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### Pilot Study of Quantitative Methods for Differentiating Pharyngeal Swallowing Mechanics by Dysphagia Etiology

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#### Abstract

Quantitative analysis of modified barium swallow (MBS) imaging is useful to determine the impact of various disease states on pharyngeal swallowing mechanics. In this retrospective proof of concept study, kinematic analysis and computational analysis of swallowing mechanics (CASM) were used to demonstrate how these methods differentiate swallowing dysfunction by dysphagia etiology. Ten subjects were randomly selected from four cohorts of dysphagic patients including COPD, head and neck cancer (HNC), motor neuron disease, and stroke. Each subject was age- and gender-matched with healthy, non-dysphagic controls. MBS videos of 5 ml thin and 5 ml thick bolus trials from each subject were used. A MATLAB tracker tool was adapted and updated to collect and compile data for each video (n = 160). For kinematic measurements, a MANOVA was performed with post-hoc analyses to determine group differences. For CASM measurements, a morphometric canonical variate analysis with post hoc analysis was performed to determine group differences. Kinematic analyses indicated statistically significant differences between HNC cohort and controls in distance measurements for hyolaryngeal approximation (p = .001), laryngeal elevation (p = 0.0001), pharyngeal shortening (p = 0.0002), and stage transition duration timing (p = 0.002). Timing differences were noted between the stroke cohort and controls for pharyngeal transit time (p = 0.007). Multivariate morphometric canonical variate analysis showed significant differences between etiology groups (p < 0.0001) with eigenvectors indicating differing patterns of swallowing mechanics. This study demonstrated that swallowing mechanics among cohorts of dysphagic patients can be differentiated using kinematics and CASM, providing different but complementary quantitative methods for investigating the impact of various disease states on swallowing function.

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#### Keywords

Dysphagia; Swallowing mechanics; Modified barium swallow; Quantitative methods; Kinematics; Morphometrics; Aspiration

#### Introduction

Multiple interdependent elements of swallowing mechanics underlie the transport of a bolus from the oral cavity through the pharynx into the esophagus while simultaneously protecting the airway. Various disease states can disrupt swallowing mechanics resulting in impaired swallowing performance (dysphagia) [1, 2]. Understanding the complexity and interplay of swallowing mechanics with risk factors, such as a disease state, is important for targeted rehabilitation [3, 4]. The modified barium swallow (MBS) examination, a standard in diagnostic imaging studies of swallowing function, can be utilized to analyze pharyngeal swallowing mechanics [5, 6]. Quantitative analysis of swallowing mechanics, such as kinematic analysis and Computational Analysis of Swallowing Mechanics (CASM), can be achieved using digital tools to reduce data from imaging files [7, 8].

Kinematic analysis has been the standard for determining how various risk factors impact swallowing mechanics. Displacement (kinematic) measurements of various anatomical landmarks during swallowing and timing (temporal) measurements of bolus transit at critical points of the swallowing process can be determined on MBS imaging using open source or commercially available digital tools [6, 8]. These physiological data are widely used to determine differences among various elements of swallowing mechanics in clinical and research settings [9–12].

CASM is a research method that utilizes multivariate morphometric analysis to infer changes in multiple elements of the swallowing mechanism associated with variables of interest, including dysphagic etiologies [13–16]. Data collected for CASM are frame-by-frame coordinates of anatomical landmarks delineating muscle groups and skeletal structures underlying the elements of pharyngeal swallowing mechanics during a swallow (Fig. 1). The resulting shapes of these coordinate data are analyzed using multivariate morphometric (also called geometric) analysis. Shape change is visualized using eigenvectors which show the variance and interaction of each element of pharyngeal swallowing mechanics included in the analysis [17].

The purpose of this pilot study was to compare how kinematics and CASM characterize the impact of disease etiology on the swallowing mechanism. This study comprises cohorts from four dysphagic patient populations, including post-treatment squamous cell carcinoma of the oropharynx (HNC), stroke, chronic obstructive pulmonary disease (COPD), and motor neuron disease (MND). Each patient was then age- and sex-matched with a healthy, non-dysphagic control. Each of these patient populations has a well-known comorbidity of dysphagia [18–21]. We used kinematic analysis and CASM independently to test the following hypotheses: swallowing mechanics of each test group differ from an age- and sex-matched control group (H1), swallowing mechanics differ by dysphagia etiology (H2), and

impaired swallowing mechanics of each test group is predictive of penetration-aspiration status (H3).

#### Methods

#### Subjects and Imaging

A database of de-identified video swallows from multiple study cohorts was utilized for this retrospective case-controlled study. Four sets of ten subjects each were randomly selected using a Microsoft Excel randomization function from four cohorts of dysphagic patients including two types of neurogenic dysphagias (Stroke and MND) and two types of structural dysphagias (HNC and COPD). Random sampling was stratified by sex to achieve an even distribution of male and female subjects. For each test subject, an age- and sex-matched control derived from a large normative database was included. Each subject underwent an MBS examination utilizing the Modified Barium Swallow Impairment Profile©™ standardized protocol digitally recorded at 30 frames per second [22]. Swallow tasks from the Modified Barium Swallow Impairment Profile©™ protocol for analysis included the second trial of barium-infused 5-ml thin liquid and the 5-ml pudding task (Varibar®, E-Z-EM, Inc.) administered via teaspoon by the examining speech-language pathologist. For the 5 ml thick bolus swallow, the 5 ml pudding trial was extracted in all patient cohorts except HNC due to missing data. For the HNC test and control group, the 5 ml honey swallow was extracted. The Varibar products offer a 40% w/v ratio of barium sulfate concentration for all bolus types. When mapped onto the International Dysphagia Diet Standardisation Initiative (IDDSI) the Varibar pudding and honey-thick are level 4 (extremely thick) [23]. The shear rate of Varibar pudding is approximately 5000 mPa at 30 s-1 and Varibar honey-thick is approximately 3000 mPa at 30 s - 1 both at 25 degrees Celsius [24]. In sum, 160 singleswallow videos were (i.e. 2 swallows each from 40 patient subjects and 2 swallows each from 40 age- and sex-matched controls). Inclusion criterion included adequate imaging quality to allow for identification of all landmarks required for coordinate mapping. All imaging data were de-identified and shared under Institutional Review Board (IRB) approval from host institutions with ethics permission granted by the author's IRB to conduct research.

Each video was trimmed using QuickTime and analyzed using a MATLAB tracker tool developed by Natarajan and colleagues [25] which was adapted and reformatted by two authors (YT and PH) to include the requisite functionality for this pilot study. The tracker tool was originally created to map coordinates of anatomical landmarks that represent functional muscle groups underlying pharyngeal swallowing mechanics [25]. These coordinates were designated for each of the 10 anatomical landmarks for each frame of the video and exported to one text file representation.

#### MATLAB Tracker Tool v5.1

The MATLAB tracker tool was tailored to extract timing and distance kinematic variables commonly reported in the research literature. Additional features include distance measurement tools, standardized unit normalization, valleculae and piriform residue area tracers, pharyngeal area tracers for pharyngeal constriction ratio (PCR) calculation, a robust

compiler tool, and an anatomical alignment function for eigenvector visualization of CASM results [26, 27] (Fig. 2). A workflow of how the tracker tool and other MATLAB functions were used is provided in Fig. 3.

The user assigned specific frames as time points throughout the swallow including bolus hold position, bolus crossing of the ramus of the mandible, hyoid burst, and upper esophageal sphincter (UES) closure. Hyoid burst was operationally defined as the first rapid anterosuperior movement of the hyoid associated with a pharyngeal swallow response. Using these designated time points, the tracker tool calculated oral transport time, stage transition duration, and pharyngeal transport time. The semi-automated tracker tool function was used to annotate anatomical landmarks frame-by-frame to map the action of muscles that displace the hyoid, larynx, tongue base, position of the UES, and head and neck posture [7].

After timing buttons were selected and coordinates were annotated, the tracker tool program determined kinematic variables. Hyoid burst and UES closure time frames selected by the user designated each frame related to pharyngeal swallowing. Displacement measurements were calculated using coordinates annotated in every pharyngeal swallowing frame and stored in an array. A search function found the maximum displacement distance in pixels within an array. Pixels were converted to centimeters based on a radiopaque referent in the image (a 1.9 cm penny). Pixels were also converted to C2-C4 vertebrae lengths using a within subject mean of the C2-C4 distance measurements [28]. Displacement measurements included in this study were hyoid excursion in reference to the vertebrae, hyolaryngeal approximation, laryngeal elevation, pharyngeal shortening, and base of tongue retraction ratio. Operational definitions for timing and distance variables in this study are listed in Table 1.

The MATLAB tracker tool was tailored to include a compiler function to aggregate data points from selected videos. Three components were included in the compiler: kinematic variable aggregation, coordinate aggregation, and classifier assignment. Coordinate aggregation and classifier assignment were essential steps toward multivariate morphometric analysis, or CASM. Kinematic aggregation provided one text file of five distance measurements and three timing values from each video for subsequent statistical analysis. For this study, the compiler function reported 1280 total kinematic values from 160 videos representing two swallows each from the 80 subjects. Coordinates were compiled from every frame representing pharyngeal swallowing (n = 2718 frames). A data balance function that randomly selects the maximum equal numbers of observations per pharyngeal swallow was performed resulting in 7 frames per swallow (n = 1120). Each set of 10 coordinates was assigned a unique identifier. The classifier assignment function was used to designate categorical variables to each of these unique identifiers. Categorical variables for the present study include: cohort group (e.g. stroke versus healthy control), binary penetrationaspiration score (PAS) status (PAS 1-2 versus PAS 3-8), and bolus type (5 mL thin versus 5 mL thick). The coordinates and classifier variable files were imported into MorphoJ integrated software for multivariate morphometric analysis [29].

MorphoJ was used to generate.svg files of eigenvector results indicating the magnitude and direction of the variance at each coordinate associated with a classifier variable of interest. These vectors represented the inferred muscle action underlying hyoid movement, laryngeal elevation, tongue base retraction, pharyngeal shortening, and head and neck posture. However, the vectors were in reference to a mathematically derived centroid, which assumes unlimited degrees of freedom, whereas the movement of these coordinates was constrained by anatomy (i.e. the mandible and cranial base moved in reference to the vertebrae, not a mathematical centroid). To represent this anatomical constraint, a matrix transformation was performed applying a MATLAB Procrustes superimposition to these vector data. First, the shape defined by the tip of eigenvectors 3, 4, & 5 (representing the C1, C2, and C4 vertebrae) was translated, scaled, and rotated such that the average length of eigenvectors 3, 4, and 5 were minimized. Then, the remaining eigenvectors were translated, scaled, and rotated to align within the proper anatomical context.

#### PAS

A speech-language pathologist (SLP) and author (SR) with six years of experience interpreting MBS studies reviewed each video and assigned a score using the Penetration– Aspiration Scale (PAS) [30]. The PAS is an 8-point scale used to describe the presence or absence of laryngotracheal invasion of ingested bolus material. Ten percent of the videos were randomly selected for intra-rater testing and for inter-rater testing by a second SLP with fourteen years of experience. Intraclass correlation coefficients confirmed acceptable intra- and inter-rater reliability levels of ICC = 0.98 and ICC = 0.99, respectively. In subsequent analyses, these scores were reduced into a categorical variable as follows: scores of 1–2 were considered within functional limits, and scores of 3–8 were indicative of penetration-aspiration.

#### Statistical Analyses of Kinematic Data

Kinematic variables were analyzed using Excel Real Statistics Resource Pack. To evaluate H1, a MANOVA of distance measurements and timing measurements comparing each test group with the respective control was performed with post-hoc ANOVA to determine p-values and effect sizes using root mean square standardized effect (RMSSE). Significance for the MANOVA was set at p < 0.05 with the post hoc ANOVAs subjected to a Bonferroni correction. To evaluate H2, a MANOVA of kinematic distance measurements and timing measurements of all test groups was performed using Pillai's trace (V), a positive-valued statistic ranging from 0 to 1, where an increase in value indicates a greater effect contributed to the model. To test H3, logistic regressions were performed using a binary penetration-aspiration status (PAS 1–2 = within normal limits versus PAS 3–8 = penetration-aspiration) as the outcome variable.

#### Statistical Analyses of CASM Data

Aggregate coordinate and classifier text files were imported in MorphoJ for multivariate morphometric analysis. A Procrustes fit was performed on all coordinates to control for size differences and correct for image rotation and camera movement. No outliers were identified using the MorphoJ outlier function. Discriminant function analysis (DFA) comparing test groups with age- and sex-matched controls was performed to evaluate H1. A canonical

variate analysis (CVA) by test group was performed to evaluate H2. In morphometric analysis, a DFA is used to determine pairwise shape differences, whereas a CVA is used to determine the impact of multiple independent variables on shape differences. To test H3, regressions were performed of DFA scores of group vs. control as the independent variable and DFA scores of penetration-aspiration status as the dependent variable. Permutation tests were performed in all analyses.

#### Results

#### H1 Kinematics: Differences Between Dysphagia and Control Groups

MANOVA results of kinematic distance measurements between each test group (H1) with respective age- and sex-matched controls resulted in significant differences for HNC group  $(V=0.40, F(5,34) = 4.54, p = 0.003, \eta^2 = 0.40)$ . MANOVA results of kinematic timing measurements testing H1 comparing each test group with respective age- and sex-matched controls resulted in significant differences for HNC ( $V=0.29, F(3,36) = 4.83, p = 0.006, \eta^2 = 0.29$ ), and stroke ( $V=0.27, F(3,36) = 4.51, p = 0.009, \eta^2 = 0.27$ ). All significant results showed a small effect size ( $\eta^2$ ). P-values and RMSSE effect sizes resulting from post hoc ANOVAs comparing distance and timing variables between each test and control group are reported in Table 2 a–b.

#### H2 Kinematics: Differences Between Dysphagia Etiology Groups

MANOVA results of kinematic distance measurements testing H2 showed statistically significant differences between test groups with V = 0.65, F(15,222) = 4.13, p < 0.0001,  $\eta^2 = 0.22$ . MANOVA results of kinematic timing measurements testing H2 showed statistically significant differences between test groups with V = 0.26, F(9,228) = 2.43, p = 0.01,  $\eta^2 = 0.09$ . While the model showed significance, the effect size ( $\eta^2$ ) indicated a small difference for distance measurements and no difference for timing variables.

#### H3 Kinematics: Swallowing Mechanics and Penetration–Aspiration Status

Logistic regressions of a binary penetration-aspiration status on kinematic distance and timing variables by group resulted in significant findings showing an increase in pharyngeal transport time was predictive of penetration-aspiration status in the stroke cohort ( $X^2 = 5.42$ , p = 0.02, U = 0.22), and reduced hyoid excursion was predictive of penetration-aspiration status in the MND cohort ( $X^2 = 4.61$ , p = 0.03, U = 0.36). Here, U functions are analogous to an  $r^2$  statistic indicating how much of the variance is explained by the variable.

#### **CASM H1: Differences Between Dysphagia and Control Groups**

Pairwise DFA results revealed significant differences (p < 0.0001) between each test and control group with Mahalanobis distances ranging from 2.42–2.82. Eigenvectors characterizing the differences in swallow mechanics between test and control groups are visualized in Fig. 4a–d. Eigenvectors for the COPD cohort indicated increased kyphosis of the vertebrae, slight head flexion, increased pharyngeal shortening and anteriorly positioned larynx during pharyngeal swallowing compared with controls. Eigenvectors for the MND cohort showed an elevated hyolaryngeal complex and tongue base with some head and neck extension during pharyngeal swallowing compared with controls. Eigenvectors for the HNC

cohort indicated reduced hyolaryngeal excursion and tongue base retraction with some flexion of the head and neck during pharyngeal swallowing compared with controls. Eigenvectors for the stroke cohort showed a reduction in all pharyngeal swallowing mechanics with moderate reduction of hyolaryngeal excursion, pharyngeal shortening, and tongue base retraction with notable extension of the head and neck when compared with controls.

#### CASM H2: Differences Between Dysphagia Etiology Groups

CVA results of the test groups showed significant differences (p < 0.0001) between all test groups with Mahalanobis distances ranging from 2.62–3.66 (Fig. 5). The neurogenic etiology mechanics (MND and Stroke) and non-neurogenic etiology mechanics (COPD and HNC) stratified as the first canonical variate describing 55% of the variance. Eigenvectors of the second canonical variate, representing 30% of the variance, indicated stratification by dysphagic etiologies that reduce hyolaryngeal excursion (stroke and HNC), and those with exaggerated hyolaryngeal movements (COPD and MND).

#### CASM H3: Swallowing Mechanics and Penetration–Aspiration Status

Multivariate regressions of DFA scores of penetration-aspiration status on DFA scores of group vs. controls are visualized in Fig. 6a–d. Results are as follows: stroke, multivariate regression coefficient = 0.70, predicting 11.9% of the variance; MND, multivariate regression coefficient = 0.63, predicting 11.16% of the variance; COPD, multivariate regression coefficient = -0.15, predicting 0.30% of the variance; HNC, multivariate regression coefficient = 0.09, predicting 0.10% of the variance.

#### Discussion

This proof of concept study aimed to demonstrate differences in pharyngeal swallowing mechanics using two types of quantitative analyses: a conventional kinematic approach and a novel multivariate shape change analysis (CASM) to characterize swallowing mechanics. We used these two techniques to document differences across four patient cohorts with swallowing disorders (HNC, stroke, COPD, and MND) against age- and sex-matched healthy, non-dysphagic controls. This study revealed that both kinematic analysis and CASM are useful to differentiate swallowing mechanics by dysphagia etiology.

Using kinematic analyses, we demonstrated significant differences in distance measurements in the HNC cohort and timing variables in both stroke and HNC to address H1. However, significant effect sizes (RMSSE > 0.2) in Table 2 a–b indicate some comparisons were underpowered. Statistical significance was achieved in cohorts with larger effect size changes (RMSSE = 0.84–0.99). For the remaining variables with a significant effect size, a post hoc two-tailed pairwise power analysis on the basis of means was performed. To obtain 80% statistical power, a sample size of n = 60 would be needed for the stroke and HNC cohorts and a sample size of n = 175 for the MND and COPD cohorts. Interestingly, even with a small sample, we did find a difference in the distance measurements among dysphagic etiologies (H2). Finally, using logistic regression by group, we identified that

Using CASM, we demonstrated significant differences in swallowing mechanics for each test and control group comparison in support of H1. Eigenvectors allowed for visualization of differences and interactions of the multiple elements of swallowing mechanics for each group. CASM also showed that pharyngeal swallowing mechanics differ among dysphagic etiologies (H2). Regressions of morphometric discriminant function scores agree with the kinematic results showing that mechanics associated with stroke and MND were predictive of penetration-aspiration status than mechanics associated with other dysphagia etiologies in the present sample.

Kinematic measurements of distance and time are more easily understood as dependent variables than geometric morphologies in morphospace. It is easier to comprehend the mean difference in laryngeal elevation in centimeters versus results that are mathematically abstracted such as a Mahalanobis distance. Furthermore, while timing variables can be factored into CASM, it is not reported as a discrete variable. In studies where a measured time interval is important, such as assessing sensory deprivation (i.e. in post-treatment oropharyngeal cancer), kinematic temporal variables are preferred.

A challenge in kinematic analysis is whether to include all elements of swallowing mechanics since including more variables invites a statistical penalty. A further challenge is assessing how these multiple elements of swallowing mechanics function together under various conditions (i.e., risk factors, patient characteristics, and bolus types) to achieve swallowing performance goals. Thus, while a result of a dependent variable in kinematics is more easily understood, the results of how multiple kinematic variables interact within the context of patient anatomy under various conditions is less evident.

On the other hand, CASM utilizes a geometric representation of the swallowing mechanism to compute how multiple variables of interest impact multiple elements of swallowing mechanics. Geometric analysis compares differences in shapes, but not sizes. Consider, for example, the shape difference between a 3 mm equilateral triangle and a 3 km equilateral triangle. While this approach controls for size differences between subjects, results cannot be translated into actual distance measurements. Eigenvectors indicate the relative magnitude and direction of variance in gestalt mechanics, in other words the shape representing the interaction of multiple elements of swallowing mechanics. Further, multivariate morphometric analysis can show how these elements of swallowing mechanics covary with independent variables such as risk factors, bolus condition, or swallowing performance outcomes. For example, CASM can depict how hyolaryngeal movement, tongue base retraction, pharyngeal shortening, and head and neck posture covary together in relation to penetration-aspiration status while controlling for other known variables [13]. So, while the dependent variable in CASM may be more difficult to comprehend, the results of CASM provide visualization of how multiple elements of swallowing mechanics interact associated with a variable of interest, such as dysphagia etiologies.

A potential limitation of CASM is that statistically significant *p*-values are readily found requiring the investigator to determine whether these differences are functionally significant or not. It is important to note the Mahalanobis distance (or D-statistic), which in morphometrics, functions like a z-score. In the present study the Mahalanobis distances, all above 2.0, were significant. In addition, the eigenvector results revealed functional differences in swallowing mechanics that were obscured using univariate kinematic methods. Visualization of how disease etiology impacts the interaction of multiple elements of swallowing mechanics provides substantial opportunity for hypothesizing structure to function relationships. For example, in a previous CASM study of COPD, vectors led to a new hypothesis about the impact of uncoupled swallowing and respiratory function [31]. CASM has also been used in a stroke population to document the impact of focal stroke lesions on the swallowing mechanism [13]. In the current study, the vectors characterizing swallowing in the MND sample may indicate a hyperreflexive response to the bolus stimulus. A future investigation using CASM to investigate HNC could determine the impact of different tumor sites or treatment options on the swallowing mechanism. Additionally, CASM has been used to quantitatively test patient-specific interventions [31].

It should also be noted that DFA assumes independent observations, whereas CASM requires multiple observations per subject. It has been shown in other studies that this can lead to false positives [32]. Methods in this study were patterned after a proposed solution involving permuting a balanced data set to mitigate the problem [32]. Positive findings in a cohort CASM study should be approached cautiously.

Another limitation to address in a future study is to increase the number and diversity of swallows per subject to reduce within-subject variability. Combining honey and pudding into a "thick" bolus classification also needs to be justified before future use. Further, some cohorts had far fewer instances of penetration-aspiration to provide meaningful results for H3. Specifically, the HNC cohort had only one subject with a penetration-aspiration status, which explains the unusual scatter plot in Fig. 4c. Other timing measurements, such as laryngeal vestibular closure time, or additional CASM coordinates that represent the function of the pharyngeal constrictors in the pharyngeal stripping wave, could be included [33]. Additionally, penetration-aspirations status could be stratified by timing of aspiration events relative to the swallow, or by using other swallowing performance variables such as the Normalized Residue Ratio Scale [27]. These data capture capabilities are programed in the MATLAB tracker tool. In spite of these limitations, both approaches were useful to differentiate mechanics by dysphagia etiology on a small sample of patients per cohort.

Built into the MATLAB tracker tool is a strategy to organize and manage large data sets. Future directions include improving semi-automated landmark tracking through machine learning. This coupled with coordination of multisite usage sets the stage for big data analysis using both kinematics and CASM that could effectively characterize swallowing mechanics associated with multiple dysphagia etiologies. Automating CASM to allow for faster, and thus, more feasible analysis in a clinical setting, may even aid the healthcare provider in clinical decision-making and rehabilitation of swallowing impairment.

The number of subjects per group and incidence of penetration-aspiration swallows in the present study is far too small to draw generalizable conclusions. The present pilot study was not intended to definitively phenotype swallowing mechanics associated with dysphagia etiologies but to demonstrate the capacity of kinematics and CASM to address such research questions. This study shows that both approaches are useful for comparing swallowing mechanics by group or associated swallowing performance variables, with each method having advantages and limitations (Table 3).

In summary, kinematic analysis and CASM are useful quantitative methods to determine differences in swallowing mechanics among various dysphagic populations. Kinematic analysis has the advantage of measuring time as a continuous variable and should be used where this is important for research. The advantage of CASM lies in visualizing the association of various risk factors, treatment plans or swallowing performance with multiple elements of swallow mechanics with a cohort or an individual patient. Use of this MATLAB tracker tool provides a means to collect data for kinematic and CASM big data analyses.

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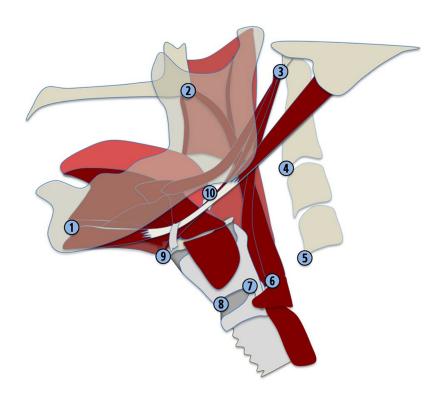
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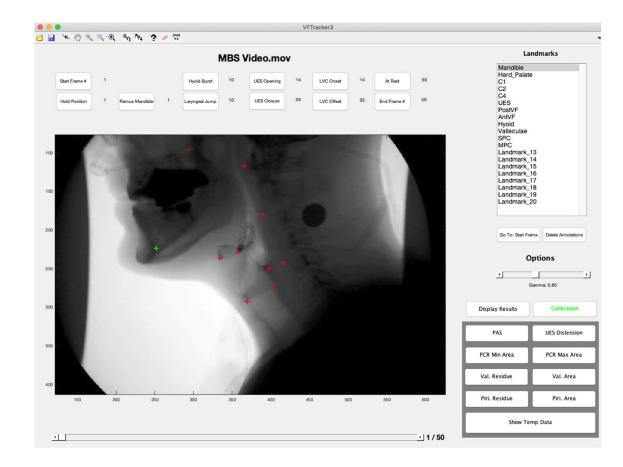
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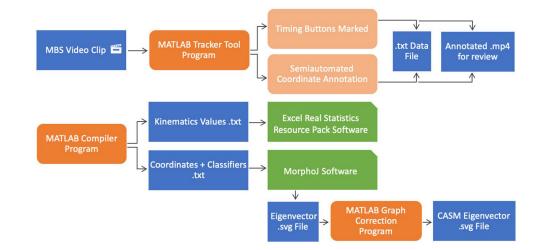
#### Fig. 1.

Coordinates map anatomical landmarks relevant to head and neck posture [1–5], proximal attachments of swallowing musculature [1–3] and distal attachments of musculature underlying hyoid movement, laryngeal elevation, pharyngeal shortening, and tongue base retraction [6–10]. Coordinate data are used for kinematic distance measurements and CASM



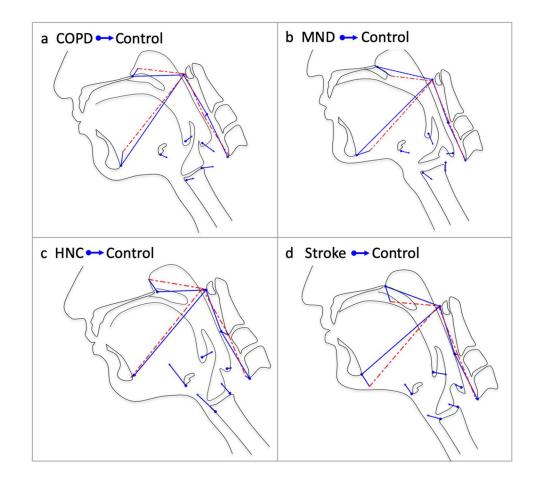


The graphical user interface and functions of the MATLAB tracker tool by Natarajan et al., were expanded to allow for kinematic data to be calculated concurrent with data collection required for morphometric analysis



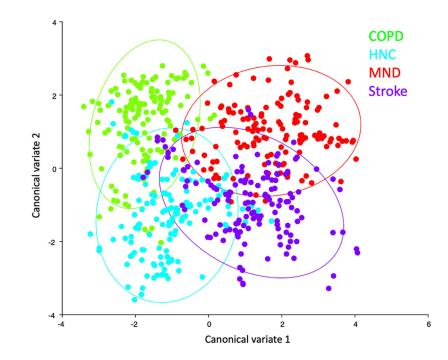
#### Fig. 3.

Workflow with data files in blue, MATLAB programs in orange, and analysis software in green. A user annotates individual video swallow files with MATLAB tracker tool to produce a.txt data file and annotated.mp4 video file (useful for visual review). The MATLAB compiler program searches all.txt data files and aggregates a.txt file of kinematic values, and two.txt files required for morphometric analysis in MorphoJ. The MATLAB graph correction program places eigenvectors within anatomical context



#### Fig. 4. a

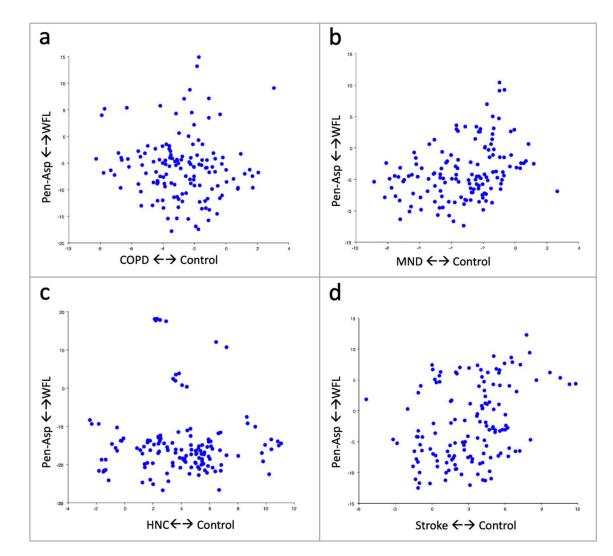
**a**–**d** DFA eigenvectors of indicate the impact of dysphagia etiologies on the functional anatomy during swallowing compared with controls (H1). The vectors represent relative changes in multiple elements of swallowing associated with each dysphagia etiology with the dots and blue lines showing the mean position of anatomical landmarks in the dysphagic group and the arrowhead and dashed red lines the control group (e.g. the stroke vectors indicate reduced hyolaryngeal elevation, pharyngeal shortening, and tongue base retraction with head and neck extension as compared to controls)



#### Fig. 5.

Morphometric CVA results (H2) indicate that pharyngeal swallowing mechanics cluster by dysphagia etiology (see color key) with neurogenic dysphagias (Stroke and MND) and structural dysphagias (HNC and COPD) aligning with canonical variate 1. Each dot represents a configuration of ten coordinates taken from a single video frame. Mathematical differences in geometric configuration, representing changes in swallowing mechanics, are calculated and plotted

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#### Fig. 6. a

**a-d** Regressions of morphometric discriminant function scores of penetration-aspiration status (Pen-Asp) vs. within functional limits (WFL) on dysphagic etiologies indicates the variability and relationship of swallowing mechanics to penetration-aspiration status within each group

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## Table 1

Operational definitions of spatial and temporal variables used in this study (# = coordinates pictured in Fig. 1)

<b>Operational defini</b>	Operational definitions for kinematic variables	
Spatial variables	Hyoid excursion (normalized to vertebrae)	Hyoid excursion (normalized to vertebrae) The orthogonal distance between the line connecting C1-C4 (#3, #5) and the hyoid bone (#9)
	Hyolaryngeal approximation	The distance between hyoid bone (#9) and the anterior vocal fold (#8)
	Laryngeal elevation	The distance between the C1 disk (#3) and posterior vocal fold (#7)
	Pharyngeal shortening	The distance between the posterior edge of the hard palate (#2) and the upper esophageal sphincter (#6)
	Base of tongue retraction ratio	The orthogonal distance between the line connecting C1-C4 and the pit of the valleculae (#10)
Temporal variables Oral transit ti	Oral transit time	The time between the start of the swallow and the bolus crossing of the ramus of the mandible
	Pharyngeal transit time	The time between the bolus crossing of the ramus of mandible and the closure of the upper esophageal sphincter
	Stage transition duration	The time between the bolus crossing of the ramus of mandible and hyoid burst

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	Hyoid Excursion	cursion	Hyolaryng	HyolaryngealApproximation Laryngeal Elevation Pharyngeal Shortening Base of Tongue Retraction Ratio	Laryngea	I Elevation	Pharynge	al Shortening	Base of Tongu	ie Retraction Ratio
vs. control	p-value	RMSSE	p-value	RMSSE	p-value	RMSSE	p-value	RMSSE	p-value	RMSSE
HNC	0.02	0.57	0.001	0.84	0.0001	66.0	0.0002	0.93	0.12	0.36
Stroke	0.08	0.40	0.70	0.09	0.37	0.20	0.10	0.38	0.88	0.03
COPD	0.39	0.19	0.08	0.40	0.39	0.19	0.23	0.27	0.16	0.32
MND	0.17	0.31	0.57	0.13	0.71	0.08	0.25	0.26	0.36	0.21
	Oral	Oral Transit Time		Stage Transition Duration Pharyngeal Transit Time	Pharyng	real Transit	Time			
vs. controls	p-value	lue RMSSE	SE p-value	e RMSSE	p-value	RMSSE	E			
HNC	0.04	0.48	0.002	0.74	0.019	0.55				
Stroke	0.91	0.02	0.019	0.55	0.007	0.64				
COPD	0.34	0.22	66.0	0.00	0.16	0.32				
MND	0.40	0.19	0.79	0.06	0.60	0.12				

With a Bonferroni correction, alpha = .01 and .0167 for distance and timing variables, respectively. Italic values indicate statistically significant *p*-values. Root mean square standardized effect (RMSSE) was used to report effect size differences with significant values ( .20) in bold

# Table 3

Overview comparison of kinematic analysis and computational analysis of swallowing mechanics (CASM) research methods

	Kinematic analysis	CASM
Dependent variables	Univariate physical measurements of distance and time	Eigenvector-based mathematical representation of geometric morphology. Time can be factored in as a covariate
Multivariate analysis and results	Indicates statistical associations of multiple variables	Indicates structural changes in swallowing mechanics associated with multiple independent variables of interest
Applications	Can be used to show statistical differences in cohort or population studies	Can be used to visualize swallowing mechanics in patient-specific, cohort, or population studies
Limitations	Does not visually assess covariance of the multiple elements of swallowing mechanism	Temporal variables cannot be extracted to calculate time differences in swallowing events
Key advantage(s)	Results reported in actual time and distances are easy to comprehend. (Table $2a-b$ )	Vectors representing differences in multiple swallowing mechanics are visualized within anatomical context (Fig. 4a–d)