Lee LA, Cheney FW. Management of the difficult airway: a closed claims analysis. *Anesthesiol J Am Soc Anesthesiol* 2005;103(1):33–39.
- Piazza C, Paderno A, Grazioli P, et al. Laryngeal exposure and margin status in glottic cancer treated by transoral laser microsurgery. *Laryngoscope* 2018;128(5):1146–1151.
- Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J* 1985;32(4):429–434.
- Roh J-L, Lee Y-W. Prediction of difficult laryngeal exposure in patients undergoing microlaryngoscopy. *Ann Otol Rhinol Laryngol* 2005;114(8):614–620.
- Kheterpal S, Martin L, Shanks AM, Tremper KK. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology* 2009;110(4):891–897.
- Kheterpal S, Healy D, Aziz MF, et al. Incidence, predictors, and outcome of difficult mask ventilation combined with difficult laryngoscopy: a report from the multicenter perioperative outcomes group. *Anesthesiology* 2013;119(6):1360–1369.
- Iseli TA, Iseli CE, Golden JB, et al. Outcomes of intubation in difficult airways due to head and neck pathology. *Ear Nose Throat J* 2012;91(3):E1–E5.
- Ohya T, Iwai T, Luan K, et al. Analysis of carotid artery deformation in different head and neck positions for maxillofacial catheter navigation in advanced oral cancer treatment. *Biomed Eng Online* 2012;11:65.
- Welch KC, Foster GD, Ritter CT, et al. A novel volumetric magnetic resonance imaging paradigm to study upper airway anatomy. *Sleep* 2002;25(5):532–542.

10. Trudo FJ, Geffer WB, Welch KC, Gupta KB, Maislin G, Schwab RJ. State-related changes in upper airway caliber and surrounding soft-tissue structures in normal subjects. *Am J Respir Crit Care Med* 1998;158(4):1259–1270.
11. Paydarfar JA, Wu X, Halter RJ. MRI- and CT-compatible polymer laryngoscope: a step toward image-guided transoral surgery. *Otolaryngol Head Neck Surg* 2016;155(2):364–366.
12. Wu X, Paydarfar JA, Halter RJ. Quantifying anatomic deformations during laryngoscopy. *Ann Biomed Eng* 2018;46(6):912–925.
13. Besl PJ, McKay ND. A method for registration of 3-D shapes. *IEEE Trans Pattern Anal Mach Intell* 1992;14(2):239–256.
14. Stubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. *PM R* 2011;3(11):1041–1054.
15. Kim J, Shin ES, Kim JE, Yoon SP, Kim YS. Neck muscle atrophy and soft-tissue fibrosis after neck dissection and postoperative radiotherapy for oral cancer. *Radiat Oncol J* 2015;33(4):344–349.
16. King SN, Dunlap NE, Tennant PA, Pitts T. Pathophysiology of radiation-induced dysphagia in head and neck cancer. *Dysphagia* 2016;31(3):339–351.
17. Morse D, Rosas IO. Tobacco smoke-induced lung fibrosis and emphysema. *Annu Rev Physiol* 2014;76:493–513.
18. Lee C-H, Ko Y-C, Huang H-L, et al. The precancer risk of betel quid chewing, tobacco use and alcohol consumption in oral leukoplakia and oral submucous fibrosis in southern Taiwan. *Br J Cancer* 2003;88(3):366–372.
19. Suda K, Shiotsu H, Nakamura T, Akai J, Nakamura T. Pancreatic fibrosis in patients with chronic alcohol abuse: correlation with alcoholic pancreatitis. *Am J Gastroenterol* 1994;89(11):2060–2062.
20. Bataller R, Brenner DA. Liver fibrosis. *J Clin Invest* 2005;115(2):209–218.