

# Digital Morphometrics

## A New Upper Airway Phenotyping Paradigm in OSA



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**BACKGROUND:** OSA is associated with changes in pharyngeal anatomy. The goal of this study was to objectively and reproducibly quantify pharyngeal anatomy by using digital morphometrics based on a laser ruler and to assess differences between subjects with OSA and control subjects and associations with the apnea-hypopnea index (AHI). To the best of our knowledge, this study is the first to use digital morphometrics to quantify intraoral risk factors for OSA.

**METHODS:** Digital photographs were obtained by using an intraoral laser ruler and digital camera in 318 control subjects (mean AHI, 4.2 events/hour) and 542 subjects with OSA (mean AHI, 39.2 events/hour).

**RESULTS:** The digital morphometric paradigm was validated and reproducible over time and camera distances. A larger modified Mallampati score and having a nonvisible airway were associated with a higher AHI, both unadjusted ( $P < .001$ ) and controlling for age, sex, race, and BMI ( $P = .015$  and  $P = .018$ , respectively). Measures of tongue size were larger in subjects with OSA vs control subjects in unadjusted models and controlling for age, sex, and race but nonsignificant controlling for BMI; similar results were observed with AHI severity. Multivariate regression suggests photography-based variables capture independent associations with OSA.

**CONCLUSIONS:** Measures of tongue size, airway visibility, and Mallampati scores were associated with increased OSA risk and severity. This study shows that digital morphometrics is an accurate, high-throughput, and noninvasive technique to identify anatomic OSA risk factors. Morphometrics may also provide a more reproducible and standardized measurement of the Mallampati score. Digital morphometrics represent an efficient and cost-effective method of examining intraoral crowding and tongue size when examining large populations, genetics, or screening for OSA.

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**KEY WORDS:** digital morphometrics; modified Mallampati; OSA; tongue; upper airway

**ABBREVIATION:** AHI = apnea-hypopnea index

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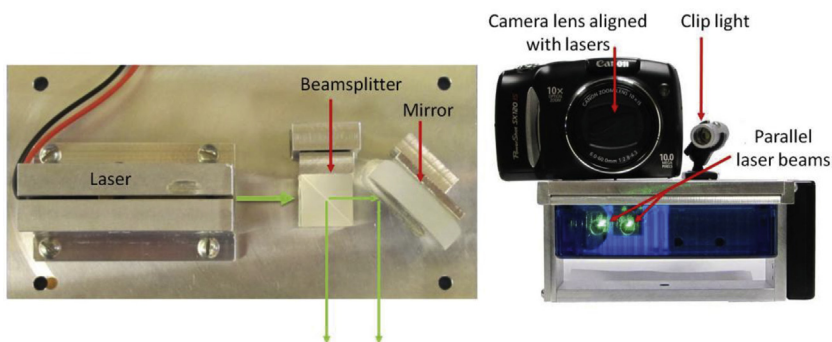


Figure 1 – Laser ruler device. Left shows the interior mechanics of the laser ruler device with the beam splitter and mirror positioned to project two parallel laser beams. Right shows the laser ruler with the camera and clip light attached to the device.

The prevalence of OSA in the adult population is estimated to be approximately 34% for men and 17% for women, with 13% and 6%, respectively, having moderate-to-severe OSA (apnea-hypopnea index [AHI]  $\geq 15$ ).<sup>1,2</sup> Increased OSA risk is associated with aging, obesity, and male sex.<sup>3,4</sup> Although obesity is the most important risk factor,<sup>3-7</sup> studies show that craniofacial abnormalities (ie, reduction in mandibular size) and upper airway soft tissue enlargement increase the prevalence and severity of OSA.<sup>8-11</sup> Larger tongue, lateral pharyngeal walls, tonsils, soft palate, and total pharyngeal soft tissue volumes, as well as a shorter maxilla, smaller mandibular enclosure, and greater mandibular retroposition, have all been shown to increase OSA risk when measured according to MR and CT images.<sup>9,10,12-15</sup> Although these studies provide important insights, such imaging techniques can be time-consuming, expensive, and expose subjects to varying levels of radiation.<sup>8-10,12-14</sup>

Alternative phenotyping methods have primarily relied on qualitative studies of tonsil size, Mallampati score, and pharyngeal narrowing.<sup>16-19</sup> The Mallampati score, originally described with the tongue extended, is a measure of pharyngeal crowding used to predict difficulty in intubation.<sup>20</sup> Modified Mallampati is scored with the tongue in the mouth and used to measure pharyngeal crowding while better representing the tongue position during sleep.<sup>18,20</sup> In an attempt to obtain more quantitative morphometric measurements, calipers have been used to measure the oral cavity and craniofacial dimensions.<sup>21,22</sup> Calipers allow for quantification;

however, there are few data on reproducibility, and the process is cumbersome and unpleasant.

Lee et al<sup>23</sup> described a novel photographic technique to quantify craniofacial measures without calipers. A washer of known size was affixed to the subject's face and used to calibrate measures taken from digital photographs. Using this technique, mandibular length was found to be shorter in subjects with OSA than in control subjects. In the present study, we extended this approach to quantify intraoral measures related to soft tissue structures. However, because a washer cannot be placed within the oral cavity, we used a projected laser ruler for calibration (Fig 1). The laser ruler, consisting of two parallel beams a known distance apart, was used to convert photographic measurements from pixels to centimeters, allowing for objective quantification of intraoral structure sizes.

The primary goal of the present study was to objectively and reproducibly quantify pharyngeal structures by using digital morphometrics based on a laser ruler and to assess differences between subjects with OSA and control subjects and associations with AHI. We hypothesized that larger intraoral structures measured via photography would be associated with higher AHI and increased risk of OSA. Furthermore, we hypothesized that there would be decreased visibility of the pharyngeal airway and a higher modified Mallampati score in subjects with OSA compared with control subjects.

Portions of this investigation have been presented as abstracts.<sup>24-27</sup>

## Subjects and Methods

Additional details are presented in e-Appendix 1 and e-Tables 1-4.

### Study Population

Subjects with OSA were defined as having an AHI  $\geq 10$  events/hour and control subjects as having an AHI  $< 10$ , as in previous

studies.<sup>7,28</sup> Tables 1 and 2 provide descriptions of the photographs and measurements.

### Overnight Polysomnography

Subjects underwent either an overnight in-laboratory polysomnography (n = 787 [91.5%]) or a home study with an Embletta Gold portable monitor (Natus Medical Incorporated) (n = 73 [8.5%]). Studies were scored

**TABLE 1 ]** Descriptions of Primary Facial Photographs (Intraoral and Soft Tissue) Analyzed

Photograph	Description	Measures
Photograph P1	Picture taken from the front, with subject's mouth open maximally, tongue within the mouth and no phonation	Modified Mallampati score; lateral mouth width; vertical mouth height; mouth area; tongue width; airway visibility
Photograph P2	Picture taken from the front, with subject's mouth open maximally and tongue extended out of the mouth and downward maximally	Standard Mallampati score; lateral mouth width; tongue length; tongue width; tongue area
Photograph P3	Picture taken from the side (profile), with subject's mouth open maximally and tongue extended out of the mouth and downward maximally	Tongue length; tongue area; tongue thickness; tongue curvature
Photograph P4	Picture taken from the front, with subject's mouth open maximally, tongue depressed in the mouth and no phonation	Airway width; uvula length, width and area at the airway

**TABLE 2 ]** Descriptions of Intraoral and Craniofacial Measures Obtained via Photography

Variable	Unit	Photograph (P)	Description
<b>Quantitative measures</b>			
Lateral mouth width	cm	P1, P2	The lateral width of the opening of the intraoral cavity, measured as a horizontal line drawn between the right and left corners of the mouth
Vertical mouth height	cm	P1	The maximal vertical height of the opening of the intraoral cavity, measured as a vertical line drawn from the inner edge of the upper lip to the inner edge of the lower lip
Mouth area	cm <sup>2</sup>	P1	The total area of the opening of the intraoral cavity, measured as a polygon bounded by the inner edges of the lips and the corners of the mouth
Tongue width	cm	P1, P2	The maximum width of the extended tongue, measured as the widest horizontal line drawn across the tongue
Tongue length	cm	P2	The length of the extended tongue in the median, measured as the longest vertical line drawn down the center of the visible tongue
Tongue area	cm <sup>2</sup>	P2, P3	The visible surface area of the extended tongue, measured as a polygon bounded by the visible edges of the tongue
Tongue length	cm	P3	The length of the extended tongue, measured as a straight line between the junction of the superior edge of the tongue and the upper lip to the tip of the tongue, as seen from the profile
Tongue thickness	cm	P3	The thickness of the extended tongue, measured as a straight line drawn perpendicular to the tongue through the thickest portion of the tongue completely visible beyond the intraoral cavity
Tongue curvature	cm	P3	The length of the superior surface curve of the tongue, measured as a curved line drawn from the junction of the tongue and the upper lip to the tip of the tongue, as seen from the profile image
Uvula length	cm	P4	The medial vertical length of the uvula, measured as a vertical line drawn from the measured uvula width at the junction of the uvula and airway to the tip of the uvula
Uvula width	cm	P4	The maximum horizontal width of the uvula, measured as a horizontal line drawn across the uvula at the junction of the uvula and upper airway
Uvula area	cm <sup>2</sup>	P4	The visible surface area of the uvula that hangs in the upper airway, drawn as a polygon following the edges of the uvula and connecting with a straight line across the uvula
<b>Categorical measures</b>			
Modified Mallampati score	1-4	P1	Scoring of visibility of structures in the upper airway in photographs with the tongue in the mouth
Standard Mallampati score	0-4	P2	Scoring of visibility of structures in the upper airway in photographs with the tongue extended

(Continued)

TABLE 2 ] (Continued)

Variable	Unit	Photograph (P)	Description
Pharyngeal airway visibility	0-1	P1	Dichotomous scoring of visibility of airway in photographs with the tongue in the mouth
Presence of tongue ridging	0-1	P1, P2, P4	Dichotomous scoring of evidence of tongue ridging on frontal intraoral photographs
Tonsil hypertrophy grade	0-4	P1, P2, P4	Grading of visible tonsil size based on encroachment of tonsils on palatopharyngeal arches and upper airway
Pharyngeal narrowing grade	1-4	P1, P2, P4	Grading of pharyngeal narrowing based on intersection of palatopharyngeal arches and tongue width

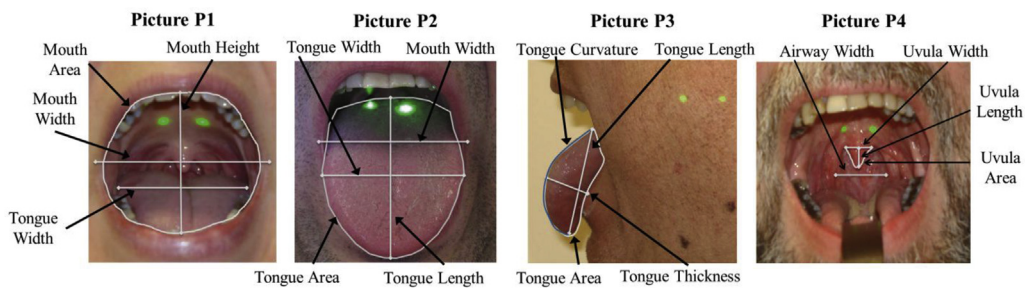


Figure 2 – Intraoral photographs with indicated measurements. The four photographs used to obtain measurements of intraoral structures are shown, with indicated measurements. The tongue within the mouth photograph (P1) shows the mouth width, height, and area and tongue width. The tongue-extended photograph (P2) shows the tongue width, length, and area as well as mouth width. The profile tongue-extended photograph (P3) shows tongue length, curvature (in blue), thickness, and area. The tongue-depressed photograph (P4) shows the uvula width, length, and area at the soft palate and airway width.

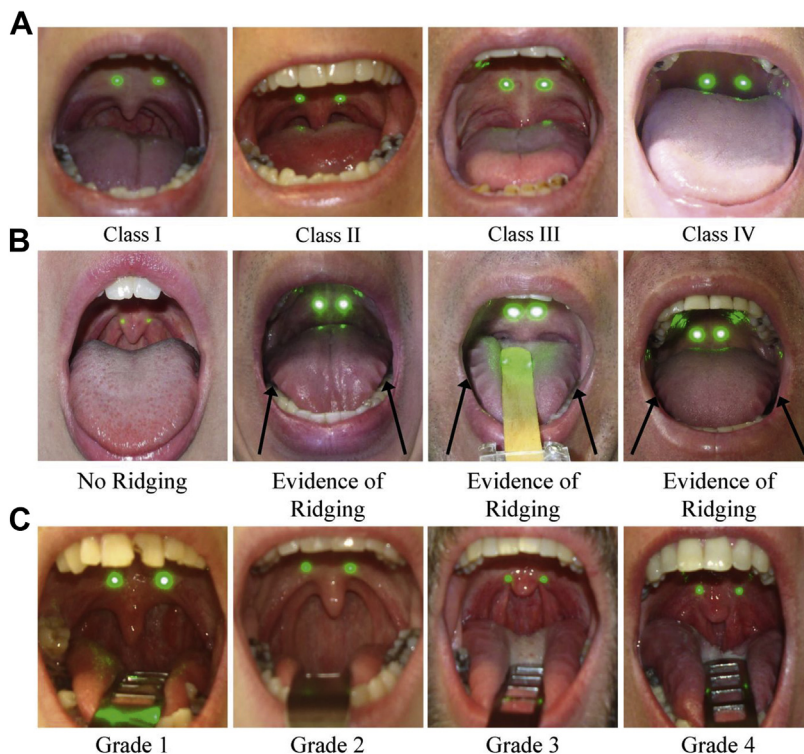


Figure 3 – A-C, Examples of the categorical photographic variables. (A) Modified Mallampati score: Representative examples of each modified Mallampati class obtained from photograph P1 are shown. Class I indicates full visibility of the uvula and tonsillar fossa. Class II indicates visibility of the upper portion of the uvula and partial visibility of the airway. Class III indicates visibility of the hard palate and base of the uvula. Class IV indicates visibility of the hard palate and no visibility of the soft palate. In addition to modified Mallampati scores, we derived a measure of airway visibility using these photographs; the airway is visible in Class I and Class II, but it is not in Class III and Class IV. (B) Tongue ridging. Representative examples of the absence of ridging and evidence of ridging (black arrows) are shown, from photograph P1, P2, or P4. If evidence of tongue ridging is visible in any frontal intraoral photo, subjects are then graded for presence of tongue ridging. (C) Pharyngeal narrowing. Representative examples of each grade of pharyngeal narrowing are shown, from photograph P1, P2, or P4. Grades are based on the location of the intersection between the palatopharyngeal arch and the tongue, relative to tongue width. Grade 1 indicates that the arch intersects at the edge of the tongue. Grades 2, 3, and 4 indicate that the palatopharyngeal arch intersects at 25%, 50%, and 75% or more of the tongue width, respectively.



by a trained sleep technologist and reviewed by certified sleep physicians according to methods of the American Academy of Sleep Medicine.<sup>29</sup>

### Laser Ruler

Digital photographs were obtained by using a digital camera and intraoral laser ruler, composed of a right angle beam splitter and mirror aligned such that two parallel beams project forward a known distance apart (Fig 1). A camera was attached to the laser ruler to allow for digital photographs to capture the projected laser beams adjacent to measures of interest. The distance between the lasers (1.0 or 1.5 cm depending on the device) was used to calculate quantitative measures from the photograph.

### Morphometric Photographs

For each photograph, subjects were seated with their head in a neutral position and line of sight parallel to the floor.<sup>29</sup> The camera and laser

ruler were placed between 35 and 50 cm from the subject. Subjects were instructed to open their mouths maximally for 4 intraoral photographs (Table 1) in the frontal or profile position (Fig 2): tongue in the mouth without phonation (frontal photograph), tongue extended (frontal photograph), tongue extended (profile photograph), and tongue depressed without phonation (frontal photograph). We also obtained categorical measures of pharyngeal airway visibility, modified and standard Mallampati scores, tongue ridging, tonsil hypertrophy grade, and pharyngeal narrowing grade (Fig 3).

### Statistical Methods

Methods, sample size and power, and Hochberg multiple comparisons correction are given in e-Appendix 1.<sup>30,31</sup>

## Results

### Validation and Reproducibility

Details on validation and reproducibility are given in e-Appendix 1.

### Measurement Visibility

We assessed our ability to measure the different structures overall and between subjects with OSA and

control subjects (e-Table 4). Due to study design (adding new photographs and measurement variables to the paradigm), the number of subjects with OSA and control subjects with available data varied. Measurements capturing the size of the mouth and tongue were obtained in at least 89% of photographs (range, 89.2%-99.0%). Tongue width with the tongue in the mouth was obtained in a slightly lower proportion of subjects with OSA than in control

**TABLE 3 ]** Descriptive Statistics of Demographic Characteristics and Photographic Measures

Measure	All Patients		Control Subjects (AHI < 10)		Subjects With OSA (AHI ≥ 10)		P
	No.	Estimate	No.	Estimate	No.	Estimate	
Age	860	47.4 ± 13.7	318	42.7 ± 13.9	542	50.2 ± 12.8	< .0001
BMI	860	36.1 ± 9.9	318	32.1 ± 8.6	542	38.5 ± 9.8	< .0001
Sex							.021
Male	412	47.9%	136	42.8%	276	50.9%	
Female	448	52.1%	182	57.2%	266	49.1%	
Race							< .001
White	405	47.7%	159	50.6%	246	45.9%	
African American	387	45.5%	122	38.9%	265	49.4%	
Other	58	6.8%	33	10.5%	25	4.7%	
AHI	860	26.2 ± 28.9	318	4.2 ± 2.8	542	39.2 ± 29.4	< .0001
ln(AHI+1)	860	2.72 ± 1.17	318	1.46 ± 0.66	542	3.46 ± 0.67	< .0001
Modified Mallampati score, P1							.018
Class I	35	4.5%	20	7.1%	15	3.0%	
Class II	79	10.1%	34	12.1%	45	9.0%	
Class III	127	16.3%	47	16.7%	80	16.1%	
Class IV	538	69.1%	180	64.1%	358	71.9%	
Airway visibility, P1							.007
Visible	114	14.6%	54	19.2%	60	12.0%	
Not visible	665	85.4%	227	80.8%	438	88.0%	
Mouth width, P1	808	6.18 ± 0.86	308	6.08 ± 0.87	500	6.24 ± 0.85	.011

(Continued)

TABLE 3 ] (Continued)

Measure	All Patients		Control Subjects (AHI < 10)		Subjects With OSA (AHI ≥ 10)		P
	No.	Estimate	No.	Estimate	No.	Estimate	
Mouth height, P1	780	5.14 ± 1.03	298	5.10 ± 1.08	482	5.16 ± 1.01	.377
Mouth area, P1	786	24.0 ± 7.0	301	23.3 ± 7.5	485	24.4 ± 6.6	.025
Tongue width, P1	742	5.13 ± 0.56	290	5.00 ± 0.53	452	5.21 ± 0.57	<b>&lt; .0001</b>
Standard Mallampati score, P2							<b>.002</b>
Class I	26	3.6%	14	5.2%	12	2.6%	
Class II	72	9.9%	38	14.1%	34	7.4%	
Class III	201	27.6%	78	29.0%	123	26.7%	
Class IV	430	59.0%	139	51.7%	291	63.3%	
Mouth width, P2	725	6.02 ± 0.77	282	5.94 ± 0.81	443	6.07 ± 0.75	.027
Tongue width, P2	798	5.23 ± 0.73	306	5.10 ± 0.71	492	5.30 ± 0.73	<b>.0001</b>
Tongue length, P2	740	5.82 ± 1.23	277	5.84 ± 1.21	463	5.80 ± 1.25	.711
Tongue area, P2	750	25.9 ± 7.9	281	25.3 ± 7.7	469	26.3 ± 8.1	.110
Tongue length, P3	624	4.30 ± 0.81	245	4.28 ± 0.81	379	4.31 ± 0.82	.574
Tongue area, P3	622	5.54 ± 1.94	243	5.37 ± 1.96	379	5.65 ± 1.93	.085
Tongue thickness, P3	626	1.47 ± 0.30	246	1.41 ± 0.31	380	1.51 ± 0.28	<b>&lt; .0001</b>
Tongue curvature, P3	615	5.31 ± 1.25	242	5.33 ± 1.32	373	5.29 ± 1.20	.671
Airway width, P4	148	2.17 ± 0.65	88	2.19 ± 0.61	60	2.14 ± 0.71	.687
Uvula length (airway), P4	169	0.57 ± 0.28	91	0.56 ± 0.25	78	0.59 ± 0.31	.455
Uvula width (airway), P4	358	0.89 ± 0.20	165	0.86 ± 0.18	193	0.90 ± 0.22	.057
Uvula area (airway), P4	166	0.38 ± 0.22	89	0.35 ± 0.18	77	0.41 ± 0.25	.082
Global Mallampati score							<b>.001</b>
Class I	17	2.1%	10	3.3%	7	1.4%	
Class II	70	8.6%	36	11.9%	34	6.7%	
Class III	174	21.5%	75	24.7%	99	19.5%	
Class IV	549	67.8%	182	60.1%	367	72.4%	
Tongue ridging							.721
Absent	209	25.8%	75	25.1%	134	26.2%	
Evident	601	74.2%	224	74.9%	377	73.8%	
Tonsil hypertrophy							.073
Grade 0	106	31.6%	56	35.9%	50	27.8%	
Grade 1	91	27.1%	47	30.1%	44	24.4%	
Grade 2	74	22.0%	30	19.2%	44	24.4%	
Grades 3 and 4	65	19.3%	23	14.7%	42	23.3%	
Pharyngeal narrowing							<b>.001</b>
Grade 0	37	8.7%	20	10.5%	17	7.3%	
Grade 1	156	36.9%	84	44.2%	72	30.9%	
Grade 2	172	40.7%	71	37.4%	101	43.3%	
Grade 3	58	13.7%	15	7.9%	43	18.5%	

Data are presented as mean ± SD unless otherwise indicated. P values for differences in photograph (P) measures significant after Hochberg correction are shown in bold.

subjects (89.3% vs 93.6%;  $P = .042$ ). Obtaining measurements of airway width or uvula size was more difficult due to lack of visibility, and measures were less

likely to be obtained in subjects with OSA (12.6%-40.6%) compared with control subjects (29.7%-55.7%). Results for these measures should be interpreted

cautiously given their availability on a subset of the population (specifically, younger, less obese subjects who are less likely to have apnea). This outcome is also true for global measures of tonsil hypertrophy and pharyngeal narrowing.

### Subject Demographic Characteristics

The study sample consisted of 542 subjects with OSA and 318 control subjects. Subjects with OSA were older, heavier, more likely to be male, and more likely to be African American (Table 3). Given these differences, statistical models were used to control for these variables; there was a reasonable overlap in age and BMI between subjects with OSA and control subjects to allow for statistical adjustment (e-Fig 1).

### Associations Between Photography Measurements and OSA Status

In unadjusted comparisons of means and frequencies between subjects with OSA and control subjects (Table 3), nominally ( $P < .05$ ) or statistically (after Hochberg correction) significant differences for a number of

photography-derived measures were recorded. Subjects with apnea had higher scores on all measures of Mallampati, less airway visibility, larger mouth width and area, and larger tongue width and thickness. These subjects also had more severe pharyngeal narrowing within the subpopulation where this measure was quantifiable.

We next examined the relationship between photograph variables and the likelihood of OSA (Table 4). In unadjusted models in photograph P1, larger tongue width was significantly associated with increased odds of OSA, whereas larger mouth width, mouth area, and a nonvisible airway were nominally associated. Similarly, a higher modified Mallampati score was nominally associated with OSA risk; subjects in Class IV had a 2.65 times increased odds of OSA compared with subjects in Class I. In photograph P2, larger tongue width and a higher standard Mallampati score were significantly associated with OSA risk, and mouth width was nominally associated. When examining the size of the tongue in the profile tongue-extended photograph (P3), a 1 SD increase in tongue thickness was significantly

**TABLE 4 ]** Associations Between Photographic Measures and OSA Status

Measure	Unadjusted		Age-, Sex-, and Race-Adjusted		Age-, Sex-, Race-, and BMI-Adjusted	
	Estimate <sup>a</sup>	<i>P</i>	Estimate <sup>a</sup>	<i>P</i>	Estimate <sup>a</sup>	<i>P</i>
<b>Photograph P1</b>						
Modified Mallampati score	Overall	.022	Overall	.120	Overall	.213
Class I	1.00 (ref)	...	1.00 (ref)	...	1.00 (ref)	...
Class II	1.76 (0.79- 3.94)	.166	1.92 (0.82-4.53)	.134	2.24 (0.88-5.66)	.089
Class III	2.27 (1.06-4.85)	.035	2.45 (1.09-5.49)	.029	2.51 (1.05-6.02)	.039
Class IV	2.65 (1.33-5.30)	.006	2.36 (1.13-4.93)	.022	2.27 (1.02-5.02)	.044
Airway not visible	1.74 (1.16-2.59)	.007	1.52 (0.99-2.34)	.057	1.33 (0.83-2.12)	.233
Mouth width	1.21 (1.04-1.39)	.011	1.15 (0.98-1.35)	.095	1.03 (0.86-1.22)	.766
Mouth height	1.07 (0.92-1.24)	.369	1.02 (0.87-1.19)	.817	0.97 (0.81-1.14)	.687
Mouth area	1.19 (1.03-1.38)	.022	1.15 (0.98-1.35)	.087	1.04 (0.88-1.24)	.644
Tongue width	1.46 (1.25-1.71)	<b>&lt; .0001</b>	1.33 (1.12-1.58)	<b>.001</b>	1.10 (0.91-1.32)	.347
<b>Photograph P2</b>						
Standard Mallampati score	Overall	<b>.002</b>	Overall	.099	Overall	.375
Class I	1.00 (ref)	...	1.00 (ref)	...	1.00 (ref)	...
Class II	1.04 (0.42-2.57)	.926	1.80 (0.68-4.79)	.240	1.44 (0.50-4.20)	.500
Class III	1.84 (0.81-4.18)	.146	2.38 (0.98-5.77)	.055	1.94 (0.75-5.07)	.173
Class IV	2.44 (1.10-5.42)	.028	2.64 (1.12-6.24)	.027	2.01 (0.79-5.10)	.142
Mouth width	1.19 (1.02-1.38)	.025	1.11 (0.94-1.32)	.218	1.04 (0.87-1.25)	.642
Tongue width	1.33 (1.15-1.54)	<b>&lt; .001</b>	1.26 (1.07-1.48)	.006	1.09 (0.91-1.31)	.324
Tongue length	0.97 (0.84-1.13)	.713	0.97 (0.82-1.13)	.673	0.85 (0.71-1.01)	.067
Tongue area	1.13 (0.97-1.31)	.114	1.10 (0.93-1.29)	.256	0.95 (0.80-1.14)	.584

(Continued)

**TABLE 4 ] (Continued)**

Measure	Unadjusted		Age-, Sex-, and Race-Adjusted		Age-, Sex-, Race-, and BMI-Adjusted	
	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P
<b>Photograph P3</b>						
Tongue length	1.05 (0.89-1.23)	.574	1.03 (0.87-1.23)	.731	0.92 (0.76-1.12)	.411
Tongue area	1.15 (0.98-1.36)	.085	1.09 (0.92-1.30)	.321	0.97 (0.80-1.17)	.724
Tongue thickness	1.43 (1.21-1.70)	<b>&lt; .0001</b>	1.29 (1.07-1.54)	.007	1.12 (0.93-1.36)	.230
Tongue curvature	0.96 (0.82-1.13)	.664	0.95 (0.80-1.13)	.594	0.88 (0.73-1.06)	.167
<b>Photograph P4</b>						
Airway width	0.93 (0.67-1.30)	.675	0.87 (0.60-1.24)	.436	0.83 (0.55-1.26)	.378
Uvula length (airway)	1.12 (0.83-1.52)	.445	1.22 (0.86-1.72)	.266	1.02 (0.71-1.48)	.911
Uvula width (airway)	1.22 (0.99-1.51)	.061	1.04 (0.82-1.32)	.747	1.10 (0.85-1.43)	.460
Uvula area (airway)	1.32 (0.97-1.81)	.079	1.35 (0.94-1.95)	.109	1.19 (0.81-1.75)	.364
<b>Global measures</b>						
Global Mallampati score	Overall	<b>.002</b>	Overall	.072	Overall	.369
Class I	1.00 (ref)	...	1.00 (ref)	...	1.00 (ref)	...
Class II	1.35 (0.46-3.95)	.584	1.57 (0.51-4.89)	.434	1.61 (0.46-5.63)	.452
Class III	1.89 (0.69-5.18)	.219	1.94 (0.67-5.62)	.224	1.66 (0.52-5.36)	.394
Class IV	2.88 (1.08-7.69)	.035	2.56 (0.91-7.19)	.075	2.11 (0.68-6.56)	.199
Evident tongue ridging	0.94 (0.68-1.31)	.721	1.03 (0.73-1.46)	.854	1.15 (0.79-1.68)	.458
Tonsil hypertrophy	Overall	.076	Overall	.012	Overall	.034
Grade 0	1.00 (ref)	...	1.00 (ref)	...	1.00 (ref)	...
Grade 1	1.05 (0.60-1.84)	.869	1.58 (0.84-2.96)	.153	1.63 (0.83-3.23)	.158
Grade 2	1.64 (0.90-3.00)	.105	2.47 (1.26-4.84)	.008	2.74 (1.31-5.74)	.008
Grades 3 and 4	2.05 (1.08-3.86)	.027	2.99 (1.42-6.29)	.004	2.45 (1.11-5.44)	.027
Pharyngeal narrowing	Overall	<b>.002</b>	Overall	.002	Overall	.073
Grade 0	1.00 (ref)	...	1.00 (ref)	...	1.00 (ref)	...
Grade 1	1.01 (0.49-2.07)	.982	1.33 (0.62-2.86)	.467	1.43 (0.63-3.26)	.393
Grade 2	1.67 (0.82-3.42)	.158	2.33 (1.08-5.03)	.032	2.11 (0.92-4.82)	.076
Grade 3	3.37 (1.41-8.08)	.006	4.10 (1.61-10.47)	.003	3.03 (1.13-8.14)	.028

P values for differences in photograph measures significant after Hochberg correction are shown in bold.

<sup>a</sup>Estimates presented as OR (95% CI) from logistic regression models (unadjusted or controlling for indicated covariates) for OSA associated with a 1 SD increase in continuous measures or compared with the indicated reference category for categorical measures.

associated with a 1.43 times increased odds of OSA. Significant associations were also seen in global categorical measures, with a more severe Mallampati score and worse pharyngeal narrowing associated with a higher likelihood of OSA. Subjects with a pharyngeal narrowing grade of 3 had a 3.37 times increased odds of OSA compared with subjects with a grade of 0. None of the airway or uvula measures in photograph P4 showed significant associations in the subset with available data.

Table 4 also illustrates covariate-adjusted associations with OSA status. In partially adjusted models controlling for age, sex, and race, larger tongue width remained significantly associated with increased OSA risk (after Hochberg correction), whereas tongue

thickness, pharyngeal narrowing, and more severe tonsil grade remained or became nominally significant. After additional adjustment for BMI, only tonsil hypertrophy grade remained nominally associated.

#### Associations Between Photography Measurements and AHI

We next examined associations between photographic measures and continuous AHI (Table 5). In unadjusted models for photograph P1, larger mouth width, tongue width, a nonvisible airway, and higher modified Mallampati score were significantly associated with higher AHI; larger mouth area showed nominal



TABLE 5 ] Associations Between Photographic Measures and In(AHI+1)

Measure	Unadjusted		Age-, Sex-, and Race-Adjusted		Age-, Sex-, Race-, and BMI-Adjusted	
	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P
Photograph P1						
Modified Mallampati score	Overall	<b>.0001</b>	Overall	<b>.002</b>	Overall	.015
Class I	0.00 (ref)	...	0.00 (ref)	...	0.00 (ref)	...
Class II	0.40 (-0.06 to 0.86)	.085	0.38 (-0.05 to 0.81)	.083	0.38 (0.00 to 0.76)	.049
Class III	0.54 (0.11 to 0.97)	.014	0.52 (0.12 to 0.92)	.011	0.42 (0.06 to 0.78)	.021
Class IV	0.77 (0.38 to 1.16)	< .001	0.65 (0.28 to 1.02)	.001	0.51 (0.19 to 0.84)	.002
Airway not visible	0.45 (0.22 to 0.68)	< <b>.001</b>	0.37 (0.15 to 0.58)	<b>.001</b>	0.23 (0.04 to 0.43)	.018
Mouth width	0.13 (0.05 to 0.21)	<b>.001</b>	0.08 (-0.01 to 0.16)	.067	0.01 (-0.06 to 0.08)	.799
Mouth height	0.04 (-0.04 to 0.12)	.320	0.00 (-0.08 to 0.08)	.946	-0.03 (-0.09 to 0.04)	.478
Mouth area	0.10 (0.02 to 0.18)	.016	0.06 (-0.03 to 0.14)	.179	-0.00 (-0.08 to 0.07)	.915
Tongue width	0.25 (0.17 to 0.34)	< <b>.0001</b>	0.17 (0.09 to 0.26)	< <b>.001</b>	0.05 (-0.03 to 0.12)	.218
Photograph P2						
Standard Mallampati score	Overall	< <b>.0001</b>	Overall	<b>.002</b>	Overall	.035
Class I	0.00 (ref)	...	0.00 (ref)	...	0.00 (ref)	...
Class II	0.04 (-0.47 to 0.56)	.868	0.34 (-0.16 to 0.84)	.183	0.19 (-0.25 to 0.64)	.395
Class III	0.48 (0.01 to 0.95)	.047	0.58 (0.13 to 1.04)	.011	0.40 (-0.00 to 0.80)	.053
Class IV	0.72 (0.26 to 1.18)	.002	0.71 (0.27 to 1.15)	.002	0.46 (0.06 to 0.85)	.023
Mouth width	0.12 (0.03 to 0.21)	.007	0.06 (-0.02 to 0.15)	.159	0.02 (-0.06 to 0.09)	.655
Tongue width	0.20 (0.12 to 0.29)	< <b>.0001</b>	0.16 (0.08 to 0.24)	< <b>.001</b>	0.06 (-0.01 to 0.13)	.102
Tongue length	0.01 (-0.07 to 0.10)	.806	0.01 (-0.08 to 0.09)	.895	-0.06 (-0.13 to 0.02)	.130
Tongue area	0.10 (0.01 to 0.18)	.027	0.07 (-0.01 to 0.15)	.097	-0.01 (-0.08 to 0.06)	.757
Photograph P3						
Tongue length	0.04 (-0.06 to 0.13)	.447	0.02 (-0.06 to 0.11)	.603	-0.04 (-0.12 to 0.04)	.335
Tongue area	0.09 (-0.00 to 0.18)	.053	0.04 (-0.04 to 0.13)	.319	-0.03 (-0.11 to 0.05)	.416
Tongue thickness	0.24 (0.15 to 0.33)	< <b>.0001</b>	0.15 (0.06 to 0.24)	<b>.001</b>	0.06 (-0.02 to 0.14)	.153
Tongue curvature	-0.01 (-0.10 to 0.08)	.817	-0.01 (-0.10 to 0.08)	.801	-0.05 (-0.13 to 0.02)	.178
Photograph P4						
Airway width	0.01 (-0.18 to 0.20)	.908	-0.03 (-0.20 to 0.14)	.739	-0.02 (-0.17 to 0.12)	.780
Uvula length (airway)	0.09 (-0.08 to 0.26)	.308	0.11 (-0.05 to 0.26)	.174	0.04 (-0.10 to 0.17)	.606

(Continued)

TABLE 5 ] (Continued)

Measure	Unadjusted		Age-, Sex-, and Race-Adjusted		Age-, Sex-, Race-, and BMI-Adjusted	
	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P	Estimate <sup>a</sup>	P
Uvula width (airway)	0.14 (0.02 to 0.25)	.021	0.01 (-0.11 to 0.12)	.926	0.03 (-0.07 to 0.12)	.588
Uvula area (airway)	0.17 (-0.00 to 0.34)	.054	0.12 (-0.03 to 0.28)	.124	0.07 (-0.07 to 0.21)	.319
Global measures						
Global Mallampati score	Overall	<b>&lt; .0001</b>	Overall	<b>.001</b>	Overall	.034
Class I	0.00 (ref)	...	0.00 (ref)	...	0.00 (ref)	...
Class II	0.20 (-0.41 to 0.81)	.525	0.23 (-0.35 to 0.81)	.437	0.17 (-0.34 to 0.68)	.521
Class III	0.55 (-0.02 to 1.13)	.060	0.50 (-0.04 to 1.05)	.069	0.30 (-0.18 to 0.78)	.218
Class IV	0.82 (0.27 to 1.38)	.004	0.69 (0.17 to 1.22)	.010	0.44 (-0.03 to 0.91)	.066
Evident tongue ridging	-0.09 (-0.27 to 0.09)	.345	-0.04 (-0.21 to 0.14)	.693	0.04 (-0.12 to 0.19)	.656
Tonsil hypertrophy	Overall	.005	Overall	<b>.0001</b>	Overall	<b>.001</b>
Grade 0	0.00 (ref)	...	0.00 (ref)	...	0.00 (ref)	...
Grade 1	-0.07 (-0.39 to 0.26)	.683	0.19 (-0.10 to 0.49)	.204	0.14 (-0.12 to 0.40)	.280
Grade 2	0.30 (-0.04 to 0.64)	.088	0.52 (0.20 to 0.83)	.001	0.43 (0.16 to 0.71)	.002
Grades 3 and 4	0.52 (0.17 to 0.88)	.004	0.73 (0.39 to 1.07)	< .0001	0.54 (0.24 to 0.84)	.001
Pharyngeal narrowing	Overall	<b>&lt; .0001</b>	Overall	<b>&lt; .0001</b>	Overall	<b>.001</b>
Grade 0	0.00 (ref)	...	0.00 (ref)	...	0.00 (ref)	...
Grade 1	0.10 (-0.32 to 0.52)	.637	0.26 (-0.13 to 0.65)	.187	0.31 (-0.04 to 0.65)	.083
Grade 2	0.30 (-0.11 to 0.71)	.155	0.45 (0.06 to 0.84)	.023	0.32 (-0.02 to 0.67)	.065
Grade 3	0.97 (0.49 to 1.45)	< .001	1.02 (0.57 to 1.47)	< .0001	0.77 (0.37 to 1.18)	< .001

P values for differences in photograph measures significant after Hochberg correction are shown in bold.

<sup>a</sup>Estimates presented as estimated mean change (95% CI) in ln(AHI+1) (natural log) from linear regression models (unadjusted or controlling for indicated covariates) associated with a 1 SD increase in continuous measures or compared with the indicated reference category for categorical measures.

significance. Airway visibility, modified Mallampati score, and tongue width remained statistically significant after adjusting for age, sex, and race. When including BMI, airway visibility and modified Mallampati score remained nominally significant. In photograph P2, larger mouth width, tongue width, and tongue area, as well as a higher standard Mallampati score, were all significantly or nominally associated with higher AHI. Adjusting for age, sex, and race, the standard Mallampati score and tongue width remained significantly associated; only the standard Mallampati score was nominally associated after BMI adjustment. Larger tongue thickness on photograph P3 was significantly associated with more severe AHI in the unadjusted and partially adjusted models but not after additional adjustment for BMI. Similarly, larger uvula width (P4) was nominally associated with AHI in unadjusted analyses only. For global categorical measures, more severe Mallampati score, tonsil hypertrophy grade, and pharyngeal narrowing grade were nominally or significantly associated with higher AHI values in all models.

#### Multivariate Associations With OSA Measures

Multivariate regression with backwards selection was used to examine whether there were independent effects among all variables from photographs P1, P2, and P3, which were visible in at least 89% of photographed subjects, as well as clinical factors (age, BMI, sex, and race). A total of 430 subjects had data for all measures and were included in multivariate models; there were no significant differences in age, sex, race, BMI, or AHI between included and excluded subjects.

When examining associations with OSA status, the backwards selection algorithm resulted in a final model, including sex ( $P = .003$ ), age ( $P < .0001$ ), and BMI ( $P < .0001$ ) as important clinical predictors, as well as significant independent associations for tongue area ( $P = .008$ ) and curvature ( $P = .003$ ) from the profile tongue-extended photograph. Thus, the results suggest that profile measures of the tongue capture unique aspects related to OSA risk.

Similarly, when examining associations with AHI, selected clinical covariates included sex ( $P < .0001$ ), age ( $P < .0001$ ), and BMI ( $P < .0001$ ). A number of photography-derived variables showed significant independent associations in the final model, including standard Mallampati score ( $P = .028$ ), tongue width ( $P = .0005$ ), and tongue length ( $P = .022$ ) from the frontal photograph with the tongue extended maximally,

and tongue length ( $P = .031$ ) and curvature ( $P = .020$ ) from the profile tongue-extended photograph. Once again, these results suggest that photography variables provide additional information after accounting for clinical factors.

#### Discussion

This investigation confirms data from other imaging studies<sup>17-23,29,32-34</sup> showing associations between intraoral anatomy and OSA but using a less invasive, higher throughput, and more cost-efficient method. Previous noninvasive studies have attempted to phenotype intraoral anatomy but have been limited to primarily qualitative studies and have not quantified pharyngeal structures.<sup>16</sup> Our validated method of digital morphometrics using a laser ruler provides an efficient and reproducible method to quantify mouth and tongue sizes, as well as airway visibility measures, in a high proportion of photographed individuals.

Using our method, we examined the relationship between intraoral measures and both AHI and OSA status in a large sample. Measurements of intraoral crowdedness showed the strongest associations. A higher Mallampati score and nonvisible airway were both risk factors for more severe OSA, even after controlling for age, sex, race, and BMI; subjects with OSA tended to have more crowded or less visible airways than control subjects. Pharyngeal airway visibility is a dichotomous analogue of the modified Mallampati score measuring pharyngeal crowding and may represent a more efficient first-stage screening tool for identifying subjects with increased OSA risk. This relationship between increased apnea severity and intraoral crowdedness was also reflected in associations with AHI for both tonsil hypertrophy and pharyngeal narrowing grade, within a subset of the population.

Mouth width and area were also associated with OSA status, although significance was lost after full covariate adjustment. A small lateral mouth opening will contribute to decreased pharyngeal airway visibility and increased modified Mallampati score. Similarly, larger tongue width and tongue thickness were associated with increased likelihood of OSA and higher AHI. Associations remained significant when controlling for age, sex, and race but were lost after adjustment for BMI. Because BMI is related to tongue size and tongue fat,<sup>7,35</sup> it is not surprising that statistical significance was lost. However, measures of tongue size and morphology could provide additional insights into appropriate treatment approaches that are not obvious based on

BMI alone. Supporting the idea that photography measures of the tongue may capture unique aspects of OSA risk, several measures of the tongue showed significant associations ( $P < .05$ ) in multivariate analyses, even in the presence of age, sex, and BMI. These associations, as well as possible interactions among variables, should be examined within independent datasets.

### *Limitations and Strengths*

The study's limitations and strengths are discussed in [e-Appendix 1](#).

### *Utility of Digital Morphometrics*

The overall potential of our digital morphometric analysis paradigm may be its ability to predict or model the likelihood of developing OSA based on airway pharyngeal visibility and tongue size. Photography could be used to determine anatomic risk factors for OSA in large population studies or screening studies.

Obtaining and storing photographs also allows for future assessments of intraoral structures. This approach is not possible if, for example, a study is recording the Mallampati score based only on visual inspection of the airway. Thus, digital morphometrics may provide a more reproducible and standardized objective measurement technique for capturing the Mallampati score, which may provide clinical benefit. Although the size of intraoral structures has been shown to be predictive of OSA,<sup>16</sup> most large trials and cohorts evaluating patients with sleep apnea have not assessed upper airway anatomy, instead relying on clinical measures of overall obesity. OSA is one of the few diseases in which detailed physical examination is largely ignored.

Digital morphometrics represent an efficient and cost-effective method of examining intraoral crowding and tongue size for large population genetic studies and/or

examination of differences across ethnicity; the process can be expanded to include craniofacial structures as described previously.<sup>23</sup> Combining the intraoral digital morphometric analyses described here with craniofacial assessments allows for comprehensive phenotyping of OSA risk factors. Future studies should examine sensitivity and specificity for predicting OSA using individual or combinations of photographically derived phenotypes. Moreover, digital morphometrics could be used to efficiently observe subjects through weight loss and address relationships between BMI, AHI, and tongue size. As the relationships between intraoral structures and apnea are documented, digital morphometrics could be used to help identify optimal, personalized OSA interventions.

### **Conclusions**

We showed that a digital camera and laser ruler can be used to quantify intraoral anatomy, particularly for measures of the tongue and mouth, airway visibility, and Mallampati score. Using the techniques described, we obtained reproducible measures of a number of OSA-related anatomic risk factors in a large proportion of photographed subjects. Measures of tongue size were associated with increased OSA risk and higher AHI, independent of age, sex, and race. Categorical measures of airway visibility and modified Mallampati score showed associations with AHI, independent of BMI, age, sex, and race and differed between subjects with OSA and control subjects. Multivariate modeling suggests that photographic measures capture unique aspects of OSA risk and severity. Thus, our photography techniques represent a promising tool for high-throughput, cost-effective intraoral phenotyping or OSA screening, which until now has required more expensive imaging.

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