Computed Tomography Data to Generate a Reproducible, Anatomically Accurate Hemilaryngeal Model

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Abstract

Objective. The study aims to demonstrate the reproducibility and feasibility of creating a hemilaryngeal model with a medialized vocal fold (VF) using 3-dimensional (3D) modeling techniques in both healthy larynges and those affected by cancer.

Study Design. Three-dimensional modeling of human larynges.

Setting. Tertiary academic referral center and regenerative medicine laboratory.

Subjects and Methods. Computed tomography (CT) scans from 10 healthy control and 10 patients with laryngeal cancer were segmented and imported into 3D modeling software. The larynx was cut sagittally to create a hemilaryngeal model and the vocal fold medialized. Measurements were taken from the CT and 3D model data and compared.

Results. All control modeling data closely matched the CT data and were not statistically different from each other. There was a significant correlation between subglottic anteroposterior diameter and VF length (\(r^2 = 0.78, P = .0008\)), and it may be a valuable tool to infer true VF dimension in cases where disruption has occurred. The modeling data from patients with cancer did not show statistical difference to the control data, showing that accurate modeling can also be achieved in patients with laryngeal cancer.

Conclusion. CT scan-based 3D modeling of the larynx and VF is possible and reproducible. The results closely match those previously reported in the literature and can also be replicated in cases with laryngeal cancer. This study paves the way for future de novo fabricated laryngeal scaffolds that can be synthesized using 3D printers and tailored to meet surgical demands.

Keywords

larynx, regenerative medicine, 3D modeling, CT, model
With this in mind, the aim of this study was to first demonstrate the reproducibility of creating a representation of a hemilarynx with a fixed and medialized VF using 3-dimensional (3D) modeling techniques in control patients and comparing this to their own computed tomography (CT) data. The second aim of this study was to demonstrate the feasibility of modeling a hemilarynx in patients with laryngeal cancer, in whom destruction of the laryngeal and VF framework is present, and compare that to control and previously published data.

Results of this study can help future laryngeal regenerative medicine approaches create bespoke laryngeal models, either for direct 3D printing purposes or to design the shape of regenerative medicine constructs.

**Methods**

**CT Images**

This study was given an exemption from our institutional review board (Mayo Clinic Arizona). Deidentified CT images (10 control and 10 patients with cancer) were selected and obtained through the otolaryngology and radiology departments. Only high-resolution (minimum slice thickness of 0.75 mm), standard head and neck protocol images were included. Only scans with an open glottis were selected for the control patients. Open glottis images were not available for the laryngeal cancer group. The files were deidentified and exported as digital imaging and communications in medicine (DICOM) files.

**Segmentation**

Segmentation was performed using the freeware software 3D Slicer (version 4.6.2; The Slicer Community, Open Source software, Brigham and Women’s Hospital, Boston, Massachusetts). DICOM images were first imported into 3D Slicer, a region of interest (ROI) was created to encompass the larynx, and then the volume was cropped. A threshold effect was applied to only select the air-filled larynx (usual threshold range: -3000 to -250) and on occasion modified using the “PaintEffect” or “EraseLabel” tool. A model was then created from the selected areas.

**3D Modeling of the Hemilarynx**

The model was imported into Meshmixer (version 11.0.544; Autodesk, San Rafael, California). The model was then transversely cut superiorly and inferiorly to only include the larynx using the “plane cut” tool (ca 2-3 cm from vocal fold superiorly and ca 3-4 cm inferiorly). The model was subsequently plane cut (no fill) through the midline to create a raw hemilarynx model. The “sculpt” tool (size, 30; strength, 25) was then used to medialize the VF, with as little as possible disruption to the height and shape of the VF. The “robust smooth” tool was used to smooth out any irregularities created from the sculpting process or from the segmentation.

This process generates a surface contour of the airway lumen of a 3D hemilarynx mesh model of 0 mm thickness (in 3D modeling software, 3D surfaces are created as 0-mm meshes that can then be expanded or offset). Using the “offset” function in Meshmixer, a 3D hemilarynx model of desired thickness can then further be created (Figure 1).

In the cancer group, the contralateral unaffected hemilarynx was modeled. For future applications, this can then be mirrored to the opposite affected side to design a construct.

**CT Measurement**

DICOM files were imported into OsiriX Lite (version 8.5.1; PixMeo SARL, Bernex, Geneva, Switzerland). The images were then viewed using 3D multiplanar reconstruction (MPR) and reconstructed via an axial plane through the VF to ensure accurate measurement of VF dimensions. Specifically, the axial plane was used to measure the distance of VF to midline and VF length by combining both membranous and cartilaginous VF. The coronal plane was used to measure VF height in the center of the VF and the superior and inferior VF angles while the subglottic anteroposterior (AP) diameter just below the level of the true VFs was measured using the sagittal plane (Figure 2).

In the cancer group, measurements were taken from the contralateral hemilarynx not affected by neoplastic invasion.

**3D Hemilarynx Measurement**

The final 3D models were measured using the Meshmixer “measure” function. The same dimensions were measured in the 3D model as in the CT data.

**Statistical Analysis**

Statistical analysis was performed using a Student t test in GraphPad Prism (version 6.0; GraphPad Software, La Jolla,
The mean (SD) age for the patients with laryngeal cancer was 72 (8.88) years, and all patients were male. All patients had a diagnosis of squamous cell carcinoma (SCC), ranging in stage from T1 to T4. The patients with laryngeal cancer consisted of 8 (80%) patients who subsequently underwent a total laryngectomy and 2 patients (20%) who had KTP laser-assisted excision. Seven (70%) patients had a history of primary radio- or chemoradiotherapy to the larynx.

**Control Larynx Dimensions (CT and Model)**

The mean (SD) VF length in the control patients was 17.74 (3.49) mm, the height of the VF was 5.00 (0.67) mm, the subglottic AP diameter was 19.14 (3.73) mm, the subglottic lateral diameter was 13.27 (2.45) mm, the superior VF angle was 60.24° (14.76°), the inferior VF angle was 39.48° (9.37°), and the distance of the VF to midline was 1.72 (0.88) mm. There was a significant difference between male and female VF length, height, and subglottic AP diameter (Table 2).

These dimensions were then compared to the 3D model data. All modeling data closely matched the CT data (Figure 3) and were not statistically different from each other. The VF was successfully medialized and performed in a repeatable fashion (1.7 ± 0.88 mm in the CT data vs 0.48 ± 0.30 mm, P = .0001).

A significant correlation was noted between subglottic AP diameter and VF length \( r^2 = 0.78, P = .0008 \) (Figure 4) in the CT data and may be a valuable tool to use for VF modeling in cases where the true VF dimension may not be discernible due to closed glottis or neoplastic destruction (Figure 5).

**Cancer Larynx Dimensions (Model)**

The mean (SD) VF length of the models in the patients with cancer was 18.00 (1.08) mm and the VF height was 5.47 (0.51) mm. The mean (SD) subglottic AP diameter was 19.07 (1.89) mm, the superior VF angle was 63.7° (11.75°), the inferior VF angle was 47° (8.56°), and the distance to midline was 0.19 (0.25) mm (Table 2). It is important to note that all patients with T4 cancer (n = 5) were excluded from the CT analysis data since neoplastic infiltration or glottic closure precluded accurate measurements of true VF dimension. These results were similar to those found in sex-matched control models with no significant differences (Figure 6). While the age of the male control patients and male patients with cancer was statistically different (P = .014), their VF length was not (P = .153).

**Discussion**

Few methods are available for the reconstruction of hemilaryngeal defects after organ-sparing partial laryngectomies. New techniques are being investigated and include the use of aortic homografts, decellularized grafts, and synthetic biomaterials. Our laboratory is currently investigating the ability to synthesize de novo biosynthetic scaffolds using 3D (bio)printers based on data acquired from the patient’s own CT scans. However, before this can be achieved, reliable and accurate CT extraction and modeling of the larynx and VF must be demonstrated. The present study demonstrates that...

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**Table 1. Patient Demographics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controls (n = 10)</th>
<th>Patients with Cancer (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Female</td>
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<td>0</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>46.2 ± 17.7</td>
<td>72 ± 8.88</td>
</tr>
<tr>
<td>Diagnosis, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>T1</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>T2</td>
<td>10</td>
<td>0</td>
</tr>
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<td>T3</td>
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<tr>
<td>T4</td>
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<td>0</td>
</tr>
<tr>
<td>N0</td>
<td>90</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
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</tr>
<tr>
<td>Cancer elsewhere</td>
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</tr>
<tr>
<td>Infectious</td>
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<td>0</td>
</tr>
<tr>
<td>Neck mass</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Treatment, %</td>
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<td></td>
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<tr>
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<tr>
<td>KTP laser</td>
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<td>0</td>
</tr>
<tr>
<td>Prior RT/CT</td>
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<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: CT, chemotherapy; RT, radiotherapy; SCC, squamous cell carcinoma.
Table 2. Larynx Dimensions.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Control Patients</th>
<th>Patients with Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>VF length, mm</td>
<td>20.62 ± 1.99</td>
<td>14.86 ± 1.65</td>
</tr>
<tr>
<td>VF height, mm</td>
<td>5.45 ± 0.48</td>
<td>4.56 ± 0.55</td>
</tr>
<tr>
<td>Subglottic AP diameter, mm</td>
<td>22.22 ± 2.68</td>
<td>16.08 ± 0.81</td>
</tr>
<tr>
<td>Distance from midline, mm</td>
<td>1.75 ± 0.34</td>
<td>1.69 ± 1.27</td>
</tr>
<tr>
<td>VF superior angle, deg</td>
<td>58.74 ± 14.76</td>
<td>61.74 ± 14.65</td>
</tr>
<tr>
<td>VF inferior angle, deg</td>
<td>39.86 ± 5.78</td>
<td>39.1 ± 12.76</td>
</tr>
</tbody>
</table>

Abbreviations: AP, anteroposterior; VF, vocal fold.

Figure 3. Comparison of computed tomography and model data in the control group showing a nonsignificant difference between the two, apart from distance to midline, which was created deliberately. VF, vocal fold.

Figure 4. Correlation between vocal fold (VF) length and subglottic anteroposterior (AP) diameter in the control group ($r^2 = 0.78$, $P = .0008$).

Figure 5. Representative coronal image showing disruption of the vocal fold and laryngeal architecture caused by neoplastic infiltration, making measurement and modeling difficult.
this is possible not only in control patients with normal larynges but also in patients with laryngeal cancer.

To evaluate the first aim of this study, in showing reproducibility of the 3D modeling process, CT data of 5 female and 5 male patients without laryngeal cancer were compared to the 3D models that were created. There was a close association between the dimensions obtained from the CT and from the model data. The differences between the two were not statistically significant, except for distance of the VFs to midline. This difference was created deliberately to allow for the contralateral VF to adduct toward the modeled VF and achieve glottic closure.

These results of the present study are in keeping with previously reported data on vocal fold dimensions for vocal fold length \(^{11-14}\) and height. \(^{12,13}\) In a study of 10 professional female singers, Vorik et al\(^ {11}\) measured laryngeal dimensions using CT scan data during phonation and found that the mean VF length was 18.3 to 19.4 mm and elongated with increased pitch. Their measurements of subglottic AP diameter also closely matched our results. A recent study by Mobashir et al\(^ {12}\) described various anatomical measurements of VFs and larynges in freshly excised human larynges after laryngectomy for laryngeal carcinoma. The mean (SD) VF length was 24.9 (2.5) mm in males and 17.5 (2.2) mm in females. The mean VF height was 6.02 mm in males and 4.74 mm in females. These measurements are slightly greater than those in the present study. Similar results have been reported by Jotz et al\(^ {16}\) in a study of 100 human fresh cadaver larynges, 50 men and 50 women, with a mean (SD) VF length of 24.46 (2.66) mm in men and 17.9 (2.15) mm in females, and by Ara et al\(^ {14}\) (23.12 vs 17.9 mm) and Eckel and Sittel\(^ {10}\) (22.09 vs 17.55 mm). VF height was also similar to previously reported results by Jotz et al\(^ {16}\) (6.07 mm in males and 5.03 mm in females) and by Qiao et al\(^ {17}\) in a sonographic study of VFs (6.23 vs 4.90 mm).

While clear sex differences have been observed in the present study as well as the literature, no difference in VF length as a function of age was observed. Jotz et al\(^ {16}\) examined larynges in patients over the age of 40 years and found that when comparing VF length in patients of the same sex but different age groups, there was no significant difference. The results of the present study replicate these findings. While there was a significant difference between the age of the male controls and patients with cancer (mean, 45.8 vs 72 years, respectively, \(P = .014\)), there was no significant difference in VF length (\(P = .153\)). While VF length changes significantly in the early years of life, it seems that in adults, there is little morphometric change in laryngeal dimension.

Overall, the measurements of VF dimensions match those reported in the literature, with a slight reduction in dimension of VF length as being observed compared to anatomical measurements; our results match other reported radiographic-acquired measurements.\(^ {8,18}\) This may be due, in part, to CT scanning by laryngeal calcification, leading to a slight underestimation of true combined membranous and cartilaginous VF length; the different measurement modality; anatomical vs CT measurement; or changes that occur on explantation and sectioning of the larynx.

Accurate determination of VF and larynx dimensions in the cancer cases was often difficult and sometimes impossible due to local disruption or destruction of the VF or

![Figure 6. Comparison of control data (computed tomography [CT] and models) with cancer models in male patients, showing reliable and consistent results. VF, vocal fold.](image-url)
laryngeal framework by neoplastic infiltration (Figure 5).
In these cases, either the contralateral hemilarynx can be used, or previously published results in the literature and the present study on normal laryngeal dimensions can be used to help sculpt a final 3D model. In addition, none of the cancer CTs had an open glottis, making true and false vocal folds nearly indistinguishable and making measurement of the true VF height sometimes impossible. This could potentially be addressed by creating an “open-glottis” CT protocol for patients considered for CT rendering and laryngeal reconstruction. Furthermore, a significant correlation was found between the subglottic AP diameter and the VF length. This association can be used to infer VF length in cases where determination of VF length is not possible, for example, due to local neoplastic destruction. Therefore, in situations where accurate determination of VF dimensions is not possible prior to laryngeal modeling, a combination of proxy measurements and known VF dimensions can be used to create a medialized VF for the purpose of laryngeal reconstruction. The present study demonstrated that it is still possible to create accurate and reproducible models of the larynx in patients with significant neoplastic involvement and destruction.

In summary, the results of this study show that CT scan-based 3D modeling of the larynx and VF is possible and reproducible. The results closely match those previously reported in the literature and can also be replicated in cases with laryngeal cancer. This study paves the way for future de novo fabricated laryngeal scaffolds that can be synthesized using 3D printers and tailored to meet surgical demands.

Author Contributions

Justin M. Hintze, contributed to conception and design, retrieval of literature and analysis of articles; drafted and revised work; finally approved; accountable for all aspects of work; Cheryl E. Myers, contributed to conception and design, retrieval of literature and analysis of articles; drafted and revised work; finally approved; accountable for all aspects of work; Michael J. McPhail, contributed to conception and design, retrieval of literature and analysis of articles; drafted and revised work; finally approved; accountable for all aspects of work; Yourka D. Tchoukalova, contributed to conception and design, retrieval of literature and analysis of articles; drafted and revised work; finally approved; accountable for all aspects of work; David G. Lott, contributed to conception and design, retrieval of literature and analysis of articles; drafted and revised work; finally approved; accountable for all aspects of work.

Disclosures

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