## Relationships between Craniofacial Morphology, Sex, and Deglutitive Hyoid Bone Movement

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**Abstract:** *Purpose*: The purpose of this study was to examine the relationship between six craniofacial measures and superior and anterior hyoid bone movement during a liquid swallow.

*Method*: Twelve White adults (6 males, 6 females) between 19-27 years of age participated. Video fluoroscopic recordings were obtained while participants swallowed 7 ml of liquid barium in the upright position. Six craniofacial measures (i.e. Frankfort-mandibular angle, nasion to menton, anterior tubercles C1 to C4, nasion to sella, sella to basion, and nasion-sella-basion angle) were obtained at rest on all participants and used to determine their association with hyoid bone displacement.

*Results*: Males demonstrated larger craniofacial dimensions than females with the exception of nasion-sella-basion angle. Significant sex differences were noted for nasion to menton (p = .05). There were no statistically significant correlations (p < .05) or predictive relationships between maximum anterior and superior hyoid bone displacements and the six craniofacial measures.

*Conclusion*: The present study demonstrated differences in craniofacial morphology related to sex, however, no correlation or predictive relationship between craniofacial measures and hyoid bone movement during swallowing of a 7 ml liquid bolus were observed. Limitations include a small sample size, lack of descriptive anthropometric features (e.g. height and weight), and limited number of swallows per subject. Future studies should include larger sample sizes and investigate the effects of bolus volume and abnormal craniofacial morphology on hyoid bone movement.

Keywords: Videofluoroscopy, Deglutition, Hyoid Excursion, Hyoid Elevation, Craniometry.

## **1. INTRODUCTION**

Superior and anterior movements of the hyoid bone assist in providing a safe swallow [1]. Perlman et al. [2] demonstrated that individuals with reduced hyoid bone elevation are 3.7 times more likely to present with aspiration than individuals with adequate hyoid bone movement during swallowing. These findings further elucidate the importance of hyoid bone excursion in safe swallowing. Contraction of the anterior suprahyoid muscles (i.e. anterior belly of the digastric, geniohyoid, and mylohyoid) assist to pull the hyoid bone anteriorly and superiorly. Superior movement of the hyoid bone protects the entrance to the airway while anterior movement contributes to opening the upper esophageal sphincter [1, 3, 4]. Hyoid bone movement amplitudes during liquid swallows have been shown to be affected by factors including age and sex [5-8].

Kang *et al.* [5] examined 69 healthy, Asian adults (20 males, 49 females) between 26-78 years of age (M = 54.2 years) and observed the maximal superior excursion of the hyoid bone and duration of supraglottic

closure to increase with age. Logemann et al. [6] examined age effects of multiple swallowing parameters during thin liquid swallows including hyoid elevation in 16 males between 21-94 years of age. The authors demonstrated that the extent of hyoid elevation in relation to the first cricopharyngeal opening and maximal extent of hyoid elevation and anterior hyoid movement was significantly reduced in older males compared to younger males, and this effect remained significant in all three parameters, even after accounting for differences in neck length. Logemann et al. [7] examined similar parameters in women and demonstrated no statistically significant age effects for measures of anterior or superior hyoid movement. However, following comparison of the gender groups from each study, the authors demonstrated significantly reduced hyoid excursion in females compared to males. Although effects for age were observed in separate studies of males and females, findings comparing datasets from both studies provided evidence of sex effects for hyoid excursion regardless of age [7].

Perry *et al.* [8] compared hyoid bone movement during swallowing in 12 White adults (6 males, 6 females) in the upright and supine positions. Females displayed a significantly more posterior hyoid position

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in both upright and supine positions at rest and at maximal anterior displacement during swallowing compared to that of males. Males exhibited a significantly greater amount of superior displacement in both positions than females. These results support the notion that sex may be associated with variations in hyoid bone displacement. Previous studies examining relationships in hyoid bone movement are limited by methodological factors between studies such as small, variable sample sizes, different bolus volumes, and differences in methods used to capture hyoid excursion [9]. However, few studies have examined the relationship between craniofacial morphology and swallowing physiological variables, including hyoid excursion.

Ishida et al. [10] examined the relationship between dental arch and hyoid movement by measuring the width and length of a dental model in 12 healthy adults (7 males, 5 females) between the ages of 20-28 years. The authors found no significant correlations between the width or length of the dental arch and superior movement of the hyoid bone. Mays et al. [11] examined the relationship between the Frankfort mandibular plane angle (FMA) and hyoid bone displacement in 12 healthy adults (7 males, 5 females) between the ages of 20-29 years during liquid swallows of 12 ml and 24 ml. The Frankfort horizontal plane passes through the inferior orbital rims and the superior edges of the external auditory meatus. The FMA is calculated by intersecting the Frankfort plane with a line through the mandibular plane, a plane coursing along the inferior edge of the mandible body (Figure 1). The authors demonstrated a significant, inverse correlation between the FMA and anterior hyoid bone movement. That is, larger FMA was found to be significantly correlated with reduced anterior displacement of the hyoid bone during liquid swallows. Superior displacement of the hyoid bone and FMA were not significantly correlated. Males demonstrated significantly greater superior displacement of the hyoid bone while swallowing 12 ml boluses compared to females, suggestive of an effect for sex on superior displacement of the hyoid bone, and potentially bolus size, as a significant sex difference was only observed for 12 ml boluses.

Stepovich *et al.* [12] compared various craniofacial measures, including FMA and nasion to sella distance, to hyoid bone movement during normal swallows and during swallows with the tongue stabilized. The tongue stabilization condition was included in five of the 28 subjects in an attempt to minimize hyoid bone movement between consecutive roentgenograms. The

authors demonstrated differences in hyoid bone position based on the FMA. However, no correlations were found between the FMA, occlusal planes, and the hyoid bone plane (i.e. a horizontal axis that passes through the greater horns of the hyoid bone). Stepovich *et al.* [12] concluded that head movement must be eliminated and fixed points must be used to compare hyoid bone movement to craniofacial measures.

The suprahyoid muscles originate at multiple craniofacial points including the mandible, base of the skull, and the tongue before inserting into the hyoid bone. Because of the presence and complexity of multiple anchor points for muscle attachments, variations in craniofacial morphology may impact the superior and suprahyoid musculature, anterior movements of the hyoid bone, and ultimately, normal swallowing. Understanding the relationship between deglutitive hyoid bone movement and craniofacial morphology has clinical implications for patients with craniofacial anomalies or differences (e.g. micrognathia, midface hypoplasia, etc.). If certain craniofacial features negatively affect hyoid movement, then patients with craniofacial differences may be at an increased risk for aspiration. Few researchers have investigated the relationship between craniofacial morphology and swallowing physiology.

The purpose of this study was to replicate the study by Mays et al. [11] and to examine the association between additional cranial measures and superior and anterior movement of the hyoid bone during liquid bolus swallows. However, unlike the study by Mays et al. [11], the present study did not evaluate the effect of bolus size. Instead, images of swallows of 7 ml were used from Perry et al. [8]. This value was originally selected by Perry et al. [8] to approximate the average of a similar study using two volumes at 5 ml and 10 ml [13] to minimize the risks associated with radiation. Replication is important because of the estimated incidence of type I and type II errors in research. Replication studies can refute or provide further support for previously completed studies [14]. This study utilized previously reported hyoid bone movement data [8] to examine the interaction of craniofacial morphology on hyoid bone movement among the same 12 participants. It was hypothesized that FMA and the cranial base angle would be negatively correlated with anterior hyoid bone movement, in agreement with Mays et al. [11]. In addition, it was expected that vertical cranial measures (nasion to menton, C1 to C4) would be positively correlated with superior hyoid bone movement.

## 2. METHODS

#### 2.1. Participants

Twelve White adults (6 males, 6 females) between the ages of 19-27 years participated. Participants reported no history of neurological, musculoskeletal, or swallowing disorders. All participants presented with a normal class I occlusion. Participants also reported a negative history of adenoidectomy, tonsillectomy, or any other oropharyngeal structural or functional abnormalities. The Institutional Review Board of the University of Illinois at Urbana-Champaign approved the study and each participant gave informed consent prior to the study procedures.

## 2.2. Image Data Collection

Video fluoroscopic data collection methods have been previously described [8]. In brief, participants were instructed to maintain a fixed head position and forward gaze. A small transparent box half-full of waterdistilled barium was fastened to the side of each participant's head with the barium fluid level parallel to the floor in order to guarantee a true horizontal position. A line was drawn along that fluid level, and during recording the participant's head was positioned so that the fluid line was parallel with the floor in the upright position.

Prior to each original recording, 1.5 ml of barium was injected transnasally *via* a syringe attached to a short feeding tube to outline oral and pharyngeal structures. Aradiopaque metric ruler was inserted into each participant's mouth for calibration between studies. Swallows were limited to two swallows, one consistency (liquid barium), and one volume (7 ml, chosen as an average of a similar study using 5 ml and 10 ml volumes) due to the risks associated with radiation [13]. Each participant was recorded with lateral-view video fluoroscopy (General Electric Advantix) swallowing 7 ml of non-flavored, low-density liquid barium twice. The bolus was presented orally *via* a flexible catheter attached to a calibrated syringe to prevent any spillage of fluid.

Two speech-language pathologists who had experience reviewing swallow studies evaluated the original videos of each swallow and determined that each participant presented with a normal swallow without any characteristics of dysphagia. Data were digitized using Micro Video DC 30 (Microsoft Corporation) and frame-by-frame images (30 frames per second) of each swallow were acquired using After Effects CS4 (Adobe Systems Inc., San Jose, CA) to export the file as an image sequence. Images were analyzed using Amira 5 (Visage Imaging, Carlsbad, CA). Flexion and extension of the head were assessed and reported as part of the original study [8] and determined to be less than 6° of difference in head position for all participants.

### 2.3. Data Analysis and Statistical Methods

Hyoid bone movement between the upright and supine position was examined in the original study [8]. Only data from the upright position were used to compare to craniofacial measures obtained herein (see Tables 1 and 2 [8]). In the original study [8], subjects completed two swallows in the upright position and measures from both were averaged. Correlations were examined between anterior and superior hyoid bone movement and six craniofacial measures. Normality assumptions were approximately met for all dependent variables as assessed formally using the Shapiro-Wilk test of normality and graphically using normal Q-Q plots and histograms of the residuals of all dependent variables. The homogeneity of variance assumption was met for all dependent variables using Levene's test of equal variances. Univariate analysis of variance was used (Statistical Package for the Social Sciences, v. 20; IBM) to examine the effect of gender on each craniofacial measure. A simple linear regression analysis was used to determine if there was a predictive relationship between craniofacial measures and maximum superior and anterior hyoid bone displacement. A level of  $\alpha$  = .05 was used to determine statistical significance.

#### 2.3.1. Hyoid Bone Displacement

Hyoid bone displacement measures are reported elsewhere [8] in detail. In brief, frames were viewed individually for each participant and three images were selected for analysis: true resting position, maximum displacement, and maximum anterior superior displacement. True resting position of the hyoid bone was defined during the pre-swallow condition of the first swallow by a primary rater and chosen relative to the maximum anterior and superior displacement. The anterior and superior position of the hyoid bone in the neck was measured on each of the three images relative to two predetermined reference lines. The first reference line (vertical line) connected the anterior borders of the second cervical vertebra to the third cervical vertebra. The second reference line (horizontal line) was drawn perpendicular to the first at the inferior border of the third cervical vertebra. Maximum anterior and superior hyoid placement for each subject was calculated by subtracting mean rest values from mean maximum anterior or superior hyoid placement values.

### 2.3.2. Craniofacial Measurements

Craniofacial measures were determined using a review of the literature and selecting skeletal regions that serve as muscle attachment sites for important supra hyoid muscles. O'Higgins *et al.* [15] reported that the most reliable and valid method of craniometry is the use of linear and angular measures because they provide the most consistent results and are the most sensitive to craniometric variations. Gribel *et al.* [16] demonstrated that linear and angular measures can be accurately and reliably used on lateral cephalograms such as x-ray images. As such, six linear and angular craniofacial measures were chosen based on being the

most reliable and well-established [12, 15-26]. Craniofacial measures were obtained on the same true, pre-swallow resting image that was used to measure the participant's hyoid bone movement. These measures are described in Table **1** and displayed on Figure **1**.

Two vertical craniofacial measures were obtained including the face height (nasion to menton distance) and cervical vertebra height (C1 to C4). The cranial base was measured as the distance from the nasion to the sella turcica, basion to sella turcica, and the angle created between the two cranial base lengths.

A primary rater (the second author) made all measurements. The primary rater reexamined 40% of the data set (i.e. five participants) chosen at random in order to assess the intra-rater reliability. Six paired *t*-

Table 1: Description of the Craniofacial Measures Collected on 12 Participants during the Res
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Craniofacial Measure	Description
Frankfort-Mandibular Angle	A line was drawn from the inferior orbital rim through the superior border of the external auditory meatus. A second line was drawn along the inferior border of the mandible. The point at which the two lines intersected was determined and the angle was calculated.
Nasion to Menton	A line was drawn from the nasion to the menton to obtain a vertical length measurement of the craniofacial region.
Anterior Tubercles C1 to C4	A line was drawn from the anterior borders of the first cervical vertebra to the fourth cervical vertebra to obtain a vertical length measurement.
Nasion to Sella	A line was drawn from the nasion to the superior-posterior border of the sella turcica to obtain a cranial horizontal length measurement.
Sella to Basion	A line was drawn from the superior-posterior border of the sella turcica to the basion to obtain a cranial base length measurement.
Nasion-Sella-Basion Angle	The nasion to sella and sella to basion lines were intersected and the angle was calculated.



**Figure 1:** Demonstration of the craniofacial measures including nasion to sella (N-S), sella to basion (S-B), nasion-sella-basion (NSB) angle, FMA, distance from C1 to C4 (C1-C4), and nasion to menton (N-M) distance.

tests were conducted to examine intra-rater differences in the six craniofacial measures. A Bonferroni correction was used to control for the family-wise error rate. There were no statistically significant differences between the first and second measures (p > .008). Pearson product-moment correlation coefficients were calculated between the first and second measures. They ranged from r = .79 to r = .98 with the lowest reliability (r = .79) for measures of the nasion-sellabasion angle.

A secondary trained rater with experience in measuring the structures of interest examined 75% of the data set (i.e. nine participants) chosen at random in order to assess the inter-rater reliability. Six independent *t*-tests were conducted to examine intrarater differences in the six craniofacial measures. A Bonferroni correction was used to control for the family-wise error rate. There were no statistically significant differences between the measures from the two raters (p > .008). Pearson product-moment correlation coefficients were calculated between the first and second measures. They ranged from r = .72 to r = .96 with the lowest reliability (r = .72) for measures of the FMA.

## 3. RESULTS

Mean craniofacial measurements as a function of gender are reported in Table 2.

Six separate one-factor analysis of variance (ANOVA) were conducted to examine the differences in each craniofacial measure as a function of gender. Males demonstrated significantly larger nasion to menton measures [F(1, 10) = 5.86, p = .04,  $\eta_p^2 = .37$ ].

There were, however, no statistically significant differences between male and female measures of FMA [*F* (1, 10) = 2.29, *p* = .16,  $\eta_p^2$  = .19], C1 to C4 [*F* (1, 10) = 1.56, *p* = .24,  $\eta_p^2$  = .14], nasion to sella [*F* (1, 10) = 0.63, *p* = .45,  $\eta_p^2$  = .06], sella to basion [*F* (1, 10) = 2.55, *p* = .14,  $\eta_p^2$  = .20], and nasion-sella-basion angle [*F*(1, 10) = 0.01, *p* = .91,  $\eta_p^2$  = .00].

The relationship between maximum anterior and superior hyoid bone displacement and all craniofacial measures was examined with correlation and linear regression analyses. There were no statistically significant correlations (p > .05) between the maximum anterior and superior hyoid bone displacements and any of the craniofacial measures (Table **3**).

Simple linear regression analyses also revealed no statistically significant predictive relations (p > .05) between the maximum anterior and superior hyoid bone displacements and any of the craniofacial measures (Table 4). That is, no craniofacial measure could be used to predict anterior or superior maximum displacement of the hyoid bone.

## 4. DISCUSSION

Although non-significant, males demonstrated greater superior hyoid bone movement during a 7 ml liquid swallow compared to females [8]. No statistically significant predictive relationships were found between gender and anterior or superior hyoid movement. These findings are similar to findings reported by Mays *et al.* [11] who observed a significantly (p < .05) greater

Table 2:	2: Means and Standard Deviations of Craniofacial Measures	as a Function of Gender
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Craniofacial Measure	Gender	Mean (SD)*
Frankfort-Mandibular Angle	Female	25.75 (2.29)
	Male	27.83 (2.47)
Nasion to Menton	Female	84.00 (3.64)
	Male	91.02 (6.10)
Anterior Tubercles C1-C4	Female	44.38 (2.08)
	Male	46.29 (3.10)
Nasion to Sella	Female	55.48 (3.66)
	Male	57.02 (3.08)
Sella to Basion	Female	29.95 (1.76)
	Male	32.57 (3.60)
Nasion-Sella-Basion Angle	Female	131.98 (7.77)
	Male	131.55 (5.65)

\*Linear measures are reported in mm. Angular measures are reported in degrees.

 Table 3: Pearson Correlation Coefficients (r) for Craniofacial Measures and Maximum Anterior and Superior

 Displacement of the Hyoid Bone during Swallowing (N = 12)

	Hyoid Bone Displacement				
Craniofacial Measure	Anterior		Superior		
	r	р	r	р	
Frankfort-Mandibular Angle	.36	.26	77	.81	
Nasion to Menton	.43	.17	.21	.52	
Anterior Tubercles C1-C4	.28	.38	06	.85	
Nasion to Sella	.43	.17	30	.34	
Sella to Basion	.46	.13	32	.31	
Nasion-Sella-Basion Angle	.43	.89	21	.52	

# Table 4: Regression Coefficients for Predicting Maximum Anterior and Superior Displacement of the Hyoid Bone during Swallowing from Craniofacial Measures (N = 12)

	Hyoid Bone Displacement					
Oranisfasial Massure	Anterior Regression Coefficient			Superior		
Cramoraciai measure				Regression Coefficient		
	Slope	Intercept	p	Slope	Intercept	p
Frankfort-Mandibular Angle	0.55 (-0.47, 1.58)	25.39	.26	-0.14 (-1.41, 1.13)	20.26	.81
Nasion to Menton	0.28 (-0.14, 0.69)	15.93	.17	0.16 (-0.37, 0.68)	2.92	.52
Anterior Tubercles C1-C4	0.41 (-0.58, 1.39)	21.86	.38	-0.10 (-1.29, 1.08)	21.17	.85
Nasion to Sella	0.51 (-0.25, 1.26)	11.80	.17	-0.41 (-1.33, 0.51)	39.73	.34
Sella to Basion	0.59 (-0.22, 1.41)	21.69	.13	-0.48 (-1.49, 0.52)	31.57	.31
Nasion-Sella-Basion Angle	0.03 (-0.40, 0.45)	36.81	.89	-0.15 (-0.63, 0.34)	35.85	.52

\*Predicted displacement of the hyoid bone during swallowing = slope X craniofacial measure + intercept. The 95% confidence intervals for the slopes are provided in parentheses under the point estimates.

amount of superior hyoid movement during a liquid swallow of 12 ml among males compared to that of females. Additionally, Leonard *et al.* [27] suggested a possible relationship between hyoid displacement and subject height for both 1 ml and 20 ml liquid swallows in an investigation of 60 healthy adults (30 males, 30 females). Subsequent Pearson r tests demonstrated relatively weak correlations of .44 for the 1 ml swallow and .37 for the 20 ml swallow. Although non-significant, perhaps greater superior movement of the hyoid observed in the present study was due to males presenting with a larger craniofacial space than that of females, which was indicated by male participants' significantly greater nasion to menton measurements (Table 3). Molfenter *et al.* [28] recently demonstrated significant sex effects for superior hyoid movement with males demonstrating a larger extent of superior hyoid movement than females. However, when the authors accounted for the size of the pharyngeal area by including a continuous covariate (C2-C4 length) which was found to have the highest correlation to true subject height, sex effects for superior hyoid movement were not significant. Despite non-significant findings in the present study, the findings from Molfenter *et al.* [28] support our hypothesis that increased craniofacial dimensions may predict hyoid movement parameters rather than differences in sex. The present study was limited by a lack of additional anthropometric

Cunningham et al.

parameters such as subject height, a parameter that Molfenter *et al.* [28] utilized to determine the craniofacial measure that would best serve as a covariate for their analysis.

Although findings from Molfenter et al. [28] and Leonard et al. [27] appear to support the hypothesis that hyoid movement may be related to differences in craniofacial size rather than sex, statistically significant predictive relationships were not found between any of the craniofacial measures and superior or anterior hyoid bone movement during 7 ml liquid swallows in the present study. These findings differ from those observed by Mays et al. [11], who demonstrated FMA and anterior hyoid bone movement to be significantly correlated. Although the present study contained the same number of participants (N = 12) and a similar age range (19-27 years) compared to that of Mays et al. [11] (20-29 years), differences between studies include bolus volume and distribution of male and female participants. Mays et al. [11] did not have an equal distribution of males and females (7 males, 5 females) and it is possible that the difference in gender distribution of participants between studies may account for the variations in findings. Mays et al. [11] examined these relationships using two bolus volumes (12 ml and 24 ml). While both bolus volumes demonstrated significant negative correlations between FMA and anterior hyoid bone movement, a 24 ml bolus demonstrated a stronger negative correlation (r = -.75) with FMA. Based on these results, it is possible that differences between the present study and Mays et al. [11] may be accounted for by differences in bolus volume, as the present study utilized a bolus volume of 7 ml compared to 10 ml and 24 ml used by Mays et al. [11].

Leonard et al. [27] demonstrated increases in the extent of superior hyoid bone movement with increases in bolus volume. Wintzen et al. [29] explained that increases in hyoid excursion as they relate to increases in bolus volume may be related to the starting and ending position of the hyoid bone during the preswallow condition. The authors demonstrated that these two positions were the same during saliva swallows, but that the pre-swallow position was located more inferiorly as bolus volumes were increased. This phenomenon might explain the variation observed between the present study and findings by Mays et al. [11]. Additional investigations of variations between studies in the deglutition literature have also demonstrated that small sample sizes are more susceptible to exhibit greater variability and that studies

utilizing less than three swallows per bolus volume may also be more susceptible to effects of individual variability [9, 30]. The present study and the study by Mays *et al.* [11] both demonstrated limitations in sample size and did not meet the criteria regarding minimum number of trials per bolus volume suggested by Lof *et al.* [30].

In the present study, males demonstrated a significantly greater vertical craniofacial height, as evident in the measure of nasion to menton. Anterior-to-posterior measures at the cranial base (i.e. nasion to sella and sella to basion) were not significantly different between males and females. Johannsdottir *et al.* [23] also found significant sex differences in craniofacial morphology related to facial height in Icelandic adults. Linear and angular measurements were made on the lateral cephalograms of 324 Icelandic adults (155 males, 169 females). Comparison data indicated that males had significantly larger anterior and posterior facial height. However, measures of hyoid excursion were not obtained.

No statistically significant predictive relationships were found between sex and nasion to sella, sella to basion, and nasion-sella-basion angle in the present study. This was expected because these three measures have been reported to differ between races, as opposed to sex [18]. Racial differences in craniofacial morphology have been previously reported [18, 23, 24, 31]. The present study only included White individuals; however, Mays et al. [11] did not indicate the race of their participants. Different racial groups present in the Mays et al. [11] study may have accounted for the significant correlation between anterior hyoid bone movement and FMA. It may be necessary to control for race in future studies examining hyoid bone movement, as craniofacial differences between racial groups may account for differences in hyoid movement.

Limitations in the present study include a small sample size and lack of additional anthropometric information such as subject height. Previous studies have demonstrated correlations between height and craniofacial measures that may be used to control for subject size when comparing sex differences in hyoid excursion [28]. Information on barium density was also not reported in the present study, and previous research has demonstrated that quantitative differences in oral-pharyngeal deglutition may be affected by the type of barium preparation [32].

## 5. CONCLUSION

This study suggests that certain craniofacial measures vary based on sex. This study does not support the hypothesis that craniofacial morphology can be used to predict superior and anterior hyoid bone movement during 7 ml liquid swallows. However, inclusion of additional anthropometric variables such as height, weight, and other craniofacial measures not included in the present study may be necessary in future investigations of hyoid bone movement. Future studies examining the relationship between craniofacial morphology and hyoid movement during swallowing of thin liquid boluses should include larger sample sizes and at least three swallows per bolus volume to account for variability between true resting position and maximal hyoid excursion across images. An evaluation of various bolus volumes and differences between individuals with craniofacial anomalies (e.g. repaired cleft palate, micrognathia) and individuals with normal craniofacial anatomy are necessary to determine the effects of craniofacial differences on hyoid bone movement.

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## CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

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