Kinematic and Temporal Variability in Healthy and Disordered Swallowing

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy

Graduate Department of Speech-Language Pathology
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Abstract
The works contained in this dissertation were motivated by a desire to better understand the variability of patient performance on videofluoroscopic assessments of swallowing. Specifically, the variation present in kinematic and temporal measures of swallowing was investigated in three main phases: narrative literature review, healthy swallowing, and disordered swallowing. The primary goals were to identify which factors explain (or do not explain) variation, to develop methods to control for variation and to investigate the association between swallowing physiology and swallowing impairment. The literature reviews revealed wide ranges of variation for kinematic (Chapter 2) and temporal (Chapter 3) measures of swallowing in the existing literature on healthy deglutition. The kinematics (Chapter 4) and timing (Chapter 5) of swallowing were investigated in a prospectively collected sample of young healthy participants stratified by height. One main objective was to investigate the impact of participant size on physiological parameters of swallowing. Finally, kinematic and temporal measures of swallowing were investigated in a sample of patients referred for swallowing assessment (Chapter 6) to explore associations between swallowing physiology and impairment. The findings of
this dissertation make several unique contributions to the dysphagia literature. It has demonstrated that inherent variation appears to exist in physiological measures of both healthy and disordered swallowing. Further, when certain sources of variation are controlled (such as participant size), men and women do not demonstrate significant differences for any of the parameters tested. Importantly, this work has demonstrated that participant size impacts the expected extent of hyoid excursion and that this variation can be controlled through normalization of hyoid movement to internal anatomical scalars. Two temporal variables trended toward detecting functional swallowing impairment. Finally, this dissertation provides the first set of normative reference values for parameters of swallowing with an ultra-thin liquid barium. Limitations are acknowledged and future work is suggested. [297 words]
Acknowledgments

It is with mixed feelings that I reach the end of this journey resulting in the culmination of my doctoral thesis. I am proud of my accomplishments and delighted to see the final product come together. However, the completion of this dissertation also signifies the end of an era, which has included some of the most rewarding and satisfying years of my life so far. There are many people to acknowledge who have contributed to this process along the way.

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Chapter 1
Introduction and Thesis Overview

Introduction

Swallowing, the act of consuming food, liquid or saliva, is required to sustain life. It is also central to most social and cultural events that humans engage in. While most people do not think twice about the seemingly simple and automatic process of swallowing, it is in fact a complex neuromuscular event that requires an intricately-timed sequence of bilateral activation and inhibition of the muscles of the lips, cheeks, tongue, palate, pharynx, larynx, respiratory system and esophagus (Ertekin & Aydogdu, 2003; Jean, 2001). Disordered swallowing function is called dysphagia and has many etiological sources ranging from neurological insult (e.g. stroke, brain injury) to structural damage (e.g. surgical, traumatic or radiation-induced changes) and progressive illness (e.g. Parkinson’s Disease). During the pharyngeal phase of swallowing, the larynx and pharynx must temporarily reconfigure from their primary biological configuration (which supports breathing), to close off the airway and allow safe passage of food and/or liquid from the mouth into the upper esophagus (swallowing configuration). Failures in the timing or the adequacy of this event place a person at risk for aspiration (the passage of material into the airway below the vocal folds) and the subsequent development of aspiration pneumonia (Martino et al., 2005).

Direct viewing of dynamic swallowing function facilitates accurate clinical assessment of the nature and severity dysphagia. Videofluoroscopy (VF) is a radiographic imaging technique that allows real-time viewing of swallowing; radio-opaque foods and liquids are swallowed under x-ray. This allows clinicians to observe the adequacy of swallowing physiology and to document the occurrence of functional impairments (such as aspiration) or the presence of material in the pharynx post-swallow (known as residue). While it is common in routine clinical practice to make online, perceptual judgments regarding swallowing physiology, careful measurements can also be made from the VF. These measurable physiological events can be broadly categorized into kinematic...
parameters (movement adequacy of a structure during a swallowing) and temporal parameters (timing of swallowing gestures).

Unfortunately, the radiographic nature of VF limits the duration and repeatability of the procedure. Typically, VF exams typically include only 3-10 swallows (Perlman, Grayhack, & Booth, 1992). Nevertheless, very important decisions regarding a patient’s health, such as the safety for oral (vs. enteral) feeding are made, based on this limited sampling of swallows. A dilemma in this regard, is that the variability of patient performance has not been clearly documented, either within or across assessments. If inherent variability in swallowing is present, this can also impact research design, given that it will influence the statistical power needed to demonstrate change on a given variable. Previous researchers have acknowledged the presence of variability (Kendall, Leonard, & McKenzie, 2003; Lof & Robbins, 1990; Rosenbek, Roecker, Wood, & Robbins, 1996) but the literature lacks a direct investigation of this phenomenon in swallowing. The objective of this dissertation is to document variability in kinematic and temporal measures of swallowing in healthy and disordered individuals. Further, my aim was to identify factors that contribute to this variability and develop methods to control for it during videofluoroscopy analysis. Finally, when sources of variability are minimized, I set out to determine which kinematic and temporal measures of swallowing are associated with swallowing impairment.

Thesis Overview

This dissertation begins with two narrative reviews summarizing the literature with respect to variability in healthy swallowing for kinematic measures (Chapter 2) and temporal measures (Chapter 3). Our goal was to document variability across studies in the literature and to identify factors that might be controllable as sources of variability.

The potential sources of variability identified in Chapters 2 and 3 highlighted gaps in our understanding of variability in healthy swallowing. This inspired me to collect a highly-controlled sample of healthy swallowing on VF in 20 (10 male) volunteers stratified by height, and explore variability in these individuals, who each swallowed the
same liquids, following a strictly controlled protocol. The documents pertaining to Research Ethics Board (REB) approval of the collection of this dataset appear in Appendix A. This dataset was used to prospectively study kinematic measures (in the form of hyoid excursion) in Chapter 4 and temporal measures in Chapter 5.

Our objective in Chapter 4 was to study the relationship between participant size and participant sex, in order to test the hypothesis that apparent sex differences in hyoid excursion in might be better explained by the size of the participant. In addition, I was interested in comparing four different methods for capturing hyoid excursion and compared the sensitivity of these methods for detecting associations between hyoid excursion and bolus volume, participant sex, and participant size. My final objective in this chapter was to demonstrate the effectiveness of normalizing hyoid excursion to an internal anatomical scalar to control for size-related differences of hyoid excursion.

In Chapter 5, I set out to understand the impact of sex, bolus volume and height on temporal measures of swallowing. My goal was to establish which temporal variables were sensitive to these factors, using a highly-controlled dataset of swallows collected from healthy individuals. The analyses in Chapters 4 and 5, allowed me to document which independent variables were significantly associated with healthy swallowing, thus allowing me to compare these findings to patients referred for videofluoroscopic assessment of swallowing.

In the final chapter, (Chapter 6) I replicated the measurement methods tested in healthy volunteers (in Chapters 4 and 5) to measure kinematic and temporal measures of swallowing in a large clinical dataset collected from patients referred for VF. The documents pertaining to REB approval for the use of this retrospective clinical dataset appear in Appendix A. In routine practice, clinicians are encouraged to make hypotheses regarding the impact of the perceptually-observed physiology on functional outcomes of swallowing. My goal in Chapter 6 was to determine whether precise measures of kinematic and/or temporal variables were independently associated with the presence of functional swallowing impairment on the same swallow. Ultimately, physiological
variables that distinguish functional from impaired swallowing can be recommended for measurement during clinical VF assessments.

Finally, the dissertation closes with a chapter summarizing the major contributions from the studies contained within and considers implications for future research.

All the experimental chapters in this dissertation are verbatim excerpts from either published manuscripts (Chapters 2, 3, and 5) or submitted manuscripts (Chapters 4 and 6). Therefore, the reader is advised that this dissertation may contain redundant information across chapters. Also, note, the referencing-style of each chapter is consistent with the requirements of the journal in which the chapter is published/submitted.
References


Chapter 2
Physiological Variability in the Deglutition Literature: Hyoid and Laryngeal Kinematics

With kind permission from Springer, this chapter was excerpted in its entirety from the following journal article Molfenter, S. M., & Steele, C. M. (2011). Physiological Variability in the Deglutition Literature: Hyoid and Laryngeal Kinematics. Dysphagia, 26, 67-74. This article can be found on the publisher’s website at http://link.springer.com/article/10.1007%2Fs00455-010-9309-x and the copyright permission can be found in Appendix B.

Abstract
A literature review was conducted on hyoid and/or laryngeal displacement during swallowing in healthy populations according to several inclusion criteria. Anterior and superior displacement measures of both structures from previously published studies were compiled for meta-analysis. Results showed a large degree of variability across studies for each structure and plane of movement. Potential sources of variation were identified, including statistical, methodological, stimulus-related, and participant-related sources.

Keywords
Swallowing, Deglutition, Hyoid, Larynx, Kinematics, Movement, Deglutition disorders

Introduction
Swallowing disorders (also known as dysphagia) are common following neurological impairments (such as stroke and brain injury). Dysphagia is also a major concern following head and neck procedures and in progressive illnesses (such as Parkinson’s disease). Dysphagia can significantly impact a person’s quality of life as well as their health status. Individuals with dysphagia are at risk for aspiration (material passing below the vocal folds and entering the lungs) and for developing pneumonia.
The gold-standard tool for assessment of dysphagia is the videofluoroscopic swallowing study (VFSS) [1]. It is a radiographic imaging protocol in which various foods and liquids are mixed with a contrast medium and swallowed under fluoroscopy allowing for direct visualization of swallowing physiology. The VFSS allows clinicians to assess the safety and efficiency of swallowing across various textures and the impact of compensatory maneuvers on swallowing function. Also, measures of structural displacement and temporal intervals can be made during VFSS analysis. Unfortunately, the VFSS procedure must be limited to a brief number of swallows (usually between 3 and 10) [2] to limit the patient’s exposure to radiation. The brevity of the exam makes interpretation susceptible to variable performance; this challenges clinical decision-making and scientific analysis.

Swallowing physiology can be quantified both spatially [3–6] and temporally [7–12]. Most prior studies of swallowing physiology in the dysphagia literature report measures of data dispersion (e.g., standard deviations); however, very few studies acknowledge or address the sizable variability in their data. Variability in swallowing physiology may threaten the representativeness and reliability of assessments and obscure change post-treatment. In this article we describe, synthesize, and discuss the physiological variability of hyoid and laryngeal displacement that is reported in the swallowing physiology literature.

**Significance of Variability**

From a clinical perspective, life-altering decisions regarding safety for oral feeding and/or compensatory strategies are based on a brief set of swallows. How confident can the clinician be that this “snapshot” view is representative of the patient’s typical performance? Management and treatment decisions may be overly cautious or dangerously bold in the presence of variability on the VFSS. From a scientific perspective, how does variability threaten data representativeness if the presentation captured by the “gold standard” is itself variable? Furthermore, in scientific studies of treatment efficacy, what is the impact of such inherent variability on the ability to measure and detect meaningful outcomes?
Certainly, some authors have acknowledged that intrasubject and intersubject variability in swallowing physiology may play an important role in the interpretation of dysphagia research. For example, Kendall et al. [13] suggest that “intrasubject variability should be analyzed and will provide information about changes in swallow sequences in the same subject at the same sitting and at different sittings.” Lof and Robbins [11] documented the existence of “high variability from trial to trial in some normal subjects” on several duration measures and suggested that “individual performance must be carefully considered when one is evaluating the potential influence of treatment.” Despite this, a systematic investigation into the variability of swallowing on VFSS has not yet been conducted. The meta-analysis in this article takes a first step in this direction by synthesizing the results of the published literature on anterior and superior displacement of the hyoid and larynx during swallowing. These movement trajectories are known to facilitate airway closure [14] and upper esophageal sphincter opening [15].

**Methods**

*Search Strategy and Inclusion Criteria*

A literature search was conducted in June 2010 to find reports of hyoid and/or laryngeal displacement in healthy populations. The electronic databases PubMed and MEDLINE were used with a combination of the following search terms: swallowing, deglutition, dysphagia, hyoid, laryn*, hyolaryngeal, displacement, kinematics, and movement. The search was limited to studies published on healthy adult humans in English. After removing duplicates, the search yielded 164 publications, which were reviewed for the following inclusion criteria: (1) VFSS as the imaging tool; (2) intact head and neck anatomical system; (3) displacement data of hyoid and/or larynx along with standard deviation (SD) or standard error of the mean (SEM); (4) reporting of both anterior and superior displacement on regular-effort liquid swallows; (5) Cartesian coordinates rotated to an anatomical plane of reference (e.g., spine); and (6) use of a scalar reference to control for magnification. After applying these criteria, 13 studies remained for in-depth analysis. The reference lists of these publications were hand-searched for additional articles but yielded no additional articles meeting the inclusion criteria.
Studies Included

A brief overview of each study that met the inclusion criteria is provided below. We restrict this overview to a discussion of methodology related to hyoid and laryngeal displacement with thin-liquid swallowing, although most of these studies involved several other measures and stimuli.

Dodds et al. [3] examined hyoid displacement of 15 (9 male) participants (age = 39 ± 19 years) who were referred for upper GI assessments but had no history or evidence of oropharyngeal dysphagia. Each participant swallowed two boluses of 2, 5, 10, 15, and 20 ml of 250% weight/volume (w/v) barium. Hyoid displacement was measured by taking the difference between the hyoid positions at rest and at maximum displacement. Data were presented as an average group value at each bolus volume and data dispersion was reported using SD.

Dantas et al. [16] reported hyoid and laryngeal displacement data from 10 healthy male volunteers who swallowed two boluses of each volume (2, 5, 10, and 20 ml) of 40% w/v barium. Hyoid displacement was calculated by comparing the rest frame to the peak frame. Data were presented as average group value at each bolus volume. Dispersion was reported in the form of SD.

Van Daele et al. [17] reported data for hyoid bone displacement from 5 males (3 in their 20 s, 2 in their 70 s). These were individuals who were referred for VFSS but judged to have normal swallowing. Each participant swallowed two 5-ml boluses. The results were averaged for each participant and dispersion was reported as SEM.

Perlman et al. [18] reported hyoid displacement data for 20 male participants (ages unknown) in two groups: half with “normal” hyoid and half with “reduced” hyoid (judged subjectively). Analysis was based on comparison of the hyoid position at rest and maximum. Each participant swallowed two boluses of an uncontrolled volume (from a cup containing either 5 or 10 ml), and each swallow was treated as distinct (not averaged) within the analysis. Only the results for the “normal” hyoid group are included in this meta-analysis.
Logemann et al. conducted two studies using identical methodology. One reports data on 16 healthy men [19] and the other on 16 healthy women [20]. In each study, the 16 participants are evenly split into young (20 s) and old (80?) and were required to swallow two 1-ml and two 10-ml boluses of “watery” barium each. Analysis was conducted using a frame-by-frame method to determine the hyoid and larynx movement trajectories. Grouped data are reported both by age and by volume. Each swallow was kept distinct in the analyses and dispersion was reported as SEM.

Ishida et al. [21] provided hyoid displacement from 12 healthy volunteers (7 male) aged 20-28 years. Each participant swallowed one 10-ml bolus of 50% w/v barium. Hyoid data were extracted by analyzing the swallow in a frame-by-frame fashion. Data were grouped by sex and dispersion was reported using SD.

Kim and McCullough [5] report hyoid displacement data from 40 (20 male) healthy volunteers in two age groups (20-51 and 70-87 years). The participants each swallowed four boluses of 50/50 barium sulfate and water: two at 5 ml and two at 10 ml. Hyoid displacement was extracted by comparing a rest frame to a maximum frame and dispersion was reported in the form of SD. While this study lacked a known scalar, the length of the C3 vertebra was assigned a fixed value of 15 mm to control for magnification. The swallows for each participant were averaged at each volume. Data were presented for each age group at each volume.

Paik et al. [22] provided data on hyoid movement trajectories in both healthy individuals (n = 9) and individuals with dysphagia (stroke, n = 7; myopathy, n = 3). The mean age of each group was in the early 60s. Each participant swallowed one 5-ml bolus of 35% w/v barium solution. Hyoid trajectories were tracked using a frame-by-frame method. Data were reported by group (control, stroke, myopathy), with SEM as the measure of dispersion. Only data from the healthy controls are included in this meta-analysis.

Kim and Han [23] reported raw hyoid displacement data for 12 young healthy male
volunteers (age = 28.6 ± 3.0 years). Each participant swallowed one 5-ml bolus of 35% w/v barium. Hyoid displacement was extracted via a frame-by-frame analysis. Means and SD were calculated from the raw data for comparison in this meta-analysis.

Kang et al. [24] examined the hyoid displacement trajectories of 69 healthy volunteers (20 male) ranging in age from 26 to 78 years old. Hyoid displacement was stratified into four age groups:<45 (n = 16), 45-55 (n = 21), 55-65 (n = 16), and >65 (n = 16). The distribution of sex across the age groups was not reported. Each participant swallowed one 2-ml bolus of 35% w/v barium. Hyoid displacement was extracted using a frame-by-frame method. Data are reported by age group with SD as the measure of data dispersion.

Kim et al. [25] compared hyoid and laryngeal movement trajectories in 8 healthy controls (4 male, mean age = 64.6 ± 11.2 years) with those of 8 pneumonectomy patients (4 male, mean age = 65.4 ± 13.2 years). Each participant swallowed one 5-ml bolus of 35% w/v barium. Movement trajectories of the hyoid and larynx were extracted in a frame-by-frame fashion. Raw data (individual scores) were reported allowing for calculation of mean and standard deviation. The data from the dysphagia group are not analyzed in this article.

Bingjie et al. [26] reported hyoid and laryngeal displacement data for 105 stroke patients (57 male, mean age = 65.2 ± 8.2 years) with dysphagia and 100 healthy male controls (mean age = 62 ± 9 years). Patients with dysphagia were split into aspirators and nonaspirators in the analysis. Each subject swallowed one 3 ml and one 10 ml bolus of thin liquid barium. Movement trajectories were reported for each group (control, nonaspirators, and aspirators) at each volume (3 and 10 ml). Only data from the healthy controls are included in this meta-analysis.

**Data Extraction**

The mean values of both anterior and superior displacement of the hyoid and/or larynx were extracted from these publications for meta-analysis. Data extraction was
limited by those variables that were reported in the original publications, given that the primary factors of interest varied across publications (i.e., group, age, bolus volume, sex). All measures were converted to millimeters for uniformity.

The corresponding measure of dispersion, SD or SEM, was also extracted from each publication. Two studies [23, 25] reported raw data, which allowed us to calculate the mean and SD manually. It is important to recognize that the SEM and SD are different mathematical functions. The SD is a true measure of data dispersion because it demonstrates how tightly each data point clusters around the mean [27]. The SD is calculated by squaring each observation, subtracting this from the mean, summing all the results, dividing this result by the total number of observations, and finally taking the square root of this value. The SEM is, by definition, always smaller than the SD because it is calculated by dividing the SD by the square root of the number of observations tested. The SEM is the standard deviation of the sampling distribution and demonstrates how representative the sample mean is of the true population mean [28]. The appropriate measure of dispersion for observational kinematic studies is the SD.

Next, confidence intervals for each study/variable were calculated. This was achieved by multiplying a specific t value (two-tailed, a = 0.05, at n - 1 df) by the SD/\[\text{SQRT}(n)\]. The product of these, plus and minus the mean, gives the 95% confidence interval for that specific mean. These findings were plotted on a modified forest plot for each structure (hyoid and larynx) in each direction (anterior and superior) and can be found in Figs. 1, 2, 3, and 4. On all figures the circles represent the mean (in mm) for each particular study (or variable, where applicable) and the error bars represent the spread of the 95% confidence interval. The study author appears to the left of the mean, with the corresponding variables (if applicable) on the right. The scales for each dimension (anterior and superior) are held constant to allow for transparent comparison across structures (hyoid versus larynx).
Results

Hyoid Displacement

Figure 1 displays the results for anterior hyoid displacement in healthy adults. The mean anterior displacement ranges from 7.6 mm in the Van Daele et al. study [17] to 18.0 mm in the Kim and McCullough study [5]. First, it is apparent that there is a wide degree of variability across these 13 studies despite the strict inclusion criteria applied to the selection of articles for this meta-analysis. Each study that includes a factor of bolus volume [3, 5, 16, 19, 20, 26] shows a consistent increase in mean anterior hyoid displacement with increasing bolus size (with the exception of the elderly group in the Kim and McCullough study). However, the mean displacement magnitude seen for a particular volume (e.g., 10 ml) varies greatly across studies. For example, the mean anterior displacement value for 10-ml swallows in the Dodds study [3] was 14.8 mm (CI: 12.93-16.67), in the Dantas study [16] it was 12.2 mm (CI: 10.94-13.96), in the young group in the Kim and McCullough study [5] it was 18.0 mm (CI: 16.66-19.34), while for the older group in the same study it was 9.9 mm (CI: 8.39-11.31). Thus, a substantial degree of variability is present across studies measuring anterior hyoid displacement. It is a well-known statistical fact that variability tends to decrease with increases in sample size. With the exception of Bingjie et al. [26], all the mean values shown in Fig. 1 are taken from sample sizes of less than 40, with many of them including fewer than 10 data points for each particular variable. The study with the tightest confidence intervals was also the study with the largest sample size [26]; this pattern will be seen across all four figures (anterior hyoid, superior hyoid, anterior larynx, and superior larynx).
Fig. 1 Mean and 95% confidence intervals for anterior hyoid excursion from the 13 studies that met inclusion criteria. ml milliliters, mm millimeters

The corresponding data for superior hyoid displacement are presented in Fig. 2. In this case, the range of variability for superior displacement is even greater than that seen for anterior displacement. The smallest mean superior hyoid displacement comes from the Ishida et al. study [21] at 5.8 mm, while the largest is 25.0 mm from the Logemann study in men [19]. Once again, there appears to be a consistent pattern of increasing displacement with increasing bolus size within studies but quite different values are seen for a particular bolus size across studies.
Fig. 2 Mean and 95% confidence intervals for superior hyoid excursion from the 13 studies that met inclusion criteria. ml milliliters, mm millimeters

*Laryngeal Displacement*

Anterior laryngeal displacement is shown in Fig. 3. The smallest mean measure of anterior laryngeal displacement in the literature was 3.4 mm [16] while the largest was 8.2 mm [19, 20]. There appears to be less variability in anterior laryngeal displacement across studies compared with anterior hyoid displacement (Fig. 1). Once again, the trend of increased displacement for larger bolus volumes is seen within studies but with a wide range of values across studies.
Fig. 3 Mean and 95% confidence intervals for anterior laryngeal excursion from the five studies that met inclusion criteria. ml milliliters, mm millimeters

Figure 4 shows the compiled data for superior laryngeal displacement, which ranges from a mean of 21.1 mm [26] to 33.9 mm [19]. The displacement values and confidence intervals span a relatively large range across studies. Again, we see highly variable outcomes for a particular bolus volume (e.g., 10 ml) across studies.

Fig. 4 Mean and 95% confidence intervals for superior laryngeal excursion from the five studies that met inclusion criteria. ml milliliters, mm millimeters
**Discussion: Potential Sources of Variability**

After a thorough search of the literature and a strict set of inclusion criteria, 13 studies detailing anterior hyoid and laryngeal displacement were analyzed and synthesized for mean displacement measures along with 95% confidence intervals. Results were plotted and examined. These revealed a high degree of variability across studies for all movement trajectories. Potential sources of this variability are discussed below.

*Methodological Sources*

The inverse relationship between sample size and variability was repeatedly demonstrated with the data from the Bingjie et al. [26] study. It is plausible that a large portion of the variability in the studies reviewed was related to small sample sizes. However, the problem could also lie in the number of swallows per subject. Seven of the studies reviewed included only two swallows per bolus condition, while the others [21–25] limited their analysis to one swallow per bolus condition. Lof and Robbins [11] recommend that at least three repeated trials of swallowing at each bolus volume should be included in VFSS “in an effort to balance the need to capture the individual variability with the negative effects of radiation exposure.” This recommendation was not followed in any of the studies that were reviewed. Future studies should maximize both the number of participants and the number of swallows per condition to potentially reduce variability.

Measurement techniques can also account for variability across studies. Take, for example, the methodology used to extract hyoid bone displacement. While the majority of studies reviewed tracked the position of the hyoid on each frame throughout the swallow, 5 of the 13 studies obtained distance measures by comparing a single frame at rest to another single frame at maximum displacement [3, 5, 16–18]. The choice of the rest frame itself appears to be susceptible to some variability. Some researchers defined the rest frame to be the moment before the hyoid starts moving [17, 18], while others defined it based on the bolus’s location in the mouth/pharynx [5]. Others do not define the rest frame at all [3, 16]. This method of deriving displacement measures from single
frames at rest and maximum displacement assumes that the frame of maximum anterior displacement is the same as the frame of maximum superior displacement. This remains to be proven. Furthermore, researchers [21, 29] have shown that the hyoid is not stable at rest. Importantly, Wintzen et al. [30] showed that the start position and end position of the hyoid were the same for saliva swallows but that the preswallow position of the hyoid lowered with increasing bolus volumes; this was attributed to a lowering of the floor of mouth musculature to accommodate bigger bolus sizes. This finding could single-handedly explain the observed pattern of increased displacement for increased bolus volumes in the studies reviewed.

Another potential methodological source of variability is the choice of the plane of reference used when deriving displacement measures. Based on our inclusion criteria, all of the selected studies rotated the X,Y coordinate system to an anatomical reference. With the exception of one study [21], the Y axis was aligned to the spine via a line drawn through the anterior inferior corners of two cervical vertebrae (most often C2 through C4), with the X axis intersecting perpendicular to Y. Ishida et al. [21] define the X axis via markers on the teeth (occlusal plane), with Y perpendicular to X. Work by Nakane et al. [31] compares different planes of reference in young and elderly subjects. They suggest that Camper’s plane (similar to the occlusal plane: an X axis defined by points on the nose and tragus) is the preferred method because it is less susceptible to morphological changes of aging (i.e., osteophytes on the spine) and does not require markers to be fixed to the dentition. Differences in anatomical references may account for some variation in hyoid and laryngeal movement trajectories, especially in elderly subjects.

**Statistical Sources**

Given that three or more swallows per bolus condition is preferred for capturing representative swallow performance [11], the statistical handling of repeated measures can also impact the manifestation of variability. The representation of variability will change if repeated measures are averaged for a participant or if each swallow is weighted equally in the analysis. Of course, those studies with only one swallow per bolus
condition are exempt from this statistical dilemma. Critical review of the seven studies with two swallows per condition reveals that not all analyses were conducted in a consistent manner. Some groups weighted each swallow equally in the analysis [18–20], while others averaged repeated measures at each volume/condition [3, 5, 16, 17]. Kim and McCullough [32] recently proposed that researchers should “investigate biomechanics by analyzing each swallow independently, rather than averaging swallows.” Meanwhile, Max and Onghena [33] provide an important tutorial in the Journal of Speech Language and Hearing Research on the proper handling of the “experimental unit.” Contrary to Kim and McCullough’s suggestion, they emphasize that repeated measures should be treated as a single case or unit and failure to do so can result in incorrect statistical conclusions. Once again, variability can manifest from this kind of distinction.

Stimulus Choice

Seven of the studies reviewed [3, 16, 21–25] provide details regarding the weight/volume (w/v) of the contrast medium that they used. A historical study by Dantas et al. [34] showed that the magnitude of maximal anterior hyoid displacement was significantly greater when using high-density barium compared with low-density barium. Interestingly, this fact could explain the higher values for anterior hyoid displacement in Fig. 1 between the Dodds study, which used 250% w/v (high-density), and the Dantas study, which used 40% w/v (low-density).

In a typical VFSS, the clinician cues the patient to swallow with a verbal command. Recent research by Daniels et al. [35] has demonstrated that the use of command swallows significantly reduces swallowing event durations. The effect of cueing on kinematic aspects of swallowing is not yet understood, but it is plausible that the hyoid may be partially pre-elevated during an intentional oral hold of the bolus; this might have the effect of reducing displacement measures, depending on the method used to extract displacement measures. None of the studies reviewed provided details regarding the use of verbal cueing; this element should be controlled in future research.
Patient Sources

Those studies that include gender in their analysis [19–21] provide evidence that variation in superior and anterior hyoid and laryngeal displacement exists for both men and women. It remains unknown whether the magnitude of variation is equal across men and women and requires future in-depth analysis.

Mays et al. [36] examined the relationship between the Frankfort Mandibular Plane Angle (FMA, a measure of craniofacial morphology) and hyoid bone displacement. They found an inverse relationship, i.e., that the greater the FMA, the smaller the anterior hyoid displacement. None of the studies reviewed provided details regarding FMA. The FMA could potentially influence the variability seen in measures of anterior hyoid displacement.

The influence of patient height on kinematic measures of swallowing has been considered by some researchers. For example, Logemann et al. [19, 20] measured the C2-C4 distance as a proxy for height and used this measure as a covariate when comparing groups (i.e., young versus old). However, in the studies reviewed, height was not factored into the mean values and may have had a significant impact on observed variability. It remains unknown if taller participants would have increased hyoid displacement. Future work should examine whether patient height can account for some of the variability observed in swallowing kinematics.

The criteria by which participants are described may also be a source of variability. Take, for example, the definition of ‘‘healthy’’ subjects in the studies discussed above. Some define healthy subjects as those referred for an assessment but with no evidence of dysphagia [3, 17], whereas others use ‘‘healthy volunteers’’ recruited from the community. It is unclear whether these groups can be expected to behave in the same way and this may be another potential source of the variability.

Lof and Robbins [11] hypothesized that patients with dysphagia may present with
significant differences in variability (either reduced or exacerbated), while their average values could appear identical to those of healthy individuals. There is a relative dearth of literature detailing swallowing kinematics in patients with dysphagia. However, in recent years, pioneering work describing hyoid and laryngeal displacement in patient populations has been conducted [22, 25, 26, 29, 32]. Unfortunately, these studies were conducted on relatively small, heterogeneous (in terms of presentation of dysphagia) samples making them difficult to compare across studies. The impact of type and severity of dysphagia on swallowing physiology variability is not yet clearly understood. Finally, after all the other sources of variability have been considered and controlled for, it is plausible to assume that some portion of the variability can be attributed to variability that is inherent to an individual’s swallow.

**Conclusions: Implications for Future Studies**

Based on a careful review of the literature and compilation of data on swallowing physiology across several studies, evidence of variability on hyoid and laryngeal displacement emerges in both anterior and superior planes of movement. For researchers, the impact of variability on statistical analysis and normative data development must be seriously considered. Clinicians should recognize the potential of variable patient performance in VFSS on management decisions. Various statistical, methodological, stimulus-related, and patient-related factors are thought to impact the degree to which this variability is apparent. Future work is needed to understand the relative contributions of each of these variables. A large-scale study that carefully controls these issues may provide researchers and clinicians with an accurate picture of variability in swallowing function to inform management decisions, treatment planning, and effect size calculations.
References


Chapter 3

Temporal Variability in the Deglutition Literature

With kind permission from Springer, this chapter was excerpted in its entirety from the following journal article: Molfenter, S. M., & Steele, C. M. (2012). Temporal Variability in the Deglutition Literature. Dysphagia, 27, 162-177. This article can be found on the publisher’s website at http://link.springer.com/article/10.1007%2Fs00455-012-9397-x and the copyright permission can be found in Appendix B.

Abstract

A literature review was conducted on temporal measures of swallowing in healthy individuals with the purpose of determining the degree of variability present in such measures within the literature. A total of 46 studies that met inclusion criteria were reviewed. The definitions and descriptive statistics for all reported temporal parameters were compiled for meta-analysis. In total, 119 different temporal parameters were found in the literature. The three most-frequently occurring durational measures were upper esophageal sphincter opening, laryngeal closure, and hyoid movement. The three most-frequently occurring interval measures were stage transition duration, pharyngeal transit time, and duration from laryngeal closure-to-UES opening. Subtle variations in operational definitions across studies were noted, making the comparison of data challenging. Analysis of forest plots compiling descriptive statistical data (means and 95% confidence intervals) across studies revealed differing degrees of variability across durations and intervals. Two parameters (UES opening duration and the laryngeal closure-to-UES opening interval) demonstrated the least variability, reflected by small ranges for mean values and tight confidence intervals. Trends emerged for factors of bolus size and participant age for some variables. Other potential sources of variability are discussed.

Keywords

Deglutition, Deglutition disorders, Temporal, Timing, Duration, Variability
Introduction

Dysphagia (disordered swallowing) may occur secondary to neurological impairment, structural changes in the head and neck, and/or progressive illness. Dysphagia has the potential to impact a person’s nutrition, hydration, and quality of life, and may lead to serious sequelae such as the development of aspiration pneumonia (as a result of material passing below the vocal folds into the respiratory system). Videofluoroscopy (VF) is considered the gold-standard tool for the assessment of dysphagia [1]. In VF, various foods and liquids are mixed with radiographic contrast media such as barium and swallowed under continuous fluoroscopy allowing for direct dynamic visualization of swallowing physiology. Using a standardized protocol, the safety and efficiency of swallowing can be assessed across various textures, volumes, and maneuvers [2]. In the analysis of VF, several different quantitative parameters can be measured, including kinematic measures of structural displacement and timing measures (durations and intervals). Given that VF involves radiation exposure, which carries a risk of stochastic biohazard, the procedure is necessarily limited to a small number of swallows (usually between 3 and 10) [3]. Molfenter and Steele [4] previously proposed that the brevity of the exam makes the accuracy of interpretation susceptible to the influence of variability in swallowing performance within a given individual; furthermore, variability across individuals impacts our ability to define a reference context of normative swallowing behavior. It can be difficult to detect and quantify the extent of both impairment and real change (either improvement or deterioration) in a patient’s swallowing against this backdrop of inherent variability [4]. Consequently, there is a need to better understand the variation that exists in swallowing physiology in order to appreciate the extent to which this constitutes a limitation on clinical decision-making and scientific analysis. In this article we report a meta-analysis of temporal variability in swallowing.

In an early and seminal publication, Lof and Robbins [5] studied the test–retest variability of nine temporal measures of swallowing in 16 healthy participants divided equally by sex and age group (middle-aged versus older adults). To our knowledge, this
is the only available publication that explores variability in temporal measures of swallowing. Each participant swallowed three 2-ml boluses of both liquid barium and paste barium. This VF protocol was then repeated an average of 97 days later for middle-aged participants and 45 days later for older participants. The authors reported data for nine durational measures and examined their relative test–retest variability using the coefficient of variation (CV). The CV is a measure that expresses the standard deviation (SD) in reference to the size of the mean, with a higher CV representing greater relative variability in the parameter of interest [6]. Among the nine timing variables that were studied, Lof and Robbins [5] reported that stage transition duration (STD) was the most volatile, with a CV of 1.14 for liquids (mean = −0.22, SD = 0.25) and 17.67 for semisolid (mean = −0.03, SD = 0.053) stimuli.

Unfortunately, there is a statistical limitation in the use of the CV for appreciating relative variability across the parameters studied by Lof and Robbins, because the measure has a tendency to become inflated in the context of small values, especially those near zero [7]. To illustrate this point, imagine a sample in which one subgroup of participants (Group A) has a mean STD of 0.01 s but a fairly large standard deviation of 0.25 s, thereby yielding a CV of 25 (CV = SD/mean). Consider, then, that a second participant group (Group B) in the same study has a higher mean STD value of 0.5 s but the same standard deviation of 0.25 s, yielding a comparative CV of 0.5. Given that the standard deviation in both groups is identical in terms of real timing (i.e., 0.25 s), it would probably strike most readers as implausible to conclude that the variability seen in Group A is 50 times greater than that seen in Group B, although this is in fact the message implied by the comparison of the two CV statistics. By simply shifting these hypothetical data away from small values by adding a fixed value of 0.5 s to all proposed group means and SDs, the CVs change to 1.47 for Group A and 0.75 for Group B, dramatically altering the magnitude of relative variability seen between the two groups from 50 to 1.96 and illustrating the tendency for the CV measure to be unduly influenced by actual numeric values. In the Lof and Robbins data set, STD was the variable that was most volatile (displaying the highest CV values), but also the variable with mean values that fell closest to zero (i.e., −0.22 s for liquids and −0.03 s for semisolids). Clearly, in
that particular study, the near-zero values of the STD parameter made the interpretations of its relative variability vulnerable to this weakness in the CV statistic; alternative methods for comparing variability across parameters and studies are needed. Currently, there are no other known studies that examine temporal variability in healthy swallowing, although other studies have described substantial variability in event sequencing [8, 9] and in the location of the bolus at swallow onset in healthy swallowing [10, 11].

In a previous meta-analysis of variability conducted on 13 studies reporting data on hyoid and laryngeal kinematics in healthy adult swallowing, Molfenter and Steele [4] inspected relative variability using means and 95% confidence intervals (CI) in order to circumvent the previously mentioned limitations of the CV statistic [7]. Where variability was found, statistical, methodological, stimulus-related, and participant-related sources were proposed. In this article we use a similar approach to describe, synthesize, and discuss the variability seen in commonly reported temporal measures of swallowing from the literature describing healthy deglutition.

Methods

Search Strategy and Inclusion Criteria

A literature search for publications reporting temporal swallowing data was completed using MedLine, with the following search terms: (deglutition) and (videofluoroscop* or modified barium) and (timing or duration or temporal). The initial search was limited to studies published in English. This yielded 183 abstracts for further review. The basic inclusion criteria were studies reporting means and SD or means and standard error of the mean (SEM) for temporal parameters during thin-liquid swallowing tasks in healthy adult humans. Studies were excluded from further analysis if they (1) did not employ VF as their instrumental method; (2) reported data for pediatric or patient populations (without clear reporting of reference data for healthy adult participants); (3) reported timing for solid stimuli only; (4) included data limited to measures taken during the performance of compensatory swallow maneuvers; or (5) if the study methods manipulated the natural process of healthy swallowing (e.g., with direct infusion of a bolus to the pharynx). Studies were also excluded if they did not report the quantitative
information necessary to calculate confidence intervals for meta-analysis and if they presented statistical results only in graph format.

*Studies Included*

After the application of these criteria, a subset of 46 publications was retained for in-depth review [5, 8, 9, 12–54]. All temporal variables and statistical data were extracted and compiled in a spreadsheet. Tallies of the frequency of occurrence for each temporal variable were made across all 46 publications. In addition, other factors regarding each study were documented, including participant age and gender distribution, bolus volume, barium density, frame rate, and method of analysis used.

*Data Extraction*

In total, 119 different temporal variables were found in the reviewed literature. Extracted variables were divided into three categories: durations, defined as the time required for a distinct physiological event during swallowing to occur (such as laryngeal closure); intervals, defined as the time or latency that elapses between two gestures in the swallow sequence (such as the time between the onset of laryngeal closure and UES opening); and partial durations, defined as subsegments of swallow durations (such as the latency between the onset of laryngeal closure and the attainment of maximum laryngeal closure, which is a segment of laryngeal closure duration). Table 1 displays the distribution of the temporal variables by category and their observed frequency within the data set of the 46 articles selected for review. Partial durations were found to be reported with low frequency, representing <10% of all measures, and therefore were not included in the subsequent analyses.

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Table 1 Number of different variables reported and their corresponding frequency of occurrence in the 46 publications reviewed
The three most-frequently occurring duration and interval measures identified in this literature review were selected for further in-depth analysis. The three most-frequently reported durations were upper esophageal sphincter (UES) opening, laryngeal closure duration (LCD), and hyoid movement duration (HMD). The three most-frequently reported intervals were stage transition duration (STD), pharyngeal transit time (PTT), and laryngeal closure (LC)-to-UES opening. The distribution of these variables across the reviewed publications is given in Table 2. It should be noted that in Table 2 the studies are listed in alphabetical order, by first author, with a corresponding study key that is also used to identify these studies in Figs. 1, 2, 3, 4, 5, 6. Study key numbers in the table and figures do not correspond to the reference list numbers and therefore are denoted in the text with italicized numbers, e.g., 7 or 8A, while reference list citations are in square brackets.

A meta-analysis was performed on the six most-commonly reported temporal parameters (3 duration and 3 interval measures), using descriptive statistics, that were clearly reported in 36 of the 46 publications selected for in-depth review. The remaining ten publications reported data for variables other than these six highest-frequency parameters. All data were converted to units of seconds for uniformity. Means and corresponding measures of dispersion, SD or SEM, were extracted from each publication. One study reported raw data, which allowed us to calculate means and SDs manually [36]. Next, 95% CIs for each study/variable were calculated. This was achieved by multiplying a specific t value (two-tailed, a = 0.05, at n-1 df) by the SD/[SQRT(n)] or SEM. By adding and subtracting this product to or from the mean, one can calculate the 95% CI for that specific mean. These 95% CIs were plotted on modified forest plots for each variable and are displayed in Figs. 1, 2, 3, 4, 5, 6. In all six figures, the diamonds represent the mean (in seconds) for each particular study (or variable, where applicable) and the error bars represent the spread of the 95% CI. The study key appears beside each data point, with corresponding information available in Table 2. The scales for intervals and durations were held constant across the figures to allow for transparent comparison of relative variability across parameters. Inspection of the modified forest plots in Figs. 1,
2, 3, 4, 5, 6 allows one to appreciate trends in the aggregate data arising from different study factors (e.g., factors of bolus volume, age, or gender). It should be noted that the recognition of these trends from visual inspection of the forest plots does not necessarily imply that variation attributable to these apparent factors of importance achieved statistical significance in the original publications.
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Table 2, Part 1. Study key by authors and variable(s) for the 36 publications that reported data for the 6 temporal variables of interest.
Table 2, Part 2. Study key by authors and variable(s) for the 36 publications that reported data for the 6 temporal variables of interest.

<table>
<thead>
<tr>
<th>Study key</th>
<th>Durations</th>
<th>Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UES opening</td>
<td>Laryngeal</td>
</tr>
<tr>
<td></td>
<td>duration</td>
<td>closure</td>
</tr>
</tbody>
</table>

| Dantas et al. [34] | 11A | ✓ | ✓ | ✓ |
| 5 ml, women | | | | |
| 5 ml, men | 11B | ✓ | ✓ | ✓ |
| 10 ml, women | 11C | ✓ | ✓ | ✓ |
| 10 ml, men | 11D | ✓ | ✓ | ✓ |
| Kahrilas et al. [44] | 12A | ✓ | ✓ | ✓ |
| 1 ml | | | | |
| 10 ml | 12B | ✓ | ✓ | ✓ |
| Kang et al. [24] | 13A | ✓ | ✓ | ✓ |
| 2 ml, < 45 years old | | | | |
| 2 ml, 45–54 years old | 13B | ✓ | ✓ | ✓ |
| 2 ml, 55–64 years old | 13C | ✓ | ✓ | ✓ |
| 2 ml, > 65 years old | 13D | ✓ | ✓ | ✓ |
| Kendall et al. [13] | 14A | ✓ | ✓ | ✓ |
| 1 cc | | | | |
| 3 cc | 14B | ✓ | ✓ | ✓ |
| 20 cc | 14C | ✓ | ✓ | ✓ |
| Kendall et al. [15] | 15 | ✓ | ✓ | ✓ |
| 3 cc | | | | |
| Kendall and Leonard [18] | 16A | ✓ | ✓ | ✓ |
| 1 cc, young | | | | |
| 20 cc, young | 16B | ✓ | ✓ | ✓ |
| 1 cc, old | 16C | ✓ | ✓ | ✓ |
| 20 cc, old | 16D | ✓ | ✓ | ✓ |
| Kern et al. [43] | 17A | ✓ | ✓ | ✓ |
| 5 ml, young | | | | |
| 5 ml, older | 17B | ✓ | ✓ | ✓ |
| 10 ml, young | 17C | ✓ | ✓ | ✓ |
| 10 ml, older | 17D | ✓ | ✓ | ✓ |
| Kim et al. [20] | 18A | ✓ | ✓ | ✓ |
| 5 ml, young | | | | |
| 10 ml, young | 18B | ✓ | ✓ | ✓ |
| 5 ml, older | 18C | ✓ | ✓ | ✓ |
| 10 ml, older | 18D | ✓ | ✓ | ✓ |
| Kim et al. [40] | 19A | ✓ | ✓ | ✓ |
| 5 ml | | | | |
| 10 ml | 19B | ✓ | ✓ | ✓ |
| Lazarus et al. [47] | 20A | ✓ | ✓ | ✓ |
| 1 ml | | | | |
| 3 ml | 20B | ✓ | ✓ | ✓ |
| 5 ml | 20C | ✓ | ✓ | ✓ |
| Leonard and McKenzie [12] | 21A | ✓ | ✓ | ✓ |
| 20 cc, young | | | | |
| 20 cc, older | 21B | ✓ | ✓ | ✓ |
| 20 cc, young (H1-B1) | 21C | ✓ | ✓ | ✓ |
| 20 cc, old (H1-B1) | 21D | ✓ | ✓ | ✓ |
| Lof and Robbins [5] | 22 | ✓ | ✓ | ✓ | ✓ |
| 2 ml | | | | | | |

Table 2, Part 2. Study key by authors and variable(s) for the 36 publications that reported data for the 6 temporal variables of interest.
<table>
<thead>
<tr>
<th>Study key</th>
<th>Durations</th>
<th>Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UES opening duration</td>
<td>Laryngeal closure duration</td>
</tr>
<tr>
<td>Logemann et al. [31]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ml</td>
<td>23A</td>
<td>✓</td>
</tr>
<tr>
<td>5 ml</td>
<td>23B</td>
<td>✓</td>
</tr>
<tr>
<td>10 ml</td>
<td>23C</td>
<td>✓</td>
</tr>
<tr>
<td>20 ml</td>
<td>23D</td>
<td>✓</td>
</tr>
<tr>
<td>Logemann et al. [23]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ml</td>
<td>24A</td>
<td>✓</td>
</tr>
<tr>
<td>10 ml</td>
<td>24B</td>
<td>✓</td>
</tr>
<tr>
<td>young</td>
<td>24C</td>
<td>✓</td>
</tr>
<tr>
<td>older</td>
<td>24D</td>
<td>✓</td>
</tr>
<tr>
<td>Logemann et al. [22]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ml</td>
<td>25A</td>
<td>✓</td>
</tr>
<tr>
<td>10 ml</td>
<td>25B</td>
<td>✓</td>
</tr>
<tr>
<td>young</td>
<td>25C</td>
<td>✓</td>
</tr>
<tr>
<td>older</td>
<td>25D</td>
<td>✓</td>
</tr>
<tr>
<td>Martin-Harris et al. [29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ml</td>
<td>26</td>
<td>✓</td>
</tr>
<tr>
<td>Mendell and Logemann [21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All bōuses pooled</td>
<td>27</td>
<td>✓</td>
</tr>
<tr>
<td>Mendell and Logemann [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>28A</td>
<td>✓</td>
</tr>
<tr>
<td>40–49</td>
<td>28B</td>
<td>✓</td>
</tr>
<tr>
<td>60–69</td>
<td>28C</td>
<td>✓</td>
</tr>
<tr>
<td>70–79</td>
<td>28D</td>
<td>✓</td>
</tr>
<tr>
<td>80–89</td>
<td>28E</td>
<td>✓</td>
</tr>
<tr>
<td>Mokhlesi et al. [41]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 ml</td>
<td>29A</td>
<td>✓</td>
</tr>
<tr>
<td>5 ml</td>
<td>29B</td>
<td>✓</td>
</tr>
<tr>
<td>Ohmae et al. [27]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ml</td>
<td>30A</td>
<td>✓</td>
</tr>
<tr>
<td>5 ml</td>
<td>30B</td>
<td>✓</td>
</tr>
<tr>
<td>Ohmae et al. [28]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ml</td>
<td>31</td>
<td>✓</td>
</tr>
<tr>
<td>Palmer et al. [48]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>straw sips</td>
<td>32</td>
<td>✓</td>
</tr>
<tr>
<td>Park et al. [32]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ml</td>
<td>33A</td>
<td>✓</td>
</tr>
<tr>
<td>10 ml</td>
<td>33B</td>
<td>✓</td>
</tr>
<tr>
<td>Pauloski et al. [54]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ml</td>
<td>34</td>
<td>✓</td>
</tr>
<tr>
<td>Stachler et al. [45]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 ml</td>
<td>35A</td>
<td>✓</td>
</tr>
<tr>
<td>10 ml</td>
<td>35B</td>
<td>✓</td>
</tr>
<tr>
<td>Taniguchi et al. [39]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ml</td>
<td>36</td>
<td>✓</td>
</tr>
</tbody>
</table>

Table 2, Part 3. Study key by authors and variable(s) for the 36 publications that reported data for the 6 temporal variables of interest.
Results

Durations

UES Opening Duration.

Twenty publications reported data for UES opening duration. Compiled results appear in Fig. 1, with corresponding study information in Table 2. First, it is apparent that this variable is distributed across a relatively small range of mean values (i.e., 0.21–0.67 s). Further, the 95% CIs for UES opening duration fall remarkably tight to the means, showing very little spread in the data. Within the UES opening duration data, it is interesting to note that every study in which two or more bolus volumes were compared demonstrated a systematic volume effect: an increase in volume resulted in a corresponding increase in mean UES opening duration (studies 2, 3, 4, 8, 9, 11, 12, 14, 17, 20, 24, 25, 29, and 30). Additionally, a systematic age effect is apparent within the UES opening duration data. Studies 17, 24, and 25 each included a comparison of data between younger and older participant groups. In each of these studies, UES opening durations were longer in the older participants. Study 11 examined a factor of gender, without evidence of any sex effect, while study 8 tested barium density and reported longer durations with higher density stimuli. These single studies do not allow us to draw any conclusions regarding trends attributable to these factors.

Laryngeal Closure Duration (LCD).

Fourteen publications reported data for LCD. Compiled results appear in Fig. 2, with corresponding study information in Table 2. Mean values for LCD ranged from 0.31 to 1.07 s. In comparison to the UES opening duration parameter, the 95% CIs for LCD are wider and reflect greater variability around each mean data point. Eight of the ten studies that tested volume effects show apparent support for the notion that LCD increases with increasing bolus volume (1, 9, 20, 24, 25, 29, 30, and 33), while two studies contain mixed results in this respect (8 and 23). The contribution of participant age to variation in LCD was tested in three studies and a trend toward increased LCD in older participants was observed in all three (13, 24, and 25). Higher barium density appeared to contribute
to longer LCD but was reported only in study 8, rendering it impossible to draw strong conclusions regarding the pervasiveness of this effect across the literature.

Fig. 1 Means (in seconds) and 95% CIs for UES opening duration as reported in the reviewed literature. Alphanumeric codes refer to studies/variables in Table 2
Hyoid Movement Duration (HMD)

Eight publications reported values for HMD. Compiled results appear in Fig. 3, with corresponding study information in Table 2. Mean HMD values were spread across a range from 0.79 to 1.39 s. Corresponding CIs appear similar in magnitude to those seen for LCD (and wider than those seen for UES opening duration). Three of four studies that tested the influence of bolus volume on HMD showed that larger volumes were
associated with longer durations (2, 8, and 30). Partial support for this trend is also apparent in study 10. Only study 13 tested the contribution of participant age to HMD, with no clear effect emerging for this variable. Higher barium density resulted in longer HMD in the single study examining this factor (study 8).

Fig. 3 Means (in seconds) and 95% CIs for hyoid movement duration as reported in the reviewed literature. Alphanumeric codes refer to studies/variables in Table 2

**Intervals**

**Stage Transition Duration (STD)**

STD is defined as the interval between the bolus entering the pharynx (usually demarcated by the bolus passing the shadow of the ramus of the mandible) and the onset of upward and forward hyoid excursion [5]. Fourteen studies reported values for STD. Compiled results appear in Fig. 4, with corresponding study information in Table 2. Mean STD values ranged from –0.22 to 0.54 s. Not only do the mean values have considerable variability across publications, but the corresponding CIs also appear to be highly variable. Seven of the 14 publications reporting this variable include variations in bolus volume, but there appears to be no clear pattern of this factor across studies. Some publications reported longer STD values with larger volumes (2, 19, 35, and 7 partially),
while others showed shorter STDs with larger volumes (14, 16, and 18). However, all four studies that included participant age as a factor in their analysis (13, 16, 18, and 21) showed a systematic trend of longer STD values in older participants. In addition, study 6 showed much higher mean values of STD and wider CIs when swallows were uncued (noncommand swallow paradigm) versus cued. Finally, of note, a subtle variation in STD definition was noted across studies. The onset of STD reported in 14, 15, 16, and 21C/D was defined as the bolus passing the posterior nasal spine (rather than the shadow of the ramus of the mandible). This variable is designated “B1-H1” by the authors. Thus, it would be logical to expect slightly longer mean values in the STD data for these studies compared to studies referencing STD to bolus movement past the mandible; this expectation is generally consistent with the data shown in Fig. 4.

**Fig. 4 Means (in seconds) and 95% CIs for stage transition duration as reported in the reviewed literature. Alphanumeric codes refer to studies/variables in Table 2**
Pharyngeal Transit Time (PTT)

PTT is defined as the interval between the bolus entering the pharynx (usually demarcated by the bolus passing the shadow of the ramus of the mandible) and the bolus tail passing through the UES [5]. Thus, it overlaps with, but extends the interval captured by the STD parameter. Fourteen publications included measures of PTT in their analysis. Compiled results appear in Fig. 5, with corresponding study information in Table 2. Mean PTT values displayed a wide range from 0.35 to 1.19 s and considerable variability in CIs. As with the STD parameter, there appears to be no clear influence of bolus volume on PTT. Some publications report longer PTT values with larger volumes (2, 8, 10, and 20), others show shorter PTT with larger boluses (11 and 14), while still others show no clear trend (16 and 29). The influence of other factors on PTT was explored in single publications only. Based on these single studies, PTT values appear to be higher in older individuals (study 16), in women (study 11), with higher barium density (study 8), and in uncued swallow conditions (study 6). However, single studies do not allow for strong conclusions to be drawn regarding the contributions of these factors. Finally, many discrepancies in naming conventions and operational definitions for PTT were noted and are discussed further below.
Laryngeal Closure (LC)-to-UES Opening Interval

Nine studies reported the time interval between onset of LC and UES opening. Compiled results appear in Fig. 6, with corresponding study information in Table 2. Mean LC-to-UES opening values display a strikingly tight range, from −0.16 to 0.02 s, with limited variability seen in the 95% CIs. No apparent trends emerge for variation in LC-to-UES opening interval based on bolus volume: This interval decreased with increasing bolus size in studies 1, 25, and possibly 29, while it increased with increasing bolus size in study 24. This interval does appear to decrease with increasing age (24, 25, and 28), although it is probably questionable to comment on apparent trends given such a narrow distribution of means. Finally, in study 1, cold temperature appeared to shorten this interval but was included only in this single study.
Fig. 6 Means (in seconds) and 95% CIs for laryngeal closure to UES opening duration as reported in the literature. Alphanumeric codes refer to studies/variables in Table 2

Aggregate Measures

Given that all six of these frequently occurring parameters are measured in a common unit (seconds), it is possible to examine the degree of variability present across the measures themselves and to characterize these parameters in terms of their relative variability. Table 3 compares the aggregate ranges found for mean values (maximum minus minimum mean values reported across studies) and 95% CI widths (maximum upper CI limit minus minimum lower CI limit computed across studies) in our meta-analysis. Table 3 summarizes this comparison exercise and also summarizes the extent to which the meta-analysis of each parameter revealed systematic trends attributable to factors of bolus volume and participant age. Based on this review, it can be seen that the LC-to-UES opening interval displays, relatively speaking, the smallest mean range and
tightest 95% CIs of the six measures reviewed. UES opening duration comes next, with a slightly larger mean range and 95% CI range. The values seen for the HMD parameter falls in the middle, displaying what might be interpreted as a typical degree of variability across these timing measures, both for mean range and for 95% CI width. By contrast, the STD, PTT, and LCD measures show large mean ranges and the widest 95% CI.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aggregate Mean Range(^a) (sec)</th>
<th>Aggregate 95% CI Width(^b) (sec)</th>
<th>Volume Effect?</th>
<th>Age Effect?</th>
</tr>
</thead>
<tbody>
<tr>
<td>UES opening duration</td>
<td>0.46</td>
<td>0.52</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>LCD</td>
<td>0.76</td>
<td>1.04</td>
<td>Yes</td>
<td>Maybe</td>
</tr>
<tr>
<td>HMD</td>
<td>0.60</td>
<td>0.96</td>
<td>Maybe</td>
<td>No</td>
</tr>
<tr>
<td>STD</td>
<td>0.76</td>
<td>1.04</td>
<td>Equivocal</td>
<td>Yes</td>
</tr>
<tr>
<td>PTT</td>
<td>0.84</td>
<td>1.07</td>
<td>Equivocal</td>
<td>Maybe</td>
</tr>
<tr>
<td>LC-to-UES-opening</td>
<td>0.18</td>
<td>0.36</td>
<td>No</td>
<td>Maybe</td>
</tr>
</tbody>
</table>

Table 3. Aggregate mean and 95% CI ranges for all variables with corresponding volume and age effects. \(^a\) Calculated by subtracting the minimum reported mean value from the maximum reported mean value across the studies reviewed. \(^b\) Calculated by subtracting the minimum value for the 95% CI lower boundary from the maximum value for the 95% CI upper boundary across the studies reviewed.

Discussion

This meta-analysis compiles data for the three most-frequently reported durations and the three most-frequently reported swallow intervals from the existing literature describing healthy swallowing. Means and CIs were plotted on modified forest plots, with scales held constant to allow for relative inspection of variability across variables. Taken together, it is apparent that not all variables behave similarly with respect to variability, despite being sampled from healthy individuals. Table 3 summarizes the impressions of relative variability gleaned from the inspection of the modified forest plots in Figs. 1, 2, 3, 4, 5, 6. Of course, it is possible that factors other than those that were directly tested in the original publications might account for some of the variability seen in these data. Here we discuss several of these potential sources of variability.

**Definitional Sources of Variability**

Methodological differences across studies may account for a portion of the variability that is seen in these data. One clear opportunity for such variability to occur
arises when different operational definitions are used for specific temporal parameters across studies. To illustrate, consider the challenge of defining hyoid movement duration. It has been pointed out that the hyoid is not stable when it is in a resting state [55, 56], making it challenging to define the onset and offset of hyoid movement, and leading to the possibility that even subtle differences in the definitions used for these indices may cause differences in the results of measures made in different studies. In fact, Kendall et al. [13] report that the postswallow hyoid position has such large SDs in their data that they have decided not to routinely include this parameter in their standardized methods for analyzing VF exams.

An associated source of variability may be related to challenges in reliable measurement of the durations that are being investigated. Agreement across raters is important not only for calculating durational measures but in selecting the frames that are used to index such measures. Difficulties in achieving adequate interrater and intrarater reliabilities for temporal measures on VF have been reported [57, 58]. In this meta-analysis, only 23 of the 46 studies reviewed reported interrater reliability, and even fewer reported intrarater reliability (16 of 46). If acceptable levels of both inter- and intrarater reliability are not established, the contributions of variable measurement by raters cannot be considered or accounted for.

The criteria by which participants are selected for inclusion may also be a methodological source of variability. The definition of “healthy” participants can be different for different research groups. For example, in most of the studies reviewed, “healthy” was undefined and could include anyone without a history of structural changes to the head and neck and/or neurological impairment and/or dysphagia. Sometimes, the source of “healthy” control participants may be fundamentally different from that for control participants in another publication. For example, Stachler et al. [45] use a control group of heavy smokers and drinkers to compare to their head and neck surgical patients. It is unclear to what extent these definitional issues may contribute to the variability present in this meta-analysis.
**Stimulus Sources of Variability**

Bolus volume emerged from this meta-analysis as a factor that influences several timing measures (see Table 3). In particular, it appears that swallow durations are impacted by bolus volume, while swallow intervals are not. UES opening duration was highly influenced by differences in bolus volume, while laryngeal closure duration and hyoid movement duration appeared to be only moderately sensitive to this factor (see Figs. 1, 2, 3).

The density of the stimulus may also be a source of variability in timing measures, as suggested in the single study (8) that examined this factor. However, while the higher-density barium preparation (250% w/v compared with 40% w/v) in that study elicited longer timing measures for all four variables included in that study (UES opening duration, LCD, HMD, and PTT), it must also be recognized that we do not have information on intermediate densities that would be necessary to clearly elucidate the effect of density on swallowing timing. Furthermore, it should be noted that only 14 of the 46 studies examined in this review reported the density of the barium used, with values ranging from 35 to 250% w/v. There is a need for clear reporting of methodological decisions like barium density in order to demonstrate the variability attributable to this factor and to inform the field regarding the potential for manipulations of this factor to reveal clinically important variations in swallowing function.

**Participant Sources of Variability**

Our meta-analysis suggests that participant age is one source of variability in swallow timing parameters. Among the parameters reviewed, UES opening duration and STD both showed systematic trends towards longer durations in older participants. By contrast, hyoid movement durations appeared to be robust and invariant across age. Other participant factors that may be considered sources of variability include differences in patient size, such as differences in spine length, which has been explored as a source of kinematic variation but has not, to date, been considered with respect to temporal measures [22, 23, 59, 60]. Variations in pharyngeal size might also be logically considered as a potential source of variability in PTT, given that this measure captures
the time for the bolus to travel through the pharynx. Future work should examine whether participant size can account for some of the variability observed in swallowing durations and intervals.

**Procedural Sources of Variability**

In 2007, Daniels et al. [37] published their groundbreaking study on the effect of verbal cueing on temporal measures of swallowing. They demonstrated that uncued swallows were initiated with the bolus head at a more posterior location in the oropharynx, thus resulting in longer temporal measures. In that study, STD and PTT measures for the uncued condition had both longer durations and wider CIs compared to values from other studies and for other variables (see 6B on Figs. 5, 6). Most of the studies included in the current meta-analysis were conducted before the Daniels et al. work was published and therefore do not report transparent information regarding the use of cueing. Future work should not only describe whether a cueing paradigm was used but also test its effect on kinematic and other temporal measures of swallowing.

Another potential source of procedural variability is related to the parameters of the fluoroscopy output, such as the frames per second (fps) capture rate. This parameter stipulates how many samples are extracted per second from the continuous fluoroscopy. The majority of studies (n = 35) reviewed reported using 25 fps or greater; however, the remaining 11 studies do not specify their frame rate. Bonilha et al. [61] have recently shown differences in ratings of standardized videofluoroscopic swallowing study measures of residue, overall impression (a physiological composite score), and penetration–aspiration scale when a simulated 15-fps condition was compared to the full 30-fps condition. The effect of frame rate on temporal measures of swallowing is unknown; however, one might speculate that higher rates of variability may be observed in lower-fps conditions due to the fact that less information is captured during the swallow.

**Individual Sources of Variability**

Finally, as has been proposed before [4], when all other sources of variability are
accounted for, it is highly plausible that each individual participant displays some level of underlying variability in both kinematic and temporal measures of swallowing, across repeated swallows and repeated VF examinations. Within this context, not all variables are likely to fluctuate to the same degree. Rosenbek et al. [1] suggest that the challenge of underlying variability for clinicians is “in deciding how many swallows to elicit and how to interpret performance on what is perforce a limited number of swallows.” We feel that underlying individual variability will be observable only in a controlled and standardized assessment paradigm that employs multiple swallows per bolus condition [46, 47]. Martin-Harris et al. [2] have shown that 5-ml thin-liquid and 5-ml nectar-thick swallows are highly sensitive to physiological measures of swallowing impairment. While this observation needs replication for temporal measures of swallowing, we advocate for the use of multiple trials of thin-liquid barium and nectar-thick barium (at controlled densities) during standardized VF assessment.

In clinical settings, it is routinely recommended that a VF include the administration of three swallows per bolus condition as a minimum for capturing individual variability while balancing radiation exposure [5]. However, 13 of the studies reviewed in this analysis reported data derived from only a single swallow per bolus condition. Under these circumstances, variability may be present but its influence unrecognized, given that the single observed swallow may not be representative of a typical swallow for that participant. In the case where multiple swallows are administered, the statistical handling of repeated measures can also impact the appreciation of variability. While the majority of studies with more than one swallow per condition averaged the repeated measure, some studies weighted each swallow equally in the analysis [22, 23, 59]. The appropriate handling of repeated measures is well recognized in the literature to influence the impression of variability in a resulting statistic [62, 63].

**Limitations**

An important caveat to note regarding this review of the deglutition literature is that we observed a startling number of inconsistencies in the naming conventions and
definitions of different temporal variables. For example, the interval between the bolus head entering the pharynx and the bolus tail passing through the UES is most commonly referred to as ‘’pharyngeal transit time’’ [21, 37, 39, 41], but it has also been called ‘’pharyngeal transit duration’’ [5], ‘’pharyngeal clearance duration’’ [42], and ‘’pharyngeal clearance time’’ [53]. Similarly, ‘’stage transition duration’’ was sometimes referred to as the ‘’pharynx-to-swallow interval’’ [45, 48].

To make matters more complex, we also observed subtle variations in operational definitions of variables, making the comparison of data across studies challenging. For example, the majority of research describes PTT as the interval between the bolus head passing the shadow of the ramus of the mandible and the tail of the bolus passing through the UES. However, it has also been defined by some as commencing when the bolus head or tail passes the faucial pillars [34, 39, 51, 64] or the posterior nasal spine [13, 15]. This same variable has also been defined as concluding when the bolus head reaches the UES [42] as opposed to when the bolus tail passes through the UES.

Langmore [65] has also discussed these challenges and pointed out that the discrepancies for this particular variable appear to stem from changing historical definitions of the boundary between the oral and pharyngeal phases. Similar subtle differences in operational definitions were noted in the literature for measures of oral transit, pharyngeal response time, STD, and onset of hyoid excursion, among others. As has been previously pointed out by Mendell and Logemann [8], some of these disparities can be attributed to different research groups choosing to time-reference swallowing data to different physiological events (such as bolus passing mandible, initial upward/forward movement of the hyoid, or UES opening). We concur with this observation given that very few discrepancies in naming conventions or operational definitions were noted for swallowing durations (which do not require a reference point) compared to swallow intervals. The only exception appeared to be for hyoid movement duration, which was also referred to as ‘’pharyngeal response duration’’ [42] and ‘’swallow duration’’ [48]. However, it is reasonable to postulate that wherever such variations in terminology and definition occur, they are likely to contribute to differences in reported mean values, but
they should not contribute directly to trends in standard deviations and data spread. This meta-analysis was limited to studies that reported temporal data in healthy adults in a way that allowed us to reconstruct means and confidence intervals. There were many publications that lacked the necessary quantitative information for inclusion. Furthermore, analysis of the influence of specific factors on temporal variability was limited to those variables analyzed and reported in the original publication.

**Conclusions**

We have compiled descriptive statistical data for the most-frequently occurring temporal variables in the healthy deglutition literature, allowing for an aggregate impression of variability in such measures to be formed. Differences in naming conventions and operational definitions were noted, especially for swallow interval measures. The three most commonly occurring measures of swallowing durations were UES opening, laryngeal closure, and hyoid movement. The three most commonly occurring measures of swallow intervals were stage transition duration, pharyngeal transit time, and laryngeal closure to UES opening. A meta-analysis of these six variables using modified forest plots has revealed that there is substantial variability in temporal measures of healthy swallowing and that not all variables fluctuate in the same way or to the same degree. Some variables demonstrated tight means and confidence intervals (laryngeal closure-to-UES opening interval and UES opening duration). Other variables appeared to be influenced by bolus volume (UES opening duration and laryngeal closure duration) or participant age (UES opening duration and stage transition duration).

We have discussed several factors that may account for a portion of the observed variability in these studies. We also propose that inherent variability in swallowing function may still exist when all these variables are controlled for. Future work should examine within-participant and across-participant variability while controlling methodological, definitional, stimulus, participant, procedural, and statistical sources of variability in both healthy individuals and different subgroups of people with dysphagia.
References


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53. Dantas RO. Effect of swallowed bolus variables on oral and pharyngeal phases of


Chapter 4

Use of an anatomical scalar to control for sex-based size differences in measures of hyoid excursion during swallowing

This chapter in its entirety is under review by IOPscience for publication in their journal *Physiological Measurement*: Molfenter, S. M., & Steele, C. M. (under review). Use of an anatomical scalar to control for sex-based size differences in measures of hyoid excursion during swallowing.

Abstract

During swallowing, the hyoid bone travels in a superior-anterior trajectory. Reduced hyoid excursion is often suspected as an explanation for swallowing dysfunction. Traditional methods for measuring hyoid excursion from dynamic videofluoroscopy x-ray recordings involve calculating change in position in absolute units (mm). This method shows a high degree of variability across studies. Typically, greater hyoid excursion has been reported in men than women. Given that men are typically taller than women, we hypothesized that controlling for participant size might reduce an important source of variability in hyoid excursion measures. We compared four methods of capturing hyoid excursion in 20 healthy volunteers (10 male), stratified by height, in a tightly controlled study. We identified an anatomical scalar (a cervical spine length measure), visible on the videofluoroscopic image, correlated with participant height. This scalar differed significantly between men and women. Further, three of four methods for capturing hyoid excursion were significantly correlated with this scalar. By incorporating the anatomical scalar as a continuous covariate in repeated measures mixed model ANOVAs of hyoid excursion, apparent sex-based differences were neutralized. Finally, we showed that transforming measures of hyoid excursion into anatomically scaled units, reduces variation attributable to sex-based differences in participant size.

Keywords
Swallowing, deglutition, dysphagia, hyoid, variation, normalization, videofluoroscopy
**Introduction**

Eating and drinking are not only important life-sustaining functions, but are also central to social activity and quality-of-life. The act of safe swallowing is a complex neuromuscular process involving a sequence of bilateral inhibition and activation of multiple muscles in the lips, tongue, palate, larynx, pharynx and esophagus (Ertekin and Aydogdu 2003). A disruption in swallowing function is called dysphagia, and can occur secondary to a variety of neurological, structural, and degenerative causes. The assessment of dysphagia frequently involves videofluoroscopy (VF), a radiographic imaging technique that allows real-time dynamic visualization of swallowing physiology. Kinematic and temporal measurements can be extracted from VF recordings, and are used to gain insight regarding the underlying reasons for and nature of dysphagia.

During the pharyngeal phase of swallowing, the pharynx must reconfigure to protect the airway while food and/or liquid moves from the mouth to the esophagus. This critical event, which prevents material from being aspirated into the lungs, is achieved in part by biomechanical displacement of the hyoid bone in a superior-anterior trajectory. Muscular connections between the hyoid bone, the larynx and the pharynx enable this movement to contribute to closure of the laryngeal vestibule and down-folding of the epiglottis for airway protection (Logemann *et al* 1992), and also to opening of the upper esophageal sphincter (UES) (Jacob *et al* 1989), allowing material to exit the pharynx. This manuscript details novel techniques for the accurate measurement of hyoid excursion using a dataset of VF swallowing recordings from 20 healthy young volunteers who swallowed a variety of volumes of ultra-thin liquid barium.

**Background**

The current standard of clinical practice with respect to interpreting VF recordings involves perceptual judgment of the adequacy of hyoid movement. Perceived reductions in hyoid movement, either in the superior or anterior direction, have been cited as contributing to, or explaining, swallowing dysfunction (see for example Perlman *et al* 1994). However, the ability to make reliable perceptual judgments regarding hyoid excursion has been questioned (Perlman *et al* 1995). Precise quantitative image-based
measurement of hyoid excursion is an alternative to perceptual judgment that is not routinely performed during clinical VF analysis. The steps involved in image-based hyoid measurement typically include defining hyoid position relative to a stable patient-defined origin (usually on the spine) to control for head movement, defining a Cartesian coordinate system relative to the patient (usually by setting the vertical axis of displacement in relation to the cervical spine), and using a measurement scale (typically absolute distance in millimeters, derived using an externally-placed scalar of known dimensions, such as a coin) (Perlman et al 1995, Zu et al 2011, Logemann et al 2002, Paik et al 2008, Kim et al 2010, Dodds et al 1988, Dantas et al 1990, Kang et al 2010). Even when this level of methodological rigor has been employed, the literature suggests that hyoid movement in swallowing is a highly variable phenomenon, even in healthy individuals. A recent meta-analysis of 13 studies that report hyoid excursion in healthy participants using the measurement methods described above, found that reported means for anterior hyoid excursion ranged from 7.6 mm to 18.0 mm, while mean superior excursion ranged from 5.8 mm to 25.0 mm (Molfenter and Steele 2011). The authors identified several possible factors that may contribute to the observed variability including: sample size (greater variability in small samples), representativeness of the data (reduced variability with repeated sampling), method used to collect hyoid excursion (frame-by-frame marking versus comparison of a rest and peak frame), the definition of rest/minimum position (i.e., pre- versus post-swallow), specifications of the coordinate system used for position measurement (origin, axes, units), measurement error (poor reliability across repeated measures), stimulus characteristics (barium concentration, viscosity, volume), protocol decisions (use of cued versus spontaneous swallows), and participant factors including sex, age, and height/size-of-the-system.

In this manuscript, we sought to conduct a study of hyoid excursion in healthy swallowing, with the goal that strict methodological control of potential sources of variability would enable us to measure the influence of participant sex and participant size (which we refer to as size-of-the-system) on hyoid excursion. Leonard and colleagues (2000) have reported statistically significant, albeit weak positive correlations between participant height and hyoid excursion (r=0.37 for 20ml boluses). This is the only study that we are aware of to date, which directly explores the relationship between an
individual’s size/height and magnitude of hyoid excursion. Perlman and colleagues (1995) proposed reporting measures of hyoid displacement in ‘cervical units’ (a participant-specific measure capturing the length of C1 to C5) and compared this approach to standard measurement (mm) using VF data from 8 healthy young male participants. They concluded that these measurement methods lead to comparable results, and that anatomical scalars can be used in lieu of external scalars. Unfortunately, because their sample was restricted to men, we cannot draw conclusions about the relationship between hyoid excursion, size-of-the-system, and sex. Others have acknowledged the possible contribution of size-of-the-system to hyoid excursion variation by size-normalizing measures of swallowing biomechanics using internal anatomical scalars (Potratz et al 1993, Kahrilas et al 1997) or by including these measures as covariates in statistical models (Logemann et al 2000, Logemann et al 2002), however, again, the interaction between hyoid excursion, size-of-the-system and sex has never been directly tested. Our hypothesis is that apparent sex differences in hyoid movement might be redundant with, and better explained by, differences in the size-of-the-system. In order to test this question, we also sought to identify an internal anatomical scalar, visible in the VF image, which would serve as a representative measure of the size-of-the-system.

When measuring hyoid excursion from VF, choices exist in what to measure. To date, evidence is lacking to clearly demonstrate whether the choice of measurement method influences the apparent effects of other independent variables, such as sex or bolus volume. In the current study, in addition to exploring the contribution of differences in size-of-the-system to variability in measures of hyoid excursion, we were interested in determining the extent to which different methods of measurement display size-based variation. Traditionally, researchers have examined the change in location of the hyoid between ‘rest’ and ‘peak’ positions and have reported separate measures for the anterior and superior planes of movement (for example, Dantas et al 1990, Dodds et al 1988, Kim and McCullough 2008, Perlman et al 1995). Others have captured the diagonal distance traveled by the hyoid from rest to peak, (i.e. the hypotenuse), rather than plane-specific vectors of movement (Leonard et al 2000); we refer to such two-point comparisons as ‘displacements’. One recognized source of variability in hyoid
displacement measures arises from difficulties in identifying a stable ‘rest’ position of the hyoid (Ishida et al 2002). Given the challenge inherent in identifying the frame of rest with confidence, a simplified approach, requiring measurement of peak hyoid position may prove more stable. A recent study by Humbert and colleagues (2012) illustrates this approach, examining the peak superior position of the hyoid (and larynx) during swallowing, relative to the C5 vertebrae.

In summary, our specific research questions were:

Q1. Of a set of 13 internal anatomical scalar candidates, visible in the VF image, which one serves best as a proxy for the size-of-the-system?
Q2. Does the size-of-the-system vary significantly by sex?
Q3. Does hyoid excursion (captured four ways in mm) vary with the size-of-the-system?
Q4. When tested in a mixed model repeated measures ANOVA, do millimeter measures of hyoid excursion (captured four ways) vary significantly by sex, size-of-the-system, and/or bolus volume?
Q5. Does adding a size-of-the-system covariate (from Q1) to the model in Q4, account for any observed sex differences in hyoid excursion?
Q6. Does changing the metric in Q4 from absolute units to scaled units (via use of the internal anatomical scalar identified in Q1), agree with the results of Q5?

Methods

The methodological procedures pertaining to this dataset were carefully chosen to control for potential sources of variability, as identified in Molfenter and Steele (2011) and have been reported in detail elsewhere (Molfenter and Steele 2012). This study was reviewed and approved by the local research ethics board.

Participants

Twenty (10 male) healthy young volunteers (under 45, mean: 31.5 years, standard deviation (SD): 5.7 years) were recruited to participate in a VF protocol. Participant recruitment was stratified by height to span a range between the national reported mean
lower and upper height quartiles for adults by sex (Shields et al 2008). Height
distribution by sex for the study sample is displayed in Figure 1.

![Height distribution by sex](image)

**Figure 1. Distribution of height by sex.**

**VF Stimuli**

Each participant performed a series of 15 swallowing tasks, 9 of which were
included in this analysis: 3 swallows each of 5ml, 10ml and 20ml liquid barium 22% w/v
suspension (Bracco Polibar suspension diluted with water). Suspensions with this
concentration of barium are called ‘ultra-thin’ in the dysphagia literature (Fink and Ross
2009). A protocol of three repetitions per volume condition was used to ensure
representative sampling of intra-participant variability, while keeping radiation exposure
time to a minimum (Lof and Robbins 1990). Sample volumes were measured using a
pipette and placed in 30ml capacity plastic cups. Based on pilot testing, 1ml above the
target volume for swallowing was pipetted into each cup to allow for residual material
likely to remain in the cup after each sip. Cups were weighed before and after drinking so
that the exact volume consumed could be determined. In the event that a participant used
piecemeal deglutition for a particular bolus (i.e., division of a sip into two or more
swallows by partitioning the bolus in the mouth), the data for that bolus were excluded
from the analysis, due to our inability to accurately measure the volume of the bolus
ingested in each sub-swallow (1 instance at 5ml and 6 instances at 20ml). Table 1 lists
means and 95% confidence intervals for the average volume swallowed by target volume.
These results confirm that despite adding extra barium to each cup, there was a tendency
for a portion of each administered bolus to remain behind as residual in the cup. All statistical analyses involved the mean values from Table 1 to represent the true volumes swallowed by participants in this study.

Table 1. Targeted volumes, pipetted volumes and actual volumes (mean and 95% CI).

<table>
<thead>
<tr>
<th>Target volume (ml)</th>
<th>Volume pipetted into cup (ml)</th>
<th>Mean volume swallowed (ml)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>3.54</td>
<td>3.42 (3.42, 3.67)</td>
</tr>
<tr>
<td>10</td>
<td>11</td>
<td>8.03</td>
<td>7.78 (7.78, 8.28)</td>
</tr>
<tr>
<td>20</td>
<td>21</td>
<td>17.34</td>
<td>16.84 (16.84, 17.85)</td>
</tr>
</tbody>
</table>

**VF Procedure**

All VFs were conducted using a Toshiba Ultimax (Toshiba America Medical Systems, Inc., Tustin, CA) in lateral view at full resolution (30 pulses per second) and captured and recorded on a Digital Swallowing Workstation (KayPentax, Lincoln Park, NJ) at 30 frames per second. A coin of known diameter (19.05 mm) was placed over the left mastoid process of each participant using medical tape to facilitate the later conversion of pixel-based measures of structural movement into millimeters. Boluses were arranged and presented in blocks of three cups of the same volume on a table within easy reach of the participant. The order of bolus volume block was randomized. Once the VF was turned on, the participant was instructed to self-feed and swallow the liquid from each block, one cup at a time, at a spontaneous, comfortable pace. Self-feeding and spontaneous swallows were used to avoid changes in swallow timing associated with cued swallowing (Daniels et al 2007). The VF was turned off after the hyoid returned to rest following the final bolus of each three-cup sequence. The average total VF exposure time (for the entire 15 task sequence) was 1.75 minutes (SD: +/-0.31 minutes).

**VF Post-Processing and Analysis**

The positions of the following structures were marked in each frame of the swallow: the anterior inferior corner of the C4 vertebra (origin); the anterior inferior corner of the C2 vertebra (Y vector); and the anterior inferior corner of the hyoid. The position of the hyoid in each frame was calculated based on its XY position relative to the origin (C4) with the Y-axis defined parallel to the spine. The positional data were then
scaled using two methods: 1) in absolute units (mm) using the external coin scalar (19.05mm) and 2) in units scaled using an internal anatomical scalar (%C2-4 spine length). Justification for this choice of particular scalar comes from the results of Q1 below. Both sets of positional data were exported to an Excel file (Microsoft) with an embedded macro that was devised to find the maximum and minimum values (in both the X and Y planes) between two user-defined frames of interest. The ‘start’ frame was designated as 10 frames prior to the sudden upward/forward movement of the hyoid associated with a swallow and the ‘end’ frame was defined as 10 frames after the epiglottis returned to a vertical position. Each swallow yielded four data points for analysis (minimum X position, maximum X position, minimum Y position, and maximum Y position). Four parameters capturing hyoid excursion were derived from the positional data: anterior displacement, superior displacement, hypotenuse displacement, and maximum XY position from the C4 origin (Fig 1).

Figure 2. Illustration of marking points and hyoid parameters, measured relative to the cervical spine (origin at C4).
Reliability Measures

Inter- and intra-rater reliability were calculated for each hyoid excursion parameter using a random selection of 10% of the swallows in the dataset, using two-way mixed intra-class correlation coefficients (ICC) for consistency. Results (Table 2) for superior displacement, hypotenuse displacement and maximum XY position all demonstrated ‘excellent’ reliability, while scores for anterior displacement achieved only ‘fair to good’ reliability (i.e., 0.40-0.75) (Fleiss 1986). One possible explanation for the lower reliability observed for anterior displacement is that head movement causes anterior-posterior movement of both the hyoid and the origin of the measurement system, but has minimal effect on the superior-inferior position of the origin. Variation in anterior-posterior position of the origin increases the opportunity for measurement error in the anterior-posterior plane between and across raters.

Table 2. Intra- and Inter-rater reliability measures for four hyoid excursion parameters. 

<table>
<thead>
<tr>
<th></th>
<th>Intra-rater Reliability</th>
<th>Inter-rater Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC 95% CI</td>
<td>ICC 95% CI</td>
</tr>
<tr>
<td>Anterior Displacement</td>
<td>0.61 -0.35-0.88</td>
<td>0.59 -0.43, 0.88</td>
</tr>
<tr>
<td>Superior Displacement</td>
<td>0.94 0.79-0.98</td>
<td>0.88 0.59-0.97</td>
</tr>
<tr>
<td>Hypotenuse Displacement</td>
<td>0.81 0.35-0.94</td>
<td>0.90 0.65-0.97</td>
</tr>
<tr>
<td>Maximum XY Position</td>
<td>0.85 0.49-0.96</td>
<td>0.79 0.26-0.94</td>
</tr>
</tbody>
</table>

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics Version 20. Two-tailed p-values < 0.05 were considered statistically significant. For the mixed model analyses of variance, a compound symmetry model structure was determined to have the best fit with the data. When main effects were significant, post hoc pairwise comparisons were conducted with Sidak adjustment for multiple comparisons. Effect sizes for pairwise comparisons were calculated using Cohen’s d and values of 0.2-0.5 were considered to show small effects, 0.5-0.8 to show medium effects and values > 0.8 to show large effects (Kotrlik and Williams 2003).
Q1. To determine which internal anatomical scalar best serves as a proxy for the size-of-the-system, 13 potential internal scalar candidates were measured in pixels using ImageJ software (National Institutes of Health, Bethesda, MD) on a single pre-swallow frame. The length of each potential scalar candidate was transformed from pixels to millimeters using the externally placed coin. Pearson’s correlations were used to examine the relationship between the various internal anatomical scalars (mm) and participant height (cm). It was decided a priori that the scalar displaying the highest correlation with height would be used to represent ‘size-of-the-system’ in the subsequent research questions.

Q2. A one-way analysis of variance (ANOVA) was run to explore the influence of sex on the size-of-the-system.

Q3. To determine whether hyoid excursion (captured four ways in mm) varies significantly according to the size-of-the system, a mixed model repeated measures ANOVA was run with a between participants factor of size-of-the-system, a within participant factor of bolus volume, and a repeated factor of trial-within-bolus-volume. Pearson’s correlation coefficients between size-of-the-system and hyoid excursion measures were also calculated.

Q4. To test the association between sex, bolus volume and hyoid excursion (captured four ways in mm), mixed model repeated measures ANOVAs using each method of hyoid measurement were run with a between participants factor of sex and within participant factor of bolus volume, and a repeated factor of trial-within-bolus-volume.

Q5. In order to test whether size-of-the-system can account for observed differences in hyoid excursion (captured four ways in mm) by sex, size-of-the-system scalar (from Q1) was added as a covariate to the Q4 model.
Q6. In order to test whether scaling hyoid movement using an internal anatomical scalar (Q1) can account for the variation attributable to size-of-the-system, the analysis from Q4 was repeated with the metric of hyoid excursion transformed from absolute units to scaled units.

Results

Q1. Correlations with height were explored for eleven spine-based and two non-spine-based scalars (see Figure 4). Pearson correlations ranged from 0.46 to 0.83 and are listed with associated two-tailed p-values in Figure 4. The length of the C2-4 unit (measured from the anterior inferior corner of C2 to the anterior inferior corner of C4) displayed the strongest correlation with true participant height ($r=0.83$, $p<0.000$) and was therefore chosen to represent size-of-the-system in subsequent analyses. Agreement for measurement of the C2-4 scalar was measured using a two-way mixed ICC for consistency on 20% of participants, selected at random, and revealed excellent consistency with scores of 1.00 (95%CI: 0.98, 1.00) for inter-rater and 0.97 (95%CI: 0.55, 1.00) for intra-rater agreement.
Q2. Results confirmed that size-of-the-system (C2-4 length in mm) was significantly greater in men (mean: 41.8 mm, SE: 0.81) than in women (mean: 34.6 mm, SE: 0.94) \([F(1, 18)=34.12, p=0.000]\). This result was associated with a large effect size (Cohen’s \(d=1.58\)).

Q3. The associations between size-of-the-system (as measured by C2-4 length) and hyoid excursion (in mm, captured four ways) are summarized in Table 3. Three of four measurement methods were significantly influenced by the size-of-the-system: superior displacement, hypotenuse displacement and maximum XY position. Anterior displacement measures did not show any dependence on size-of-the-system. Maximum XY position measures displayed the highest correlation with the size-of-the-system at \(r = 0.63\).
Table 3. Associations between four methods for capturing hyoid excursion and size of the system (as measured by C2-4 length).

<table>
<thead>
<tr>
<th>Association between hyoid measurement method and size-of-the-system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degrees of Freedom (df)</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Anterior Displacement</td>
</tr>
<tr>
<td>Superior Displacement</td>
</tr>
<tr>
<td>Hypotenuse Displacement</td>
</tr>
<tr>
<td>Maximum XY Position</td>
</tr>
</tbody>
</table>

Q4: Descriptive statistics for each hyoid excursion parameter by sex and bolus volume in absolute units (mm) are presented in Table 4. A mixed model repeated measures ANOVA with factors of bolus volume and sex found significant sex differences for all millimeter based hyoid excursion measures except anterior hyoid displacement. Male participants always demonstrated greater hyoid excursion than female participants. Only the maximum XY position measure demonstrated a significant main effect of volume. Maximal XY position of the hyoid was significantly further from the C4 origin in the 20ml condition (64.9mm, SE: 1.1) compared with both of the smaller bolus conditions (5ml mean: 61.9mm, SE: 1.1 vs. 10ml mean: 62.7mm, SE: 1.1), although this result achieved only a small effect size (Cohen’s d=0.34). Results are summarized in Table 5. Given that anterior displacement did not demonstrate sensitivity to size-of-the-system (Q3) or sex (Q4), it was not included in the remaining analyses.
Table 4. Descriptive statistics for hyoid excursion (measured four ways in mm) by sex and bolus volume. CI = Confidence Interval

|                  | MEN  | WOMEN |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|------------------|------|-------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                  | 5ml  | 10ml  | 20ml                 | 5ml                 | 10ml                | 20ml                |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Anterior         |      |       |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Displacement     | Mean (mm) |      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|                  | 15.6 | 14.7  | 16.1                 | 14.5                | 13.9                | 14.4                |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|                  | 95% CI |       | 13.9-17.4            | 12.9-16.5           | 14.3-17.8           | 12.7-16.3           | 12.1-15.6           | 12.6-16.3           |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Superior         | Mean (mm) |      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Displacement     | 19.3 | 20.3  | 21.3                 | 15.8                | 15.3                | 16.4                |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|                  | 95% CI |       | 16.1-22.5            | 17.1-23.5           | 18.1-24.5           | 12.9-19.0           | 12.1-18.5           | 13.1-19.6           |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Hypotenuse       | Mean (mm) |      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Displacement     | 25.1 | 25.3  | 27.1                 | 21.9                | 21.0                | 22.1                |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|                  | 95% CI |       | 22.2-28.0            | 22.4-28.2           | 24.1-30.0           | 19.0-24.8           | 18.1-23.9           | 19.1-25.1           |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Maximum XY       | Mean (mm) |      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| Position         | 67.3 | 69.0  | 71.8                 | 56.5                | 56.4                | 58.2                |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|                  | 95% CI |       | 64.2-70.3            | 65.9-72.0           | 68.7-74.8           | 53.5-59.6           | 53.4-59.5           | 55.0-61.3           |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |

Table 5. Results of Question 4 exploring contributions of bolus volume and sex to hyoid excursion measures (in mm) without controlling for the size-of-the-system

<table>
<thead>
<tr>
<th>Association between hyoid measurement method and sex</th>
<th>Main effect of sex?</th>
<th>Degrees of Freedom (df)</th>
<th>F Statistic</th>
<th>Significance (p value)</th>
<th>Effect size (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Displacement</td>
<td>NO</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Superior Displacement</td>
<td>YES</td>
<td>(1, 18.1)</td>
<td>4.8</td>
<td>0.042</td>
<td>0.74</td>
</tr>
<tr>
<td>Hypotenuse Displacement</td>
<td>YES</td>
<td>(1, 18.1)</td>
<td>5.2</td>
<td>0.034</td>
<td>0.72</td>
</tr>
<tr>
<td>Maximum XY Position</td>
<td>YES</td>
<td>(1, 18.2)</td>
<td>47.1</td>
<td>0.000</td>
<td>1.34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Association between hyoid measurement method and volume</th>
<th>Main effect of volume?</th>
<th>Degrees of Freedom (df)</th>
<th>F Statistic</th>
<th>Significance (p value)</th>
<th>Effect size (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Displacement</td>
<td>NO</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Superior Displacement</td>
<td>NO</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Hypotenuse Displacement</td>
<td>NO</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Maximum XY Position</td>
<td>YES</td>
<td>(1, 148.2)</td>
<td>4.9</td>
<td>0.009</td>
<td>0.34</td>
</tr>
</tbody>
</table>
Q5. When the size-of-the-system covariate was added to the statistical model from Q4, all main effects of sex were neutralized. This was true for all three measures of hyoid excursion tested (superior displacement, hypotenuse displacement and maximum XY position, all measured in mm). In other words, no significant main effects of sex on hyoid excursion were found when the model accounted for size-of-the-system. Consistent with the analysis from Q4, a significant main effect of volume was observed when hyoid excursion was captured using maximal XY position \([F(2, 143.3) = 4.09, p=0.020]\).

Q6. Our final statistical analysis involved transforming the metric of hyoid excursion from absolute units (mm) to internally anatomically scaled units (i.e., \%C2-4 length). Descriptive statistics for the hyoid excursion parameters by sex and bolus volume are shown in scaled units in Table 6. The model explored in Q4 was repeated using these scaled units. The findings from Q5 were replicated: no significant differences by sex were found, but a significantly greater distance from the C4 origin for the 20ml bolus volume was observed when hyoid excursion was captured using maximal XY position \([F(2, 143.1)=5.6, p=0.005]\), (Cohen’s \(d=0.44\), i.e. small effect size). This finding demonstrates that the use of the internal anatomical scalar controlled for sex-related differences in participant size and hyoid position.

Table 6. Descriptive statistics for scaled hyoid excursion (measured in \%C2-4 units) by sex and bolus volume. CI = Confidence Interval

<table>
<thead>
<tr>
<th></th>
<th>5ml</th>
<th>MEN 10ml</th>
<th>20ml</th>
<th>5ml</th>
<th>WOMEN 10ml</th>
<th>20ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior Displacement</td>
<td><strong>Mean</strong> (%C2-4)</td>
<td>42.7</td>
<td>43.8</td>
<td>46.7</td>
<td>41.4</td>
<td>41.3</td>
</tr>
<tr>
<td></td>
<td><strong>95% CI</strong></td>
<td>35.2-50.2</td>
<td>36.3-51.3</td>
<td>39.1-54.2</td>
<td>33.9-48.9</td>
<td>33.8-50.9</td>
</tr>
<tr>
<td>Hypotenuse Displacement</td>
<td><strong>Mean</strong> (%C2-4)</td>
<td>55.6</td>
<td>54.7</td>
<td>59.4</td>
<td>57.3</td>
<td>55.9</td>
</tr>
<tr>
<td></td>
<td><strong>95% CI</strong></td>
<td>48.8-62.4</td>
<td>47.9-61.5</td>
<td>52.5-66.2</td>
<td>50.5-64.2</td>
<td>49.1-62.7</td>
</tr>
<tr>
<td>Maximum XY Position</td>
<td><strong>Mean</strong> (%C2-4)</td>
<td>148.2</td>
<td>149.9</td>
<td>157.9</td>
<td>147.6</td>
<td>147.7</td>
</tr>
<tr>
<td></td>
<td><strong>95% CI</strong></td>
<td>141.9-156.4</td>
<td>142.6-157.1</td>
<td>150.6-165.2</td>
<td>140.3-154.9</td>
<td>140.5-160.6</td>
</tr>
</tbody>
</table>
Discussion

In this study, we sought to accurately measure the physiological phenomenon of hyoid excursion during swallowing. This important physiological event is critical for airway protection and opening of the upper esophageal sphincter (Logemann et al. 1992, Jacob et al. 1989). Traditional methods for measuring hyoid excursion have shown high levels of variability across studies (Molfenter and Steele 2011). We examined the relationship between size-of-the-system, sex and bolus volume and their impact on four different methods for capturing hyoid excursion in a dataset of healthy individuals stratified by height, swallowing controlled volumes of ultra-thin liquid barium. Strict methodological control was employed to regulate as many potential sources of variability as possible.

When previous work has reported a significant sex difference in hyoid excursion, it has typically been the case that a greater extent of hyoid excursion was seen in men compared with women (Ishida et al. 2002, Logemann et al. 2002, Leonard et al. 2000). We hypothesized that sex effects in hyoid excursion may actually reflect differences in the size-of-the-system, and that scaling measures for variations in participant size might reduce a source of measurement variability. As a first step, we identified the length of the C2-4 segment as the best of 13 possible internal anatomical scalars, based on its correlation with participant height (Q1). In Q2, we demonstrated that this size-of-the-system parameter (C2-4 length) did indeed vary significantly by participant sex (greater size-of-the-system in men). Next, in Q3, we demonstrated that three methods for measuring hyoid excursion did, in fact, vary systematically by the size-of-the-system. We found greater excursion in taller individuals for superior displacement, hypotenuse displacement, and maximum XY position measures, but not for anterior displacement. Interestingly, the correlation observed between size-of-the-system and hypotenuse displacement ($r = 0.35$, averaged across bolus volumes) is comparable to correlations reported by Leonard and colleagues (2000) between height and the hypotenuse displacement parameter ($r = 0.37$ for 20 ml).
In Q4, we were able to replicate results previously reported in the literature by demonstrating a significant sex effect when we analyzed measures of hyoid excursion without taking size-of-the-system into consideration. However, when participant size-of-the-system was added as a covariate in Q5, we were able to show that sex no longer accounted for significant differences in hyoid excursion. Thus, we were able to demonstrate, for the first time, that apparent sex differences in hyoid excursion are actually explained by differences in participant size. Predictably, when hyoid excursion was scaled to the size-of-the-system (by expressing measures in %C2-4 units as opposed to mm), the same finding was replicated: sex differences in hyoid excursion were not found (Q6). The C2-4 scalar is readily available and reliably selectable from the radiographic view captured in a standard VF exam. We advocate for clinicians and researchers to adopt the practice of scaling hyoid excursion measures using the C2-4 length to minimize measurement artifacts attributable to participant size, and to control for sex-based differences in participant size. The values in Table 6 can be used as reference values for young healthy participants swallowing ultra-thin liquid barium (22% w/v).

In this study we investigated four methods for capturing hyoid excursion: anterior displacement, superior displacement, hypotenuse displacement and maximum XY position (Figure 2). Three out of four of these methods are displacement measures, that is, they involve calculating a change in position between two frames (rest and peak). Anterior displacement, on the whole, did not yield any significant results in our study. This measure was not significantly correlated with the size-of-the-system (Q3), nor was it sensitive to sex or bolus volume effects (Q4). Further, this measure demonstrated the poorest inter- and intra-rater reliability scores. Superior and hypotenuse displacement measures were both significantly correlated with the size-of-the-system and both demonstrated significant sex effects when there was no control for size-of-the-system in the analysis. Maximum XY hyoid position performed similarly to superior and hypotenuse displacement measures, however, it was the only measurement method that revealed significant associations between hyoid excursion and bolus volume. Interestingly, this parameter also had the highest correlation with participant height.
Perhaps because this measure captures both planes of movement while also excluding the difficult-to-select rest frame, it provides the most accurate method for measuring hyoid excursion.

The findings of this study are restricted to healthy young individuals swallowing controlled, single-sip volumes of ultra-thin liquid barium. The results should not be extended to other textures, barium densities, or swallowing conditions (such as continuous drinking). Future work should focus on quantifying the contributions of size-of-the-system to hyoid excursion variation in healthy aging. This question is particularly pertinent given known age-related changes in intervertebral disk space (Buckwalter 1995, Logemann et al. 2000, Logemann et al. 2002), which may affect the utility of the C2-C4 internal scalar. Furthermore, sarcopenia (i.e., age-related changes in skeletal muscle) also has the potential to impact range of hyoid movement due to suprahyoid muscle atrophy (Robbins et al. 2005). Once scaled reference values for hyoid excursion in healthy aging adults are obtained, they can be used to accurately identify reduced hyoid excursion and to set treatment targets for rehabilitation.

**Conclusion**

Hyoid excursion during swallowing is dependent on a person’s size (size-of-the-system). Taller individuals demonstrate greater superior displacement, hypotenuse displacement and maximal XY position of the hyoid. If measurements do not control for this source of variation, apparent sex differences in hyoid excursion are seen. Using the C2-4 length as an internal anatomical scalar controls for variations in size-of-the-system, and neutralizes these apparent sex differences. Capturing hyoid excursion using the parameter of maximal XY position eliminates measurement error attributable to difficulties with rest frame selection. This parameter is sensitive to variations in hyoid excursion across bolus volume. Further research in healthy aging is required before applying reference values to patient populations.
References


Chapter 5
Variation in Temporal Measures of Swallowing:
Sex and Volume Effects

With kind permission from Springer, this chapter was excerpted in its entirety from the following journal article: Molfenter, S. M., & Steele, C. M. (2012). Variation in temporal measure of swallowing: Sex and Volume Effects. Dysphagia, online first. This article can be found on the publisher’s website at http://link.springer.com/article/10.1007/s00455-012-9437-6 and the copyright permission can be found in Appendix B.

Abstract
Temporal measures of healthy swallowing appear to be variably sensitive to bolus and participant factors based on a recent meta-analysis of studies in the deglutition literature. In this carefully controlled study of healthy young volunteers, balanced for sex and height, we sought to understand the influence of bolus volume and participant sex on the three durations and three intervals most frequently reported in the deglutition literature. Three boluses per target volume (5, 10, and 20 ml) were repeated for each participant (n = 20, 10 male) using a spontaneous swallow paradigm in lateral view videofluoroscopy. None of the temporal durations or intervals was found to be correlated with participant height above an a priori cutoff point of r > 0.3. Further, none of the temporal durations or intervals varied significantly by participant sex. Bolus volume significantly impacted upper esophageal sphincter (UES) opening duration, laryngeal closure duration, the laryngeal closure-to-UES opening interval, and the pharyngeal transit time interval, but not hyoid movement duration or the stage transition duration interval. When participants are sampled in such a manner as to represent the range of height reported to be typical for both sexes in the population, sex does not significantly influence temporal measures of swallowing.

Keywords
Deglutition, Deglutition disorders, Dysphagia, Swallowing, Temporal, Duration, Interval, Sex, Volume, Height
Introduction

The gold standard tool for the assessment and management of dysphagia (swallowing disorders) is the videofluoroscopic (VF) swallowing study, which involves administering food and liquid mixed with a radiopaque contrast agent under fluoroscopy. The VF offers real-time dynamic viewing of swallowing physiology. The pharyngeal phase of swallowing involves a complex sequence of temporal events in a relatively short span of time, which can be broadly grouped into durations (the length of time for a distinct physiological swallow event to occur) and intervals (the length of time between two gestures in the swallow sequence). Aberrant swallow timing in patient populations has been linked to laryngeal penetration and aspiration [1–3].

A recently published study examined the most frequently reported duration and interval measures in the healthy swallowing literature (36 publications) and demonstrated different degrees of variability across temporal measures and variable effects of bolus volume, sex, and age on these measures [4]. Six parameters were chosen for meta-analysis in that study: three durational measures [upper esophageal sphincter (UES) opening duration (UESD), laryngeal closure duration (LCD), and hyoid movement duration (HMD)] and three interval measures [laryngeal closure-to-UES opening (LC-to-UES), pharyngeal transit time (PTT), and stage transition duration (STD)]. Modified forest plots of means with 95% confidence interval error bars were used to compare variability across studies. Trends attributable to factors such as bolus volume and age were noted whenever information was available from the original studies. The authors concluded that a variety of factors play a potential role in contributing to the observed variability in temporal measures of swallowing, including differences across studies in operational definitions, statistical analyses, stimulus factors, participant factors, and procedural factors.

The contribution of bolus volume has been studied extensively in the healthy deglutition literature. Some temporal variables have clear and consistent trends, e.g., UESD which regularly displays longer durations for greater volumes (see, e.g., [5–12]). Other temporal variables such as STD have mixed findings; some studies have reported
longer STD values at larger volumes (see, e.g., [3, 5, 13]), while others have reported shorter durations at larger volumes (see, e.g., [8, 14]) and others still describe mixed findings [15]. A full review of trends by bolus volume for the six temporal measures of interest can be found in the Molfenter and Steele review [4].

The impact of sex on temporal measures of swallowing is unclear in the literature. Some research has demonstrated that sex has no effect (e.g., [15, 16]), while others report that women display longer durations (e.g., [10, 17, 18]). Dantas et al. [18] suggest that longer durations in women are required for safe swallowing because women are smaller than men, arguing that the relative size of the bolus to the individual is larger, therefore requiring longer swallow durations for transit and clearance.

In this study we sought to clarify the true impact of bolus volume and participant sex on timing measures in healthy swallowing using the same six timing parameters reviewed in Molfenter and Steele [4] (Table 1). Our approach was to tightly control other factors recognized as possible contributors to variability in swallow timing, including participant age, sex, and height, the volume and number of boluses administered, and the use of a spontaneous, self-fed (noncommand) paradigm. Our hypothesis was that under these conditions, duration measures (measures of a swallowing event, such as the opening of the UES) would vary significantly with changes in bolus volume because the event would require more time to be completed with larger boluses. Conversely, however, we hypothesized that interval measures of swallow timing (the time lapse between two component events) would not be influenced by bolus volume. Finally, using a sample in which participant height was systematically distributed across ranges typical for both sexes in the broader population, we hypothesized that sex would not significantly impact any temporal measures of swallowing (durations or intervals).
Table 1. Description, abbreviations, and intervals included in this study

<table>
<thead>
<tr>
<th></th>
<th>Timing Variable</th>
<th>Abbreviation</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durations</td>
<td>UES Opening Duration</td>
<td>UESD</td>
<td>UES Closure - UES Opening</td>
</tr>
<tr>
<td></td>
<td>Laryngeal Closure Duration</td>
<td>LCD</td>
<td>Laryngeal Closure - Laryngeal Opening</td>
</tr>
<tr>
<td></td>
<td>Hyoid Movement Duration</td>
<td>HMD</td>
<td>Hyoid Rest - Hyoid Onset</td>
</tr>
<tr>
<td>Intervals</td>
<td>Laryngeal Closure to UES Opening</td>
<td>LC-to-UES</td>
<td>Laryngeal Closure - UES Opening</td>
</tr>
<tr>
<td></td>
<td>Pharyngeal Transit Time</td>
<td>PTT</td>
<td>UES Closure - Bolus Past Mandible</td>
</tr>
<tr>
<td></td>
<td>Stage Transition Duration</td>
<td>STD</td>
<td>Hyoid Onset - Bolus Past Mandible</td>
</tr>
</tbody>
</table>

**Materials and Methods**

**Participants**

Twenty healthy young volunteers (10 male, 10 female) consented to undergo a standardized VF protocol. Exclusion criteria included a history of swallowing difficulty, neurological deficits, head/neck surgery (other than routine dental surgery, tonsillectomy, or adenoidectomy), or possible pregnancy. All participants were under 45 years old, with a mean age of 31.5 years (standard deviation = 5.7 years). Participants were strategically recruited to ensure a distribution of height that spanned both the lower and upper quartiles for nationally reported height by sex [19]. Participant height was measured in centimeters (cm) with the participant’s shoes removed and head in a neutral position using a free-standing stadiometer. Figure 1 demonstrates the distribution of participant height by sex in our sample. The local institutional research ethics board approved this study and written consent was obtained from each participant prior to study participation.

![Fig. 1 Distribution of participants by height and sex](image-url)
VF Stimuli

Each participant performed a total of 16 swallowing tasks. Nine of these swallows per participant are included in the present analysis: three swallows each of 5, 10, and 20 ml of ultrathin liquid barium, a 22 % weight/volume (w/v) suspension [20]. Three repetitions per bolus condition were included in order to sample intrasubject variability adequately while minimizing VF exposure time [16].

Each bolus was presented to the participant in a 30-ml medicine cup. Non-VF pilot testing demonstrated that residual material remained in the cup after each sip. Given that we were particularly interested in bolus volume contributions to temporal measures of swallowing, we devised a system to tightly control bolus volume. First, in order to compensate for expected residue in the cup, we carefully pipetted 1 ml more than the target sip volume into the cup. Second, each cup was weighed before and after each stimulus was swallowed so that the exact volume consumed could be determined. Finally, whenever piecemeal deglutition was observed for a particular stimulus, the corresponding data were excluded from the analysis, given that we could not accurately measure the volume of the portions of the bolus ingested in each subswallow. Across the entire data set of 180 ultrathin liquid swallows, there were seven instances of piecemeal deglutition: one occurrence at 5 ml and six occurrences at 20 ml. However, despite these procedures, the post-swallow cup weights showed that participants swallowed bolus volumes that were smaller than the target volume. For the 5-ml target condition (6 ml in the cup), the average volume consumed was 3.54 ml (95 % CI = 3.42–3.67). For the 10-ml target condition (11 ml in the cup), the average volume consumed was 8.03 ml (95 % CI = 7.78–8.28). Similarly, for the 20-ml target condition (21 ml in the cup), the average volume consumed was 17.34 ml (95 % CI = 16.84–17.85).

VF Procedure

All VFs were completed using a Toshiba Ultimax fluoroscope (Toshiba America Medical Systems, Inc., Tustin, CA) with the participant seated in lateral view. VFs were conducted at full resolution (30 pulses per second) and captured and recorded on a Digital Swallowing Workstation (KayPentax, Lincoln Park, NJ) at 30 frames per second. The
cups containing the stimuli were arranged on a table within easy reach of the participant. Cups were presented in sets of three (of the same condition). The order of bolus volume was randomized by set for the three ultrathin liquid conditions. The fluoroscope was turned on and the participant was instructed to self-feed each three-bolus array of stimuli at a spontaneous, comfortable pace. This method of self-feeding and spontaneous swallows was chosen to promote natural drinking behavior and to avoid differences in swallow timing known to be associated with cued swallowing [21]. The indication for turning off the fluoroscope after the final bolus of each three-swallow sequence was visualization of the hyoid returning to rest. The mean (±SD) radiation exposure time across participants was 1.75 ± 0.31 min.

VF Post-processing and Analysis

Each three-swallow sequence was spliced out of the larger VF recording starting 30 frames before the bolus passed the shadow of the mandible on the initial swallow and finishing 30 frames after the hyoid returned to rest on the third swallow (or when the fluoroscope was turned off, in the event this occurred first). These videoclips were randomized and individually opened in ImageJ (National Institutes of Health, Bethesda, MD) and advanced frame-by-frame to identify the following seven events:

- **Hyoid onset** the first marked upward/forward movement of the hyoid associated with an immediately occurring subsequent swallow.
- **Bolus past mandible** the head of the bolus touching or passing the ramus of the mandible. In the event that the participant was not seated completely upright or perpendicular to the fluoroscopy beam, resulting in a view in which both mandibular rami were visible, the more superior ramus was used as the landmark for defining this event.
- **Laryngeal vestibule closure** the first frame depicting a seal between the posterior surface of the epiglottis and the arytenoids.
- **Laryngeal vestibule opening** the first frame depicting a release of the seal between the posterior surface of the epiglottis and the arytenoids.
- **UES opening** the first frame showing the head of the bolus passing through the UES, represented by the opening of the narrowest region between C4 and C6 [8]
(and confirmed by a visible column of barium in the proximal esophagus on the same or the immediately occurring subsequent frame).

- UES closure the first frame depicting the UES closing behind the tail of the bolus in the region between C4 and C6.
- Hyoid rest the frame depicting the lowest position of the hyoid bone post swallow, with concurrent epiglottic return and pharyngeal relaxation.

These seven frames were used to derive each of the six temporal variables of interest (Table 1). For statistical analyses, all temporal durations and intervals were converted from frames to milliseconds (ms) by dividing the frame measures by 29.97 and multiplying by 1,000. Inter- and intrarater reliabilities were tested for each temporal parameter on a random selection of 10% of the swallows by using two-way mixed intraclass coefficients (ICC) for consistency. Results appear in Table 2.

Intrarater reliability scores ranged from 0.86 to 0.99 and interrater reliability scores ranged from 0.73 to 0.98. We acknowledge that one score, UESD, demonstrated interrater reliability within only the “fair to good” range of 0.40–0.75 [22]. Closer examination revealed an average three-frame discrepancy in defining the UES closure frame between raters. We feel this discrepancy may be related to difficulty visualizing the location of the UES at the height of the swallow in healthy individuals who completely obliterate the pharynx during pharyngeal pressure generation.

Penetration-Aspiration Scale scores [23] were also rated to ensure functional healthy swallowing in this sample. All 180 swallows were rated as scores of 1 (no penetration, 167/180) or 2 (high transient penetration, 13/180), which is consistent with previous reports of healthy populations [24, 25].
Table 2. Descriptive statistics for each of the six temporal variables by bolus volume and inter- and intra-rater reliability ratings

**Statistical Analysis**

All statistical analyses were conducted using IBM SPSS Statistics ver. 20. Two-tailed p-values < 0.05 were considered statistically significant. Pearson’s correlation coefficients (r) were first used to examine the relationship between each of the six temporal variables (ms) and participant height (cm). A priori, it was decided that for variables with r > 0.3, height would be tested as a covariate in subsequent statistical models. Mixed-model repeated-measures analysis of variance (ANOVA) with a between-participant factor of sex and within-participant repeated factor of trial within bolus volume (with or without the height covariate, as explained above) were run in order to
test the influence of bolus volume and participant sex on each of the six dependent variables. When main effects were significant, post hoc pairwise comparisons were conducted with Sidak adjustment for multiple comparisons.

Results

Descriptive statistics for all six temporal variables (three durations and three intervals), separated by bolus volume and sex, appear in Table 2. Given that participant size has been proposed as a factor to explain sex differences in temporal measures of swallowing, the relationship between each temporal measure and participant height was tested. None of the variables demonstrated a correlation above $r > 0.3$ (Table 3). Therefore, height was discounted as a potential influence on swallow timing and height covariates were not included in any of the statistical models for the variables.

<table>
<thead>
<tr>
<th>Timing Variable</th>
<th>Correlation (r) with Height</th>
<th>Significance (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UES Opening Duration</td>
<td>-0.09</td>
<td>0.22</td>
</tr>
<tr>
<td>Laryngeal Closure Duration</td>
<td>-0.17</td>
<td>0.03</td>
</tr>
<tr>
<td>Hyoid Movement Duration</td>
<td>0.20</td>
<td>0.01</td>
</tr>
<tr>
<td>Intervals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laryngeal Closure to UES Opening</td>
<td>0.11</td>
<td>0.16</td>
</tr>
<tr>
<td>Pharyngeal Transit Time</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>Stage Transition Duration</td>
<td>0.07</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Table 3. Pearson’s r correlations between temporal variables and participant height (cm)

Analysis of the contributions of bolus volume and participant sex to UESD revealed a significant main effect for volume [$F(2, 149.42) = 41.306, \ p = 0.000$], while sex and the interaction term were nonsignificant. Post hoc pairwise comparisons are summarized in Fig. 2. Results revealed that UESD increased significantly with larger bolus volumes for all pairwise volume comparisons: 3.54-ml condition (mean = 282.2 ms, SE = 13.6), 8.03-ml condition (mean = 319.8 ms, SE = 13.6), and 17.34-ml condition (mean = 356.8 ms, SE = 13.8).
The investigation of the contributions of bolus volume and participant sex to LCD yielded similar results, with a significant main effect for volume \[ F(2, 149.23) = 17.980, \ p = 0.000 \] but no significant main effect for sex. The interaction term was nonsignificant. Post hoc pairwise comparisons are summarized in Fig. 3 and demonstrated significant differences in LCD for all pairwise volume comparisons, with increasing bolus volume resulting in longer LCD. The mean LCD was 451.7 ms (SE = 26.9) for the 3.54-ml condition, 489.9 ms (SE = 26.9) for the 8.03-ml condition, and 527.7 ms (SE = 27.1) for the 17.34-ml condition.
When the contributions of bolus volume and participant sex to HMD were analyzed, no significant main effects or interactions were found.

Analysis of the contributions of bolus volume and participant sex to the LC-to-UES interval revealed a significant main effect for volume \([F(2, 149.607) = 5.027, p = .008]\), while sex and the interaction term were non-significant. Post-hoc pairwise comparisons are summarized in Fig 4. Results revealed a significantly shorter LC-to-UES interval in the 17.34-ml condition (mean = -5.48 ms, SE = 13.27) compared with both the lower volumes (3.54-ml, mean = 18.81 ms, SE = 13.08 and 8.03-ml, mean = 20.02, SE = 13.05). No significant difference between the 3.54-ml and 8.03-ml condition was found.

Analysis of the contributions of bolus volume and participant sex to the PTT interval revealed a significant main effect for volume \([F(2, 149.596) = 4.690, p = 0.011]\), while sex and the interaction term were nonsignificant. Post hoc pairwise comparisons are summarized in Fig 5. Results revealed a significantly longer PTT interval in the 17.34-ml condition (mean = 527.71 ms, SE = 27.68) than in the 3.54-ml condition (mean = 470.95 ms, SE = 27.26). No significant differences were revealed between the intermediate volumes.

Fig. 4 Post-hoc pairwise comparisons of Laryngeal Closure-to-UES Opening Duration (ms) and 95 % CI by bolus volume (ml) and by participant sex. n.s. not significant
When the contributions of bolus volume and participant sex to the STD interval were analyzed, no significant main effects or interactions were found.

In summary, none of the six parameters of interest demonstrated a sex effect, while four of six variables (UESD, LCD, LC-to-UES, and PTT) demonstrated significant sensitivity to bolus volume.

**Discussion**

In the current study, we sought to understand the contributions of bolus volume and participant sex to the most frequently reported duration and interval measures of swallow timing in the healthy deglutition literature. Our sample of young, healthy participants was recruited to systematically span a population-representative range of heights in both men and women. Importantly, height for the tallest women in this sample overlaps with height for the shortest men, thus creating a sample where height does not automatically distinguish the sex groups (Fig. 1). We have demonstrated for the first time that the durational and interval measures analyzed in this study do not vary according to participant height (as measured by correlations that failed to reach a conservative criterion of > 0.3). Further, we have demonstrated that when height is distributed across population-appropriate ranges for both sexes, sex does not appear to influence temporal
We hypothesized that bolus volume would significantly impact all three duration measures of swallowing. In fact, we observed that volume significantly impacted only two of the three duration measures explored in our study: UESD and LCD. For these durations, larger bolus volumes resulted in a longer opening of the UES and longer closure of the laryngeal vestibule. We were surprised to learn that HMD did not differ by bolus volume given that previous literature has demonstrated that hyoid excursion does vary by bolus volume [11, 26–28]. One possible explanation for this is that duration of movement (in ms) does not adequately capture the complex dimensions of a swallow. For example, it may be that differences in hyoid bone movement velocity (distance over time) will explain differences peak position across bolus volumes while durations do not.

We hypothesized that bolus volume would not impact interval measures of swallow timing, but we learned that two of our three intervals (LC-to-UES and PTT) were significantly influenced by main effects of volume. Larger bolus volumes caused shorter temporal intervals between the closing of the laryngeal vestibule and the opening of the UES and longer temporal intervals between the bolus passing the ramus of the mandible and the closing of the UES (though these trends were not consistently significant between each level of volume comparison). This finding is consistent with trends reported in the literature for these two variables [4]. We were especially surprised by this finding for the LC-to-UES interval given the close temporal proximity of the two swallow gestures comprising the LC-to-UES interval and its tight confidence intervals in a previously published meta-analysis [4]. PTT, on the other hand, is an interval for which the influence of bolus volume is less surprising, given that the UES opening duration (inherently tied to this interval by its offset) has repeatedly been shown to be sensitive to bolus volume. STD is thought to represent the trigger of the pharyngeal swallow in response to arrival of the head of the bolus in the upper pharynx. It is therefore logical that this triggering does not depend on the size of the bolus.

We would like to point out that the investigations in this study were limited to measures of swallowing (durations or intervals).
temporal measures for ultrathin liquid swallowing in healthy young individuals. Importantly, this work needs to be expanded to older age groups, given the known impact of advancing age on temporal measures of swallowing [11, 17]. Logemann [11] has suggested that women have a protective “flexibility” in the oropharyngeal swallow mechanism that allows them to better compensate for aging than men. An important component of future work in healthy older adults will be to determine the sensitivity of temporal durations and intervals to aging and to ensure appropriate representation of typical population heights (as we have done here) so that participant height can be teased apart from sex as an influence on timing measures. Further, future work should focus on the relationship between various temporal durations and intervals and penetration/aspiration. Once these relationships have been tested across a variety of age spans, normative references can be established for the purpose of comparison for patient populations and to serve as treatment targets and for outcome measurement.

**Conclusion**

In this height-distributed sample of healthy young adults who swallowed three repeated boluses each of three target volumes of ultrathin liquid barium (22 % w/v), participant sex did not impact swallowing durations or intervals. Bolus volume significantly impacted UES opening duration, laryngeal closure duration, the laryngeal closure-to-UES opening interval, and the pharyngeal transit time interval. Neither hyoid movement duration nor the stage transition duration interval was influenced by bolus volume. Future work in height-representative samples of older adults is warranted.
References


Chapter 6
Comparisons of kinematic and temporal measures of deglutition by swallow profile: Functional versus impaired swallows in patients referred for videofluoroscopy

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Abstract
In this study, we undertook careful analysis of seven quantitative physiological variables related to oropharyngeal swallowing from a sample of 23 subacute patients referred for dysphagia assessment. Each patient underwent two videofluoroscopic swallowing examinations, from which we analyzed total of 111 swallows of 22% w/v ultra-thin liquid barium suspension. Our goal was to determine whether scores on any of the seven variables of interest were independently associated with the presence of functional swallowing impairment on the same swallow. Swallowing impairment was defined either as a penetration-aspiration scale score ≥ 3 and/or post-swallow pharyngeal residue judged perceptually to be filling ≥25% of the available space in the valleculae or piriform sinuses. The physiological variables of interest included: one kinematic measure (maximal hyoid position); three swallow duration measures (laryngeal closure duration, hyoid movement duration, upper esophageal sphincter (UES) opening duration); and three swallow interval measures (laryngeal closure to UES opening, stage transition duration, pharyngeal transit time). Mixed model repeated measures ANOVAs were conducted to determine the association between each parameter and swallow function, while controlling for participant sex, video order, and bolus-order-within-video. None of the seven physiological variables showed a statistically significant independent association with swallow function or sex. One variable, UES opening duration, demonstrated significantly shorter durations in the initial video and in the first bolus
administered (compared with the third). Wide confidence intervals, despite careful and reliable methodology, suggest inherent variability in physiological measures of swallowing. Limitations and future considerations are discussed.

**Keywords**
deglutition, deglutition disorders, dysphagia, swallowing, impairment, kinematic, temporal, variability

**Introduction**
Videofluoroscopy (VF) allows direct and dynamic visualization of swallowing physiology. This radiographic procedure, combined with a standard protocol, is widely used to determine patient safety for oral intake, candidacy for swallowing treatment, and treatment outcome. Several types of physiological measures can be extracted from the VF including kinematic measures of structural displacement, temporal durations (i.e., the time required for a distinct physiological event to occur) and interval measures (i.e., the time lapse between two gestures in the swallow sequence) [1]. In addition, ratings of swallowing safety and efficiency can be made to capture a patient’s functional swallowing status. The combined results of the VF exam have the potential to greatly impact a patient’s medical management and quality of life. Unfortunately, because the VF exam requires radiation exposure, it must be restricted in duration and frequency. It is therefore important to understand the sensitivity of the various possible physiological measures to swallowing impairment, and to determine whether boundary values for these measures can be identified and validated with respect to their ability to dissociate functional from impaired swallowing. Previous work has reported mixed findings for associations between physiological measures of swallowing and impairment. For example, one study demonstrates that aspirators have significantly decreased hyoid excursion compared to non-aspirators [2] while another study does not [3]. Some timing variables have been shown to differentiate patients who aspirate from those who do not, such as the initiation of laryngeal closure, stage transition duration and pharyngeal transit time [2,4-6]; other timing measures, such as laryngeal closure duration, have been reported to not dissociate aspirators from non-aspirators [5,6]. The clear
delineation of boundary values in specific physiological parameters of swallowing that characterize impairment is challenged by the fact that studies of healthy deglutition report wide ranges and considerable variability in both kinematic and temporal measures of swallowing [1,7].

In this manuscript, we explore seven selected quantitative measures of swallowing physiology, to determine whether scores on any of these measures independently dissociate functional from impaired swallowing. Using a sample of ultra-thin liquid swallows collected from subacute hospital patients referred for videofluoroscopy, we operationally defined swallowing impairment in terms of swallowing safety (i.e., penetration-aspiration scale scores ≥ 3) and/or efficiency (residues in either the valleculae and/or piriform sinuses judged perceptually to occupy ≥ 25% of the available space). The physiological variables of interest included: one kinematic measure (maximal hyoid position); three swallow duration measures (laryngeal closure duration, hyoid movement duration, upper esophageal sphincter (UES) opening duration); and three swallow interval measures (laryngeal closure to UES opening, stage transition duration, pharyngeal transit time). In addition to investigating the independent association between each of these dependent variables and swallow function, we were also interested to determine whether these parameters varied according to participant sex, video order (for repeated videos) and the bolus-order-within-video. Our hypothesis was that impaired swallows would show reduced kinematic movement, slower durations and longer intervals. Physiological variables that are shown to distinguish functional from impaired swallowing can be recommended for routine measurement during the analysis of standardized clinical VF assessments and can be explored further in terms of validity for determining the severity of dysphagia.

**Materials and Methods**

**Participants**

The swallows analyzed for this study come from a retrospective dataset of VF exam recordings collected from subacute patients who were referred for more than one VF between 2007-2010. The goal in extracting these studies was to document variability
and change in swallowing across repeated VF exams. For the present analysis, two VFs were extracted from each of 23 participants (16 male) resulting in a dataset of 46 videofluoroscopy recordings. For 18/23 participants, the two VFs were performed within an average time lag of 60 ± 29 days (mean ± standard deviation). The five remaining participants were followed as outpatients for more chronic dysphagia. The time between the two videos selected from these individuals ranged from 12-27 months. While the exact etiology of each patient’s medical condition was not captured in this retrospective study, the majority of patients were referred from stroke, acquired brain injury or geriatric rehabilitation units. The chronological order of the videos administered for each participant was documented as an independent variable (‘video order’). On average, male participants were 62.4 ± 15.9 years old and female participants were 55.7 ± 19.0 years old.

VF Procedure

All VF exams were conducted using a Toshiba Ultimax (Toshiba America Medical Systems, Inc., Tustin, CA) fluoroscope in lateral view at 30 pulses per second, and were captured and recorded at 30 frames per second. A standard recipe was used to prepare 22% w/v barium suspension (Bracco Polibar suspension diluted with water), which was used as the stimulus for all liquid swallows extracted for this analysis. This concentration of barium has previously been labeled “ultra-thin” in the literature [8].

VF Post-processing and Analysis

Bolus clips for all ultra-thin liquid swallows were spliced out of the larger VF recordings starting 30 frames before the bolus passed the shadow of the mandible and finishing 30 frames after the hyoid returned to rest (or when the fluoroscopy was turned off, in the event this occurred first). The order of the boluses within each video was documented as an independent variable (‘bolus-order-within-video’) and the first three qualifying ultra-thin liquid bolus clips from each VF were selected for analysis. Information regarding the exact volume of the boluses administered was regrettably not available (given that this was a retrospective secondary analysis of a clinical dataset), and therefore could not be included as a variable in our analysis. Nevertheless, qualifying
boluses were limited to those administered using a standard 5ml teaspoon, meaning that all boluses in this study were \( \leq 5 \text{ml} \) in volume. All instances of piecemeal deglutition (a single bolus partitioned in the oral cavity into multiple swallows) were excluded. This resulted in a complete dataset of \( n = 111 \leq 5 \text{ml} \) ultra-thin bolus clips for analysis, including not fewer than two bolus clips per VF, and not fewer than four bolus clips per participant. These clips were randomized and individually analyzed for the physiological and functional parameters of interest. Where a series of multiple swallows was employed to clear a single bolus (i.e., the entire bolus was swallowed from the oral cavity, with one or more subsequent clearing swallows), only the initial swallow in the series for that bolus was analyzed. The following parameters were measured:

1. Hyoid Kinematics
Maximal hyoid position was extracted according to procedures reported in detail elsewhere [9] and summarized here. The positions of the following structures were marked in each frame with a movement-tracking software program: a) the anterior inferior corner of the C4 vertebra (origin); b) the anterior inferior corner of the C2 vertebra (Y vector); and c) the anterior inferior corner of the hyoid. All three of these points were measured in a Cartesian coordinate system with the Y-axis defined by the line running through the origin and the Y-Vector, and the X-axis defined perpendicular to this line. The position of the hyoid in each frame was calculated based on its XY position relative to the origin (C4) within these participant-defined Cartesian coordinates. The positional data were scaled in cervical units (% C2-4 distance) to control for magnification artifact and differences in size-of-the-system across participants. All measures were exported to a Microsoft Excel file with an embedded macro which identified the maximum and minimum hyoid position values (in both the X and Y planes) between two user-defined boundary frames of interest (‘start’ and ‘end’). The ‘start’ frame was designated as 10 frames prior to hyoid movement onset and the ‘end’ frame was designated as 10 frames after the epiglottis returned to a vertical position. Between these boundary frames and using these positional data, maximum XY position of the hyoid, i.e., its destination relative to C4, was calculated in anatomically scaled units (See Figure 1).
2. Timing measures

Video clips were opened in ImageJ (National Institutes of Health, Bethesda, MD) and advanced frame-by-frame to identify the frames associated with seven specific timing events within each swallow: hyoid movement onset, bolus passing mandible, laryngeal vestibule closure, laryngeal vestibule opening, UES opening, UES closure, and hyoid rest. Operational definitions for finding each frame have been reported elsewhere [1]. These seven frames were used to derive each of the six temporal variables of interest:

Durations:

- Laryngeal Closure Duration (LCD) = laryngeal vestibule closure minus laryngeal vestibule opening
- Hyoid Movement Duration (HMD) = hyoid rest minus hyoid movement onset
- UES Opening Duration (UESD) = UES closure minus UES opening
Intervals:

- Laryngeal Closure to UES opening (LC-to-UES) = laryngeal vestibule closure minus UES opening
- Pharyngeal Transit Time (PTT) = UES closure minus bolus passing mandible
- Stage Transition Duration (STD) = hyoid movement onset minus bolus passing mandible

Prior to statistical analysis, the unit for all temporal durations and intervals was converted from frames to milliseconds (ms) by dividing the frame measures by 29.97 and multiplying by 1000.

3. Functional measures

Each swallow was also rated on functional measures of impairment. Swallowing safety was measured using the 8-point Penetration-Aspiration Scale [10] which captures the depth of and response to airway invasion. Swallowing efficiency was measured using a four-point ordinal rating scale for residue in both the valleculae and the piriform sinuses, previously described by Eisenhuber and colleagues [11]. In this scale, a score of 0 corresponds to no residue, 1 is considered ‘mild’ where the level of contrast material constitutes less than 25% of the height of the structure, 2 is considered ‘moderate’ where the level of contrast material is between 25 and 50% of the height of the structure, and 3 is considered ‘severe’ where the level of barium is greater than 50% of the height of the structure. All residue ratings were taken using the frame depicting hyoid rest. Scores of 0 and 1 were considered functional, while scores of 2 or greater were considered to be inefficient. Based on these ratings for each swallow, that swallow was designated as either ‘functional’ or ‘impaired’. A swallow with PAS ≤ 2 and with any residue ≤1 was categorized as ‘functional’ [12-14]. A swallow was categorized as ‘impaired’ if it displayed PAS ≥ 3 (safety concern) and/or residue in one or both locations ≥2 (efficiency concern). In total, 58 swallows from this clinical dataset were categorized as impaired, while 53 were found to be both safe and efficient, despite being collected from patients undergoing VF assessment for dysphagia. A specific breakdown of the frequency of the different types of functional impairment seen in this dataset can be found in Figure 2.
Reliability

All physiological measurements were conducted by a research assistant who was trained using a set of training swallow recordings to a level of excellent agreement with an experienced, certified speech-language pathologist (first author). Ten percent of swallows were chosen at random and re-rated for all parameters by the original rater (intra-rater agreement) as well as by the first author (inter-rater agreement). All ratings of swallowing function vs. impairment were made by the first author with 10 percent of the measures repeated for intra-rater reliability, while inter-rater reliability measures were made by a second experienced and certified speech-language pathologist. Reliability was measured using two-way mixed intra-class coefficients (ICC) for consistency. Results appear in Table 1. Intra-rater reliability scores ranged from 0.88 to 0.98 and inter-rater reliability scores ranged from 0.70 to 1.00. Most parameters demonstrated ‘excellent’ reliability, while inter-rater scores for two parameters (UESD and Piriform Sinus Residue) reached the high end of the ‘fair to good’ range (i.e., 0.40-0.75) [15].

Figure 2. Breakdown of swallow function by safety and efficiency.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Inter-rater</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max XY position of the hyoid (%C2-4)</td>
<td>Inter-rater 0.97</td>
<td>(0.94-0.99)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.98</td>
<td>(0.94-0.99)</td>
</tr>
<tr>
<td>LCD (ms)</td>
<td>Inter-rater 0.93</td>
<td>(0.82-0.97)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.98</td>
<td>(0.96-0.99)</td>
</tr>
<tr>
<td>UESD (ms)</td>
<td>Inter-rater 0.74</td>
<td>(0.38-0.89)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.89</td>
<td>(0.73-0.95)</td>
</tr>
<tr>
<td>HMD (ms)</td>
<td>Inter-rater 0.81</td>
<td>(0.55-0.92)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.88</td>
<td>(0.71-0.95)</td>
</tr>
<tr>
<td>LC-to-UES (ms)</td>
<td>Inter-rater 0.93</td>
<td>(0.83-0.97)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.89</td>
<td>(0.74-0.96)</td>
</tr>
<tr>
<td>PTT (ms)</td>
<td>Inter-rater 1.00</td>
<td>(0.99-1.00)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.98</td>
<td>(0.96-0.99)</td>
</tr>
<tr>
<td>STD (ms)</td>
<td>Inter-rater 1.00</td>
<td>(0.99-1.00)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.98</td>
<td>(0.95-0.99)</td>
</tr>
<tr>
<td>Vallecular Residue</td>
<td>Inter-rater 0.78</td>
<td>(0.45-0.91)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.93</td>
<td>(0.84-0.97)</td>
</tr>
<tr>
<td>Piriform Sinus Residue</td>
<td>Inter-rater 0.70</td>
<td>(0.26-0.88)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.97</td>
<td>(0.93-0.99)</td>
</tr>
<tr>
<td>Penetration-Aspiration Score</td>
<td>Inter-rater 0.91</td>
<td>(0.77-0.96)</td>
</tr>
<tr>
<td></td>
<td>Intra-rater 0.96</td>
<td>(0.91-0.99)</td>
</tr>
</tbody>
</table>

Table 1. Reliability results for all parameters in the VF_VAR dataset.

**Statistical Analyses**

All statistical analyses were conducted using IBM SPSS Statistics Version 20. Two-tailed p-values < 0.05 were considered statistically significant. For each of the 7 physiological parameters (dependent variables), a stepwise process was used to explore statistically significant differences, using mixed-model repeated measures analyses of variance (ANOVA). This process began at the level of the full model, with a between participant factor of sex, within participant factors of video order (1st, 2nd) and bolus-
order-within-video (1, 2 or 3), and a nested factor of swallow function (functional, impaired) within bolus-order-within-video. The model accounted for repeated measures at the level of bolus-order-within-video X video order. When significant effects for these factors were not found at the level of the full model, the statistical model was simplified in the following sequence: first removing video order; then sex; and finally, the repeated measures factor (resulting in a univariate analysis of swallow function across the entire pooled dataset). When main effects were significant, post hoc pairwise comparisons were conducted with Sidak adjustment for multiple comparisons. Effect sizes for pairwise comparisons were calculated using Cohen’s $d$ [16]; according to this measure, values of 0.2-0.5 can be considered to show small effects, 0.5-0.8 show medium effects and values $> 0.8$ show large effects. Additionally, visual inspection of trends in estimated marginal means was used to confirm whether separation of parameter values between functional and impaired swallows appeared to warrant further investigation using effect size calculations, even when statistical significance was not demonstrated in the ANOVA models.

Results

Table 2 details the descriptive statistics (using estimated marginal means) of the 7 parameters of interest in this study. Detailed results for ANOVA analyses follow.

Kinematic Variable

Max XY Hyoid Position. When the associations between the independent variables (swallow profile, participant sex, video order and bolus-order-within-video) and maximum hyoid position were analyzed, no significant main effects or interactions were found.
<table>
<thead>
<tr>
<th>Kinematics</th>
<th>Mean</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max XY Position (% C2-4)</td>
<td>Functional</td>
<td>147.4</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>152.7</td>
</tr>
<tr>
<td>LCD (ms)</td>
<td>Functional</td>
<td>574.5</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>530.2</td>
</tr>
<tr>
<td>UESD (ms)</td>
<td>Functional</td>
<td>372.6</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>368.1</td>
</tr>
<tr>
<td>HMD (ms)</td>
<td>Functional</td>
<td>1704.3</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>1670.6</td>
</tr>
<tr>
<td>Durations</td>
<td>Mean</td>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>--------------</td>
<td>------</td>
<td>------------------------</td>
</tr>
<tr>
<td>LC-to-UES (ms)</td>
<td>Functional</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>3.2</td>
</tr>
<tr>
<td>PTT (ms)</td>
<td>Functional</td>
<td>971.7</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>1479.2</td>
</tr>
<tr>
<td>STD (ms)</td>
<td>Functional</td>
<td>374.2</td>
</tr>
<tr>
<td></td>
<td>Impaired</td>
<td>709.5</td>
</tr>
</tbody>
</table>

Table 2. Descriptive statistics for hyoid and timing parameters by swallow function.

**Durations**

When the associations between swallow profile, participant sex, video order and bolus-order-within-video for the LCD and HMD parameters were analyzed, no significant main effects or interactions were found. However, for UESD, the analyses revealed significant main effects of video order $F(1, 79.685) = 9.052, p = .004, d = 0.47$ and bolus-order-within-video $F(1, 78.866) = 5.589, p = .005, d = 0.68$, while swallow function and sex effects were non-significant. Post-hoc pairwise comparisons for video order revealed that UESD was significantly shorter in the first video (mean: 327.6 ms, SE: 31.6) compared with the second video (mean: 413.1 ms, SE: 30.3). Further, post-hoc pairwise comparisons for bolus-order-within-video revealed that UESD was significantly shorter for the first bolus (mean: 312.2 ms, SE: 31.0) compared with the third bolus (mean: 436.2 ms, SE: 39.6) but not between the first and the second bolus or between the second and third bolus within a video.
**Intervals**

When the contributions of swallow function, participant sex, video order and bolus-order-within-video factors to swallow interval measures were analyzed (LC-to-UES, PTT, STD), no significant main effects or interactions were found. However, based on inspection of the estimated marginal means (Table 2), it was determined that the apparent separation of both the PTT and the STD parameters between functional and impaired swallows warranted further investigation using effect size calculations despite the absence of significant main effects of swallow function in the ANOVA models. Small effect sizes were found to differentiate functional from impaired swallows for both PTT ($d=0.39$) and STD ($d=0.24$).

Recognizing that grouping both types of impairment (safety; efficiency) together might obscure a finding, we also conducted post-hoc analyses using the same statistical models but replacing the swallow function variable (functional vs impaired) first with a binary aspiration parameter (PAS ≤2 vs ≥3) and then with a binary residue parameter (Eisenhuber ≤1 vs ≥2). Changing the metric of impairment did not alter the results. No statistically significant relationships between the presence of aspiration or residue were found for any of the seven physiological variables analyzed.

**Discussion**

Using mixed-model repeated measures ANOVAs, we explored whether quantitative measurements for seven physiological swallowing parameters (kinematic and temporal durations and intervals) differ according to swallow function (functional vs. impaired) on ultra-thin liquid swallows. These explorations were performed using a clinical dataset of videofluoroscopy recordings from 23 subacute patients with neurogenic dysphagia, and controlled for the effects of sex, video order, and bolus-order-within-video. We hypothesized that impaired swallows would be associated with less kinematic movement, shorter durations, and longer intervals. We were surprised to find no independent main effects differentiating swallow function from impairment for any of the seven physiological parameters studied, with impairment operationally defined as the
presence of significant penetration-aspiration (PAS ≥ 3) and/or significant residue (Eisenhuber scores ≥2).

Previous studies have looked for associations between the occurrence of aspiration and other physiological abnormalities in swallowing, and have generated mixed findings. With respect to kinematic measures of hyoid movement, Kim and McCullough found no significant group differences in measures of anterior and superior hyoid displacement between aspirators and non-aspirators [3], consistent with our results. Conversely, Bingjie and colleagues demonstrated significantly reduced superior but not anterior hyoid displacement in aspirators compared with non-aspirators [2]. Neither of these prior studies utilized scaling to account for artifacts attributable to variation in participant size in their measures of hyoid displacement [9]. It should also be noted that the lack of sex differences in both kinematic and temporal variables in the current study is consistent with previous work in healthy height/size-normalized volunteers [1,9] and provides support for the idea that apparent sex differences in physiological measures of swallowing may in fact be related to participant size.

With respect to timing measures, previous studies have reported significantly longer PTT intervals [2,6] and longer STD intervals [4] in aspirators compared with non-aspirators. While we did not find statistically significant differences in PTT and STD intervals by swallow function, our data do reveal apparent trends for longer STD and PTT intervals (with weak effect sizes) in impaired swallows. This finding supports the need to include these variables in future studies with larger sample sizes and increased statistical power. Our findings for LCD are consistent with previous work showing no statistically significant difference between aspirators and non-aspirators [5,6]. With the exception of the UESD parameter, we did not find significant differences explained by video order or bolus-order-within-video for any of the physiological variables studied. UESD was shorter in the first video compared with the second video. One possible explanation for this result is the fact that our dataset reflects progression of swallow function across two successive videos in time within each participant, and may therefore include evidence of spontaneous recovery and/or intervention effects in the
second VF. UESD was also significantly shorter in the first bolus compared to the third bolus administered within the same VF exam. Given that this dataset lacked precise volumetric control (≤5ml), we speculate that clinicians may have tended to conservatively provide their patients with a smaller volume of liquid via teaspoon on the initial bolus compared to the third bolus. This might explain the observed bolus-order-within-video effect for the UESD variable, given that the literature suggests that UESD is highly constrained by bolus volume (longer opening for larger boluses) [17-24].

The wide confidence intervals in Table 2 (especially for HMD, STD and PTT) illustrate considerable variation in these parameters despite the strict methodological controls that were employed in this study. This variability should be carefully considered by clinicians and researchers alike. We must remember that the VF exam provides only a brief ‘snapshot’ view of swallowing function and that inherent variability in swallowing physiology can threaten our ability to capture representative swallowing function to support clinical decision making. This limitation must also be considered for research design and outcomes involving VF measures. Based on the results of this study, we concur with the suggestion made by Lof and Robbins [25] that at least three swallows per bolus condition should be sampled during VF to adequately sample swallow-to-swallow variability and capture representative swallow function while keeping radiation exposure to a reasonable level.

In this analysis, we chose to analyze the association between physiological parameters and swallow performance at the level of the swallow (not at the level of the patient participant). Previous work primarily categorizes aspiration (impairment) at the participant-level, however other options include summing performance across one consistency, or across a single bolus (taking multiple swallows into account). Unfortunately, for the most part, the literature fails to provide clear operational definitions for impairment, for example, does aspiration on one swallow in a protocol deem a patient an aspirator? At least one approach described in the literature adopts the perspective that a patient’s impairment status should be based on the worst performance seen across a standard set of swallowing challenges [26]. Another study has demonstrated that defining impairment using a set of four swallows (two thin liquid and two spoon-
thick liquid) results in a less severe picture of dysphagia, than when the entire VF sequence is analyzed [27]. Continued exploration is required to determine which level (swallow, bolus, consistency, or participant) is the most appropriate for capturing swallowing impairment.

Clinicians have long been taught to examine/explore the physiological reasons that may contribute to the functional impairments they observe on VF. The results of this study appear to challenge the notion that a direct relationship between specific physiological parameters and impairment can be posited (at least for this particular group of patients when swallowing ≤5ml boluses of ultra-thin liquid). The act of swallowing is recognized as a complex, dynamic sequence of events [28,29]. Testing linear, unidirectional relationships between single parameters and impairment may very well under-represent the complexity of deglutition.

There are several limitations to acknowledge in the present study. The findings of this analysis are restricted to ≤ 5ml ultra-thin liquid (22% w/v) boluses. Although this is, to our knowledge, the first study to explore quantitative measures of swallowing impairment using this stimulus, the results should not be extrapolated to other volumes, textures and barium concentrations. Further, bolus volume was unfortunately not strictly controlled in this retrospective dataset. However, by restricting the boluses to teaspoon-administered amounts we are confident that all boluses are ≤ 5ml thus minimizing the impact of this potential source of error. Cued swallows are known to shorten swallow durations (such as STD) when compared with uncued swallows [30]. Unfortunately, swallow cueing status was not captured for this retrospective dataset. Further, we chose to define impairment as swallows with PAS ≥3 and/or residue ≥ 2. Although the frequency distribution of swallow function ratings in our sample provided a reasonable balance between impaired and functional examples, it is possible that operationalizing ‘impairment’ at different cut-points might yield different results. Finally, given that our inclusion criteria included patients who received more than one VF, the sample may be biased towards a more severe population than patients who would typically only need or receive a single VF. Future work should employ an age-balanced sample that focuses on
a wider range of volumes, textures and barium densities in patients who receive any number of VF examinations with adequate control of cueing and bolus volume.

**Conclusions**

None of the seven physiological variables that we tested showed significant independent associations with swallowing impairment in this sample of ≤5ml ultra-thin liquid swallows, though a trend towards longer STD and PTT was observed in impaired swallows. Further, none of the parameters studied differed significantly between the male and female participants in the study. UES opening duration was found to be shorter in initial videos and initial swallows. Wide confidence intervals, despite careful and reliable methodology, suggest inherent variability in physiological measures of swallowing. The results challenge the notion that clinicians can identify (and treat) a single underlying physiological cause associated with functional swallowing impairment.

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References


Chapter 7
Summary of Contributions and Future Directions

Dissertation Summary

In 2008, as a clinician working on a tongue strengthening treatment outcomes study, I was shocked to learn that our carefully controlled pre- and post-treatment videofluoroscopic (VF) swallowing analyses did not demonstrate statistically significant improvements on parameters extracted from the VF, even though I had perceived there to be clinically-significant changes in patient performance (Molfenter et al., 2009). This apparent disparity in results provided the initial motivation for me to focus my doctoral studies on a project that would help clinicians and researchers to better understand the representativeness of swallows collected using VF. How confident can a clinician be that the swallows they observe in the VF suite exemplify overall patient function in an accurate manner? How does a researcher know that the swallows they have sampled in their VF research protocols are representative of a participant’s swallowing? Ultimately, a better understanding of the variation of swallowing physiology on VF has the potential to impact both patient care and research design.

This dissertation was carried out in three phases. First, it was important to investigate the previous literature, to determine what has been documented to be ‘normal’ variation in healthy individuals. I conducted two narrative literature reviews to capture the spread of ‘normative’ values reported for kinematic variables (Chapter 2) and temporal variables (Chapter 3) of swallowing in healthy participants. The observed variation across studies was surprisingly high. It was evident that significant gaps existed regarding variation in healthy swallowing in the deglutition literature. This motivated the second phase of this dissertation, namely the collection swallowing data using a highly-controlled VF protocol from healthy young individuals, in a sample deliberately recruited to ensure a population-representative distribution of height for both sexes. Expected stimulus, procedural and participant sources of variation were controlled to the greatest extent possible. This dataset was used to perform in-depth analyses of hyoid excursion (Chapter 4) and temporal measures of swallowing (Chapter 5). In the final phase of this
dissertation, these same kinematic and temporal parameters were used to characterize swallowing from a sample of patients referred for VF (Chapter 6) to examine the independent association of these variables with swallowing impairment.

Summary of Unique Contributions

Taken together, the results of this dissertation research offer several novel insights for the dysphagia community. Each contribution and its potential impact is discussed below.

Inherent Variation in Swallowing Physiology

At every stage of this dissertation, the available evidence demonstrates that variation in swallowing physiology exists. At a broad level, the literature reviews in Chapters 2 and 3 demonstrated wide ranges of ‘normative’ values across studies. In the analysis of swallowing from patients referred for VF, we observed remarkably wide confidence intervals for several variables; for example, the 95% confidence interval for pharyngeal transit time ranged from 1108 ms to 1851 ms (Chapter 6, Table 2, page 105). Even in the analyses of the healthy dataset in Chapters 4 and 5, one can appreciate considerable variability in the confidence intervals for some parameters, such as hyoid excursion (Chapter 4, Table 6, page 70) and hyoid movement duration (Chapter 5, Table 2 page 85). This variability is evident in the context of strict control for as many potential sources of variation as possible (e.g., bolus volume; participant sex; age; the use of non-cued and self-administered swallows; representative height sampling; size-normalization in measurement; random task order; and three repetitions per condition). These data demonstrate the existence of inherent variability in swallowing physiology. It is important to note that one variable, the interval between the onset of laryngeal closure and the onset UES opening (LC-to-UES), appears to demonstrate less variation than other measures; this observation was upheld in all three phases of the dissertation research (literature reviews, healthy swallowing analysis, and disordered swallowing analysis). Beyond this one exception, there appears to be some degree of underlying, healthy functional variation in most physiological parameters of deglutition. This conclusion has the potential to impact and inform the way that clinicians and researchers design their VF
protocols. For example, the evidence from our studies that variation can be expected across repeated swallows of the same bolus volume within an individual supports an early and insightful recommendation made by Lof and Robbins (1990) that clinicians should sample at least 3 swallows per bolus condition inVF, in order to capture representative swallowing function, while minimizing the influence of inherent variability.

Hyoid Excursion is Dependent on the Size-of-the-System

Another contribution of this dissertation is the novel demonstration that hyoid excursion is dependent on the size of the participant (Chapter 4). That is, larger people can and should be expected to display a greater extent of hyoid movement. Further, in Chapter 4, it is shown that when the size-of-the-system is not taken into consideration, significant differences in hyoid excursion are apparent by sex (men display greater excursion than women, consistent with previous literature). When the size-of-the-system is taken into account, these differences between men and women vanish, demonstrating that sex differences are actually better understood as size differences. I have proposed a novel, accessible and reliable method for scaling VF measures of hyoid excursion to spine length (C2-4 distance) to control for this size-based variation. This contribution will impact future research by providing a method to limit artifact in measures of hyoid excursion attributable to the size-of-the-system. Further, the use of an internal anatomical scalar eliminates the need for the planned use of external scalars and allows post-hoc VF measures of hyoid excursion to be collected accurately.

Lack of Sex Effects for All Physiological Variables

A consistent finding across the various phases of this dissertation is the lack of any evidence of significant differences in swallowing between men and women. This conclusion is supported by the data when strict methodological procedures are employed and when size-of-the-system is taken into account, and holds for all of the physiological variables tested (kinematic and temporal). This finding was true both for healthy participants, and for patients referred for VF assessment. This is a substantial and novel
contribution to the literature; men and women do not swallow differently when other sources of variation are controlled.

*Volume Effects Depend on the Physiological Variable*

In contrast to the previous finding, of similar swallowing physiology between men and women, certain parameters displayed variation as a function of bolus volume. For example, when hyoid excursion is scaled to the size-of-the-system and captured using maximum XY position, it is sensitive to differences in bolus volume. This sensitivity to volume influences is, however, not evident when hyoid excursion is captured as a superior or hypotenuse displacement measure. Two out of three of the duration measures and two out of three of the interval measures explored in this dissertation showed main effects of volume: UES opening duration, laryngeal closure duration, LC-to-UES opening interval and pharyngeal transit time. However, hyoid movement duration and stage transition duration were found to be stable across the bolus volumes explored in Chapters 4 and 5. Table 1 (below) summarizes which variables appear to be sensitive to bolus volume in my analyses. This contribution has the potential to influence the design of future studies, given that some variables do not appear to be sensitive to volumetric differences.

In addition, it is worth pointing out two interesting observations regarding bolus volume from my analyses of healthy swallowing. First, despite adding 1ml extra liquid to each target volume to accommodate for expected bolus loss attributable to material being left behind in the cup, my method of weighing each cup before and after swallowing demonstrated that participants still drank less than the target volume (Chapter 4, Table 1, page 62). Second, when the main effects of volume are closely inspected, in all but two cases, the post-hoc pairwise comparisons reveal significant differences between 5ml and 20ml or 10ml and 20ml target volumes but not between 5ml and 10ml target volumes. It may be the case than bolus volume differences greater than 5ml are required to elicit robust changes in swallowing physiology, or that volumes above those reported to be close to, or smaller than habitual sip size challenge the swallowing mechanism in a way that elicits changes in swallowing physiology. Average natural sip size during an
instructed drinking task has been reported as 7.85ml for women and 8.40ml in men (Bennett, Van Lieshout, Pelletier, & Steele, 2009). Note, however, that pairwise comparisons of UES opening duration and laryngeal closure duration in healthy participants revealed significant volume-dependent differences for all comparisons. Given that these two parameters hold biological salience as measures related to protecting the airway across the entire timeframe when the bolus is near, or passing by, the entrance to the airway, it is reassuring to see that these parameters display sensitivity to differences in bolus volume. A reasonable recommendation related to these observations is that clinical VF examinations and future research studies should explore the influence of volume differences using comparisons greater than 5ml, and that analyses should consider both the actual volumes swallowed and the magnitude of the contrast across volume conditions.

The 22% ‘Ultra-thin’ Reference Values

Recently, Fink and Ross (2009) demonstrated that an ‘ultra-thin’ 22% w/v liquid barium suspension is more likely to elicit aspiration than a 40% w/v suspension in patients with dysphagia. This is not the first evidence that swallowing physiology may vary across different barium concentrations, although previous studies have explored this phenomenon with much more concentrated suspensions (e.g., 250% w/v vs. 140% w/v) (Dantas, Dodds, Massey, & Kern, 1989). To date, there have been no systematic investigations of swallowing physiology using the 22% w/v ultra-thin liquid barium proposed by Fink and Ross (2009) to be more representative of a “true thin liquid” like water. The tightly controlled healthy dataset in my dissertation research enables us to supply clinicians and researchers with reference values for kinematic and temporal parameters of swallowing across three volume conditions using this ultra-thin liquid barium suspension. Table 1 summarizes descriptive statistics (means and 95% confidence intervals) for nine physiological parameters with this barium stimulus. Note that references have not been split by sex because no main effects of sex were found for any of the reported parameters. Importantly, these reference values can be used for accurate power calculations in the design of future studies.
Table 1. Reference values for kinematic and temporal parameters of swallowing across 3 ‘ultra-thin’ volumes. (ms = milliseconds, %C2-4 = percentage of C2-4 vertebral length)

Not All Physiological Variables Are Created Equal

With the exception of hyoid movement duration and stage transition duration, all of the variables analyzed in this dissertation demonstrated significant variation attributable to at least one of the independent variables incorporated into the study design (bolus volume, participant size, video order, or bolus order), either in the healthy participants and/or the patient dataset. While none of the physiological variables in Chapter 6 were statistically associated with impairment, stage transition duration (and pharyngeal transit time) displayed trends and small effect sizes that dissociated functional swallowing from impairment.

Of all the physiological parameters studied, hyoid movement duration appears to be the least informative. This observation brings into question the utility of the overall duration of hyoid movement as a clinically relevant parameter of swallowing. This observation does not necessarily imply questionable utility of temporal measures of
subcomponent stages of hyoid movement that have been reported by other researchers, such as time to peak, duration of peak, or peak to rest (Gay, Rendell, Spiro, Mosier, & Lurie, 1994; Kendall, McKenzie, Leonard, Gonçalves, & Walker, 2000; Robbins, Hamilton, Lof, & Kempster, 1992).

**Limitations**

There are several limitations to acknowledge in this dissertation. First, the findings in all experimental chapters deal exclusively with physiological parameters for thin liquid swallowing. Specifically, the stimulus used for the detailed analyses of physiological measures of swallowing (in Chapters 4-6) was an ‘ultra-thin’ 22% w/v liquid barium suspension (Bracco Polibar suspension diluted with water) (Fink & Ross, 2009). The results reported in this dissertation should not be generalized to other textures/viscosities and/or barium concentrations.

The data in this dissertation are limited to a restricted set of physiological parameters and it is important to acknowledge that many other kinematic and temporal variables could be investigated. I had initially planned to include laryngeal excursion and UES opening width in my kinematic analyses; however during pilot testing, we discovered poor reliability for extracting these variables. It is likely that difficulty in visualizing the cartilaginous upper border of the larynx and the moving location of the UES during the swallow contributed to these difficulties and ultimately impacted my decision to drop these variables. With respect to timing variables, as described in Chapter 3, data regarding 119 different temporal variables can be found in the healthy swallowing literature. My decision to focus on the three most frequently reported durations and three most frequently reported interval measures was based solely on feasibility.

In order to maintain a high level of experimental control, all analyses in this dissertation were conducted on swallowing ‘clips’ extracted from the full VF recordings. This method allowed us to name clips with unique alpha-numeric codes and arrange them in a random order for blinded analyses. However, recently, our lab has questioned whether this approach is optimal for capturing swallowing impairment. We found that
when we compared a swallow-by-swallow analysis approach (i.e., separate clips for two boluses each of ultra-thin liquid and spoon-thick liquid) to an analysis approach in which the entire VF recording sequence was watched (including swallowing examples with other textures and possibly with compensatory manoeuvres), the swallow-by-swallow approach resulted in a more favourable overall impression of functional impairment (Steele, Hori, Molfenter, & Oshalla, 2012). Of course, as mentioned above, the work in this dissertation was restricted exclusively to an ultra-thin liquid stimulus, thus excluding consideration of the entire VF for the clinical dataset. Nevertheless, it is appropriate to acknowledge that the stringent methodology employed for extracting, randomizing and blindly analyzing individual clips from the VF may have obscured information regarding overall function or impairment that would be appreciable in the larger VF exam.

Patients with dysphagia often employ several swallows to clear a single bolus from the pharynx, a phenomenon known as ‘multiple swallows’. A limitation of the investigation in Chapter 6 lies in my choice to limit the analysis to the initial swallow of these multiple swallow sequences, whenever they occurred. Perhaps an analysis that extends beyond these initial swallows would demonstrate independent associations between swallow physiology and swallow function. While the physiologic parameters have not yet been measured beyond the initial swallows for these examples, in a related study arising from this dissertation, we demonstrated an association between residue in the valleculae after an initial swallow and the risk of aspiration on subsequent clearing swallows of the same bolus (Molfenter & Steele, 2013).

Another limitation we would like to acknowledge with respect to the retrospective analyses reported in Chapter 6 (patients referred for VF) lies in the fact that the data came from an existing clinical archive of VF studies. Unfortunately, we were not able to apply the same level of bolus volume control during the collection of this dataset that we were applied to the prospective, healthy dataset described in Chapters 4 and 5. To minimize the impact of this limitation, we restricted the analysis in Chapter 6 to swallows that were administered by a 5ml teaspoon, thus guaranteeing that the volume swallowed was 5ml or less. On a related note, the retrospective clinical archive did not contain sufficient
information to allow us to extract etiologic and clinical history details for the patients referred for VF.

Unfortunately, age differs significantly between the healthy participants and the patients referred for VF. This limited our ability to compare the reference values for healthy swallows in Chapters 4 and 5 with the values obtained from patients with dysphagia in Chapter 6.

**Future Directions**

In future research, it would be desirable to repeat the methods used in Chapters 4 and 5 to detail healthy swallowing in a sample of healthy older adults. Extending this process to a healthy older sample is important given that there are known processes in healthy aging that affect swallowing, and these could influence the reference values that should be used when determining whether older patients display physiological abnormalities. For example, there are known reductions with age in muscle mass (known as sarcopenia) (Robbins et al., 2005), laryngeal sensory function (Aviv et al., 1994) and cervical spine length (Buckwalter, 1995). Further, future work should focus on other barium concentrations, textures/viscosities, and swallowing conditions (such as continuous drinking). Once these reference values are obtained, they can be used to outline expected values for the development of evidence-based guidelines for the measurement of swallowing physiology on VF.

The dysphagia literature would benefit from a large-scale prospective study of patients referred to VF (with precise volumetric control) to further explore the relationships between pharyngeal transit time and stage transition duration and swallowing impairment. These variables showed trends toward differentiating functional from impaired swallowing and further research should be conducted before ruling out their utility in predicting impairment. Further, it would be interesting to investigate etiologic-specific populations with respect to patterns and physiological trends in swallowing. For example, do all patients treated with radiation therapy for head and neck cancer or all patients who have undergone cervical spine surgery have similar kinematic
and temporal profiles of swallowing? It seems probable that some physiological variables will be more or less sensitive to impairment in specific populations.

Finally, swallowing is an extremely complicated, multidimensional process and it is important to recognize that an analysis of isolated features of swallowing physiology probably under-represents the complexity of the swallow. These one-dimensional features of swallowing are overlapping in time and space and demonstrate interdependence on one another. In the future, it would be interesting to re-analyze the data, either in reference to other physiological events within the swallowing sequence (Kendall, Leonard, & McKenzie, 2003; Mendell & Logemann, 2007) or to other systems outside the swallow, such as respiration (Martin-Harris et al., 2005).

Conclusions

This dissertation was broadly motivated by a desire to better understand patient performance on videofluoroscopic assessment of swallowing. Specifically, I set out to describe variation in swallowing physiology, identify which factors explain (or do not explain) this variation, develop methods to control for sources of variation in measurement, and apply those methods to a patient population to investigate the link between physiology and impairment. Taken together, this work makes several novel contributions to the dysphagia community. I have established that inherent variation exists in measures of swallowing physiology. This dissertation has demonstrated that when certain sources of variation are controlled (such as participant size), there are no sex differences in swallowing physiology. This research shows that bolus volume impacts physiological variables differentially. I have proven that participant size impacts the expected extent of hyoid excursion and that we can control this variation by scaling measures of hyoid excursion to cervical spine length. I have established that stage transition duration and pharyngeal transit time show promise to detect functional swallowing impairment. Finally, I have provided the first set of normative reference values for physiological parameters of swallowing using ultra-thin liquid barium. In conclusion, several limitations are acknowledged and this work has, to some extent, raised more questions than it has resolved. Nevertheless, it has undeniably ignited a
passion in me to further investigate these unanswered questions in the pursuit to minimize the impact of dysphagia.
References


Appendix A: Ethics Documents

Healthy VF Ethics protocol

**Title:** Investigating variability in healthy swallowing using videofluoroscopy and acoustic pharyngometry

**Principal investigator:** Catriona M. Steele, PhD

**Co-investigators:** Sonja M. Molfenter, MHSc, PhD Candidate
                        Azadeh Yadollahi, PhD
1. Background, Purpose, Objectives

**Background**
In videofluoroscopy (VF), food and liquid are mixed with barium and swallowed under fluoroscopy allowing direct and dynamic visualization of swallowing function. This tool, paired with a standardized protocol, is considered the instrumental 'Gold Standard' for diagnostic evaluation, treatment planning, and outcome measurement of dysphagia (swallowing disorders). Measures of kinematic movement and measures of temporal duration can be extracted from VF. However, due to the radiographic exposure associated with this tool, VF assessments must be restricted in duration, usually lasting between 3 and 10 swallows per assessment (Perlman, Booth, & Grayhack, 1994), and thus representing a mere ‘snapshot’ of swallowing function. At Toronto Rehab, a recent audit showed that VF examinations typically involve up to 15 swallows. The brevity of these exams makes interpretation susceptible to variable performance; this, in turn, challenges clinical decision making and scientific analysis.

**Purpose**
The proposed study is part of the co-applicant’s (S. Molfenter) doctoral research. The ultimate purpose of the doctoral research is to provide clinicians with concrete evidence regarding swallow variability, which will inform clinical decision-making in VF.

A careful review of the swallowing literature reveals the existence of inter-subject variability on swallowing measures in healthy individuals (Molfenter & Steele, 2011). We have proposed several factors that may potentially account for variability that is apparent across studies including methodological factors (data extraction method, image rotation), subject factors (participant size, gender, age), statistical factors (weighting of repeated measures), and stimulus factors (volume, texture, barium density) (Molfenter & Steele, 2011). However, it remains unclear how much variation can be attributed to these factors and what (remaining) proportion of the variation is inherent to swallowing. Our goal is to fill this gap in the literature by analyzing a dataset of healthy swallowing that investigates the contribution of gender, height, bolus volume, barium density, and stimulus viscosity to variation in swallow performance using a repeated-measures design, controlled for age. In addition, we propose to collect acoustic pharyngometry measures of the cross-sectional area of participants' vocal tracts as a second measure of anthropometric parameters that may explain some variability in observed swallowing behaviours. This measure will be overseen by Dr. Yadollahi.

The current study will complement research already underway at Toronto Rehab, in which the extent of within- and across-subject variability is being measured on various quantitative physiological variables across repeated VF assessments in patients with dysphagia (REB # 09-029). In the proposed study, the same features of swallowing will be measured in a sample of 20 healthy adults. Together, this will allow us to determine which measures of swallowing are robust and display
minimal variability, and to calculate the magnitude of physiological differences that can be interpreted as clinically and statistically meaningful versus those attributable to inherent variability.

**Objectives**

1. To quantify the magnitude of variability on various kinematic and temporal measures of swallowing on VF in a sample of 20 healthy individuals swallowing 15 boluses balanced for volume, texture, and barium density.

2. To use the results of (1) to rank the relative variability of swallowing measures and compare to relative rankings of physiological variability observed in patients with dysphagia (REB#09-29).

3. To inform clinical decision-making by determining which features of swallowing are relatively stable and which are more volatile, affording clinicians increased confidence in decisions based on a brief set of swallows as dictated by the radiographic nature of VF.

4. To inform future research by helping investigators understand the magnitude of effect sizes required to show group differences for each physiological variable based on their inherent variability.

2. Research Methodology and Data Collection

**Participants**

20 healthy individuals (10 male) between the ages of 18 and 50 will be recruited for this study. The sample will be restricted to young individuals given that there are known effects of aging on swallowing kinematics (see for example, Kim & McCullough, 2008) and swallowing durations (see for example, Robbins, Hamilton, Lof, & Kempster, 1992). Participants will be stratified by height based on recent research from our lab showing that accounting for participant height can normalize apparent gender-based differences in hyoid resting position (Waito, Molfenter, & Steele, 2010). Male and female height stratification is based on the range of heights that span the reported means of the lower and upper quartile for height in adult Canadians (Shields, Gorber, & Tremblay, 2008). See Table 1 for details.

**Materials**

During the videofluoroscopy portion of data collection, each participant will swallow three repeated boluses in five conditions. These conditions have been selected to systematically vary factors that are hypothesized to be possible sources of physiological variability: barium density, bolus volume, and viscosity (see Table 1). The motivation for studying various bolus conditions is based on research showing inter-participant variability on each of these features; at this time, the literature lacks information clarifying the extent of within-participant variability attributable to these factors. In order to explore intra-participant variability, each bolus condition will be administered three times as recommended by Lof and Robbins (1992). The proposed total number of boluses (n=15) is similar to several previous studies in healthy adults which contain between 12-24 swallows (Bisch, et al., 1994; Gay, Rendell, Spiro, Mosier, & Lurie, 1994; Lazarus et al., 1993; Ohmae, Logemann, Kaiser, Hanson, & Kahrilas, 1996; Rofes et al., 2010).
Procedures
All VF studies will be conducted after-hours at Mount Sinai Hospital in the radiographic imaging suite. Studies will be conducted by the co-investigator (S. Molfenter) and SRRL speech pathologist (S. Hori) along with a licensed radiographic technician from Mount Sinai Hospital.

The participant will be seated upright in a chair in lateral view. All boluses will be premeasured in 30ml medicine cups and presented to the participant on a table in one of 3 predetermined randomized sequences (see Appendix A). The participant will self-administer each bolus. They will be instructed to hold the medicine cup in their hand, indicate when they are ready to drink (by raising their hand), then place the bolus in their mouth and swallow as naturally as possible. The radiographic technician will turn on the fluoroscopy only when the participant indicates that they are ready with the hand gesture. This will limit unnecessary radiation exposure.

The VF will be conducted through the hospital’s fluoroscopy equipment at full resolution (30 pulses per second) and captured and recorded on the Swallowing Rehabilitation and Research Lab’s (SRRL) portable Kay Pentax Digital Swallowing Workstation at 30 frames per second. No data will be recorded onto Mount Sinai’s PACS system.

Each participant will be scheduled for a 15 minute session, which will allow for set-up, positioning, reviewing instructions, and data collection. Pilot testing on three healthy individuals drinking the 15 proposed boluses (outside of the fluoroscopy suite) at a natural pace has demonstrated that our study will require approximately 1 minute of radiation exposure (mean drinking duration was 58.7 seconds; range 55-61 seconds), significantly less exposure time than is typical of VF exams (Moro & Cazzani, 2006; Zammit-Maempel, Chapple, & Leslie, 2007).

As an additional, optional procedure, we will invite participants to a second 15-minute data collection session in the Swallowing Rehabilitation Research Laboratory on the 12th floor at the University site of Toronto Rehabilitation Institute for measurement of the cross-sectional area of their upper airway (UA-XSA), which will be measured non-invasively by acoustic pharyngometry (Eccovision; Hood Laboratories; Pembroke, Massachusetts, USA). Acoustic pharyngometry is based on the analysis of sound waves reflected from the airways. The amplitudes of the reflections and their times of arrival at the sensing microphone will be used to generate a plot of upper airway area vs. distance from the microphone. Acoustic pharyngometry has been validated against CT scanning and MRI for assessment of UA-XSA. With participants seated upright in a dental chair and their heads in the neutral position, this device will be positioned in the mouth using a mouthpiece designed to secure the tongue in place. During the measurements, the participant’s head position will be supported by a headrest. UA-XSA will be determined at end-expiration as the mean area between the nasal and oropharyngeal junction (velum) and the glottis. The mean of four consecutive measurements will be used.
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Table 1. Study design: Each participant (<50 years old) will swallow 3 repeated boluses across 5 conditions varied by volume, viscosity and barium density in a random order under VF.

### 3. Data Processing and Analysis

**Data Processing**

In total, the dataset will consist of 300 swallows (15 swallows for each of 20 participants). Each single swallow will be extracted from the larger VF study, de-identified, and assigned a unique alphanumeric code by a trained research assistant (C. Tsang). Swallow clips will be spliced 60 frames prior to the bolus passing the shadow of the mandible and 60 frames after the hyoid bone returns to rest. The dataset will then be placed in random order prior to analysis.

**Data Analysis**

Randomized analysis will be conducted by the co-investigator (S. Molfenter) and SRRL speech pathologist (S. Hori) for the variables listed below. Each swallow will be rated on several kinematic measures, temporal measures, and ordinal rating scales (see below). Detailed descriptions of each measure are listed in Appendix B.
Results for each rating on each swallow will be entered into an excel spreadsheet. Ten percent of the sample will be randomly selected and presented in duplicate for inter-rater and intra-rater reliability measures.

1. **Objective kinematic measures** include anterior and superior hyoid excursion (Kim & McCullough, 2008), upper esophageal sphincter (UES) opening width (Leonard, Kendall, McKenzie, Gonçalves, & Walker, 2000), and pharyngeal constriction (Leonard, Rees, Belafsky, & Allen, 2011).

2. **Objective temporal measures** include stage transition duration (Lof & Robbins, 1990), pharyngeal transit time (Robbins et al., 1992), laryngeal closure to UES opening time (Mendell & Logemann, 2007), hyoid movement duration (Kang et al., 2010), laryngeal closure duration (Logemann et al., 1992) and duration of UES opening (Cook et al., 1989).

3. **Ordinal rating scales*** including bolus location at swallow onset (Martin-Harris, Brodsky, Michel, Lee, & Walters, 2007), depth of airway invasion (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996), and bolus clearance (Eisenhuber et al., 2002).

*Scores of >1 on the ordinal rating scales reflect swallowing impairment. It is anticipated that the number of scores >1 on any of these scales will be low or non-existent. However, any scores reflecting swallow impairment must be considered non-normal and removed from the analysis.

**Statistical Analysis**

Descriptive statistics for all kinematic and temporal measures will be calculated within and across participants. These values will be used to calculate the coefficient of variation (CV). Due to the volatile nature of the CV for values close to zero (van Geert & van Dijk, 2002), a constant value of 500 milliseconds will be added to all temporal data. Next, temporal and kinematic measures will be ranked from low to high variability based on the CV. These results will be compared to the complementary study in patients with swallowing disorders (REB #09-029) to determine if patterns of variability/stability are different in health versus disease.

Finally, pooled means and SDs (across all participants) will be used to calculate an average magnitude of change necessary to detect a statistical difference in group comparisons on each variable using Cohen’s $d$. A power analysis to calculate group mean difference thresholds for achieving a moderate effect (0.40) and a strong effect (0.60) will be generated for each variable. This will inform future research by helping investigators understand the magnitude of effect sizes required to show group differences for each physiological variable of interest.
4. Recruitment

**Inclusion/Exclusion Criteria**

Eligible participants must be in good health, between 18 and 50 years old, with no history of swallowing difficulty, neurological deficits or head/neck surgery (excluding routine dental surgery and/or tonsillectomy and adenoidectomy). Participants must meet height stratification criteria (see Table 1). Participants who are pregnant or are at risk of being pregnant will not be able to take part in the study. Finally, individuals who have had any radiographic investigation other than a single routine chest x-ray and single routine dental x-ray within the past year will be advised not to participate. Individuals who have occupational exposure to radiation (e.g. Speech Language Pathologists conducting VF) are encouraged to check their most recent dosimetric results. Health Canada recommends no more than 20 mSvs per year exposure. We anticipate this experiment to contribute no more than 0.14 mSv of radiation exposure.

**Recruitment**

Participants will be recruited via flyers posted on University of Toronto (U of T) campus, at U of T teaching hospitals, U of T’s Speech Language Pathology Alumni Association Facebook page, and on the SRRL website (www.srrltri.ca). The recruitment flyer appears in Appendix C. It is expected that many clinicians and students in speech language pathology will demonstrate interest in participating. First contact will be with Tasnim Shariff, who will first confirm that potential participants meet inclusion and exclusion criteria and then supply potential participants with the information sheet (Appendix D).

**Sample Size**

The proposed sample size is on par with previous work examining swallowing in healthy individuals (Daniels et al., 2009; Dantas et al., 2009; Kern et al., 1999; Martin-Harris, Brodsky, Price, Michel, & Walters, 2003; Mokhlesi, Logemann, Rademaker, Stangl, & Corbridge, 2002) and will provide sufficient evidence of variation in healthy swallowing to inform power analyses for future research.

5. Risks and benefits

**Risks**

Videofluoroscopy (VF) involves low levels of radiation exposure, which carries a risk of stochastic radiation effects. Stochastic radiation effects are effects produced at random without a threshold dose level. Their probability of occurrence is proportional to the dose received, but the severity is independent of dose. In radiation safety, the main stochastic effects are carcinogenesis and genetic mutation (Blakely, 2000).

Radiation dose is measured in millisieverts (mSv). Background radiation exposure is known to occur in everyday activities such as flying in a plane (0.005 mSv per hour) or smoking cigarettes (0.18 mSv per half pack) as well as during medical tests such as a chest x-ray (0.02 mSv) or a CT scan (10 mSv) (Green, 2011). In fact, the average Canadian is exposed to somewhere between 2 and 4 mSv of background radiation per year (Health Canada, 2003). The maximum recommended dosage for people exposed to radiation in their occupation (i.e. during medical imaging) is 20mSv (Health Canada, 2003).
Researchers have quantified the median levels of radiation exposure associated with a VF in patient populations. Zammit-Maempel and colleagues (2007) reported a median exposure time of 171 seconds and an associated dose of 0.20 mSv, while Moro and Cazzani (2006) reported a median exposure time of 149 seconds and an associated dose of 0.35 mSv. Moro and Cazzani (2006) showed that this dose (0.35 mSv) corresponds to a risk of 1 in 39,000 of developing a radiation-induced stochastic effect from a VF. Pilot testing on three healthy individuals drinking the 15 proposed boluses at a natural pace has demonstrated that our study will require significantly less exposure time than reported in the literature. The mean time required to complete 15 swallowing tasks in our pilot trial was 58.7 seconds (range 55-61 seconds). Based on this, we estimate that this study will contribute no more than 0.14 mSv of radiation exposure. Naturally, this reduced exposure time corresponds to a decrease in the associated risks reported by Moro and Cazzani (2007). We conclude that the risk of stochastic radiation effects in this study can be quantified as very rare (<0.0001%).

Ingestion of large quantities of high density barium sulfate in routine medical tests (such as an upper GI series) carries risk of nausea and/or constipation (i.e. 340 grams of barium sulfate suspended in water). The participants in this study will be provided with only 135 ml of solution total, mixed at 22% w/v or 44% w/v, totaling to just under 60 grams of barium sulfate. Thus, the amount of barium ingested will be a fraction of the amounts given in routine testing. We do not anticipate that participants will experience side-effects at this level of consumption.

In the unlikely event of an emergency, both the Speech Language Pathologist and the Radiation Technician are trained to respond appropriately by following regular emergency procedures.

There are no known risks involved with the UA-XSA measurement procedure.

**Benefits**

There is no direct benefit to the participants in this experiment.

**6. Privacy and confidentiality**

All data will be stored on a computer for offline analysis. Information gathered from participants will be kept confidential and identified using a set of unique alphanumeric codes. All hard copy data will be stored in a secure locked area in the SRRL at the Toronto Rehabilitation Institute. Access to participant information and experimental raw data will be restricted to the investigators named in this proposal. All records will be destroyed after 10 years under the supervision of Dr. Steele.

**7. Compensation**

VF data collection for each participant will take approximately 15 minutes; participants will be compensated with a $25 gift card for participation. A receipt will be provided. Participants who would like a copy of their swallowing video will be provided a DVD.
Participants to agree to the optional additional session for UA-XSA measurement will be provided with a second $25 gift card for participation in this portion of the study.

8. Conflicts of interest
We anticipate, due to professional interest, that it is likely that clinicians, lab members and students we know may wish to participate in this study. We plan to mitigate the possible risk of coercion by asking the member of our team with the least affiliation to the clinical community (T. Shariff, lab coordinator) to make the initial contact with such potential participants and to consent these individuals if they choose to participate.

Also, in the unlikely event that an incidental finding is noted on the VF (such as a diverticulum or a mass) the co-investigator (S. Molfenter), a licensed speech language pathologist, will consult the on-call radiologist and generate a clinical report documenting the observation. The participant will be informed that an abnormality was detected during the study and advised to consult their family doctor regarding further investigation of these unanticipated findings.

9. Informed Consent Process
All participants who show an interest in participating will be provided with detailed information about this study via the Participant Information Sheet (Appendix D) at least one week prior to the study date. Only after confirming they have understood all the information that is provided and after verifying they have no more questions, can they sign the consent form (Appendix D). Copies of the consent form will be provided to them.

A second (optional) consent form will be provided to each participant asking them if they consent to use of the VF for educational and teaching purposes (Appendix E).

10. Scholarly review
Not applicable.

11. Additional ethics reviews
No additional ethics reviews are planned.

12. Contracts
A service agreement with Mt. Sinai Hospital is in process. A preliminary meeting has confirmed that the diagnostic imaging department at Mt. Sinai has the capacity to accommodate and staff the videofluoroscopies required for this study. Further negotiations regarding fees for this service and scheduling will take place pending initial REB approval, and the service agreement will be forwarded to the REB for filing once signed.

13. Clinical Trials
Not applicable.
REFERENCES


**Data Collection Form**

Participant #  
_____________________

Age  
______________

Gender  
______________

Height (cm)  
______________

Radiation Technician  
______________

**Randomization # 1**

<table>
<thead>
<tr>
<th>BOLUS</th>
<th># of swallows</th>
<th>Comments</th>
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A = 5ml thin liquid barium 22% w/v  
B = 5ml thin liquid barium 40% w/v  
C = 5ml nectar thick liquid barium 22% w/v  
D = 10ml thin liquid barium 22% w/v  
E = 20ml thin liquid barium 22% w/v
VF Ratings: Objective Kinematic Measures

Superior Hyoid Movement
The maximum distance that the hyoid moves in the vertical direction, with the vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae normalized to C2-C4 distance.

Anterior Hyoid Movement
The maximum distance that the hyoid moves in the anterior direction, i.e. at 90 degrees to a vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae normalized to C2-C4 distance.

Maximum Upper Esophageal Sphincter (UES) Opening
The narrowest anterior-posterior opening during bolus passage through the UES between C4 and C6 normalized to C2-4 distance.

Pharyngeal Constriction
The area of pharynx area measured in lateral fluoroscopic view at the point of maximum pharyngeal constriction during the swallow normalized to the pharyngeal area measured with the hyoid at rest.

VF Ratings: Objective Temporal Measures

Stage Transition Duration
The interval (in milliseconds) between arrival of the head of the bolus at the lower margin of the shadow of the ramus of mandible and the onset of the first hyolaryngeal excursion associated with UES opening.

Pharyngeal Transit Duration
The interval (in milliseconds) between the first frame showing the arrival of the bolus head at the hypopharynx (i.e., beyond the shadow of the lower margin of the ramus of the mandible) to the last frame showing the tail of the bolus passing through the mid-margin of the upper esophageal sphincter.

Laryngeal Closure to UES Opening Duration
The interval (in milliseconds) between the first frame showing laryngeal closure to the first frame showing bolus entering the UES.

Laryngeal Closure Duration
The duration (in milliseconds) that the laryngeal vestibule remains completely closed.

UES Opening Duration
The interval (in milliseconds) between the first frame showing UES opening and the last frame showing the tail of the bolus leaving the UES.

Hyoid Movement Duration
The interval (in milliseconds) between the first frame showing ascent of the hyoid associated with a swallow to the frame showing the hyoid’s return to resting position.
VF Rating Scales: Ordinal Rating Scales

Bolus Location At Swallow Onset (Martin-Harris, 2008)
(Note: this feature will be rated at first frame showing upward hyoid excursion)
0 = Bolus head at posterior angle of ramus
1 = Bolus head at vallecular pit
2 = Bolus head at posterior laryngeal surface of epiglottis
3 = Bolus head at pit of pyriforms
4 = No appreciable initiation at any location

Penetration-Aspiration Scale (Rosenbek et al, 1996)
1 = Material does not enter the airway
2 = Material enters the supraglottic space, remains above the true vocal folds, and is then ejected
3 = Material enters the supraglottic space, remains above the true vocal folds, but is not ejected
4 = Material enters the supraglottic space, contacts the true vocal folds, but is then ejected
5 = Material enters the supraglottic space, contacts the true vocal folds, but is not ejected
6 = Material enters the airway, falling beneath the true vocal folds, but is then ejected above the true vocal folds
7 = Material enters the airway, falling beneath the true vocal folds, but is not ejected despite volitional clearance attempts
8 = Material enters the airway, falling beneath the true vocal folds, and there is no attempt to clear

Bolus Clearance: Valleculae and Pyriform Sinuses (Eisenhuber et al, 2002)
0 = No evidence of residual
1 = A thin coating of residual material
2 = Residual material sufficient to be obvious, but not to fill the available space to capacity
3 = Substantial residual material either filling a space to capacity or overflowing the available space
Recruitment Flyer

HEALTHY VOLUNTEERS NEEDED!

Researchers in the Swallowing Rehabilitation and Research Lab are seeking healthy volunteers to participate in a videofluoroscopic study of swallowing. In this study, you will swallow 15 different liquids mixed with barium and be able to see your swallowing mechanism at work! The study will require 15 minutes of your time and take place at Mount Sinai Hospital in the evening. Please note that this experiment involves a one-time exposure to low doses of radiation. You will be informed of the risks of radiation exposure prior to being asked to participate.

Optionally, a second 15 minute session will be scheduled at Toronto Rehab for a measurement of the dimensions of your throat using an echo-based technology similar to radar.

Volunteers will be compensated for their time.

Participants must meet the following criteria:

- Generally healthy
- Between 18-50 years old
- Not pregnant
- No history of swallowing problems
- No history of head/neck surgery (other than routine adenoid/tonsil/dental surgery)

**We are looking for people of various heights because we are interested how height influences measurements of swallowing. Please be prepared to tell us how tall you are in centimeters when you contact us.**
Title of research project: Investigating variability in healthy swallowing using videofluoroscopy

Principal Investigator: Catriona Steele, Ph.D. Research Scientist, Toronto Rehabilitation Institute
550 University Avenue, Room 12030, Toronto, ON, M5G 2A2
Phone: 416-597-3422, ext 7603
Fax: 416-597-7131

Contact person: Tasnim Shariff
Phone: 416-597-3422 Ext. 7810
E-mail: shariff.tasnim@torontorehab.on.ca

IMPORTANT: You are being invited to take part in a research study. Before you consent to participate, it is important that you read the information below about the study. It describes the purpose of the study, risks or benefits to yourself and your right to withdraw at any time during the study. Ask as many questions as necessary to be sure you understand what you will be asked to do. Make sure all your questions have been answered to your satisfaction before signing this document.

It is common for patients with stroke or brain injury to develop swallowing impairment. The primary diagnostic tool used to assess swallowing function is called a videofluoroscopy. A videofluoroscopy is an x-ray of swallowing that is recorded as a movie. It enables the speech-language pathologist and doctor to see inside the throat while the patient is swallowing.
Here is a sample image from a videofluoroscopy:

![Sample Image from Videofluoroscopy]

The aim of this study is to understand how the swallows of normal healthy people respond to differences in the tasks conducted in a videofluoroscopy exam. We are specifically interested in measuring differences attributable to: a) the volume of material swallowed; b) the viscosity of material swallowed; and c) the density of the barium that is swallowed. Better understanding of these variables in healthy individuals will help us better diagnose abnormalities in patients with swallowing disorders. We are also interested to learn how a person's size/height influences the range of movement seen in the swallowing structures (that is, do taller people exhibit larger movements?).

Should you choose to participate in this study, you will be asked to participate in a 15-minute data-collection session in a radiographic imaging suite at Mount Sinai Hospital. First, we will measure your height in centimeters. Next, you will be seated in a chair with a table containing 15 liquids in front of you. The liquids will be of various volumes, thicknesses and densities. You will be asked to swallow each of these at a comfortable pace. All the liquids will be mixed with barium. Barium is a type of x-ray contrast material that allows us to see the food or liquid on the x-ray. Barium is not harmful to swallow, but may cause nausea or constipation when consumed in large quantities at high densities (i.e. 340 grams of barium sulfate suspended in water). You will only be consuming 60 grams of barium sulfate in total and we do not expect that you will experience side-effects. During each of the swallows, a radiographic technician will turn on the x-ray to capture and record your swallowing. After the 15 swallows are completed, you will be finished the experiment.

Because we are interested in the impact of a person’s size/height on swallowing behaviours, we would also like you to consider a second, optional 15-minute session to measure the shape and dimensions of your upper airway using a technique called Acoustic Pharyngometry. This technique works like sonar or radar. A sound is introduced into your airway through a mouthpiece and it bounces back based on the length and shape of your mouth and throat. If you are willing, we will schedule this second session at your convenience,
Participants
You will be among 20 participants in this study. Participants must be between 18 and 50 years old. Participants must be able to comprehend English well enough to understand this information sheet and to follow instructions during the experiment.

If you have had major surgery to your head, neck or mouth (other than routine dental surgery, tonsillectomy or adenoidectomy) or have a history of a neurological condition (i.e. stroke) you will not be able to participate. If you have ever had a swallowing problem, you will not be able to participate.

If you have had medical x-rays other than a single routine chest x-ray, and a single routine dental x-ray in the past 12 months, you should not participate in this study. This restriction is necessary to limit the amount of radiation that you receive over a 12-month period.

If you experience occupational exposure to radiation (i.e. Speech Pathologist conducting videofluoroscopy), we recommend that you check your most recent dosimetric results. Health Canada recommends less than 20 mSv exposure per year. We anticipate that this study will contribute no more than 0.14 mSv of radiation exposure.

Potential Risks
Videofluoroscopy involves low levels of radiation exposure, which carries risk of stochastic radiation effects (such as gene mutation and cancer). Stochastic radiation effects are effects produced at random without a threshold dose level. Their probability of occurrence increases with increased radiation dose but the severity is independent of the dose. Radiation dose is measured in millisieverts (mSv). Background radiation exposure is known to occur in everyday activities such as flying in a plane (0.005 mSv per hour) or smoking cigarettes (0.18 mSv per half pack) as well as during medical tests such as a chest x-ray (0.02 mSv) or a CT scan (10 mSv). According to Health Canada, the average Canadian is experiences between 2 and 4 mSv background radiation exposure each year. Health Canada recommends that occupationally exposed workers not exceed 20 mSv per year.

Based on research in patient populations and the very short time your x-ray will take (approximately 60 seconds of exposure), we expect the radiation dose you will receive from this experiment to be less than 0.14 mSv. This is the same exposure as 20 hours of flying in an airplane and less than the radiation received from smoking a half package of cigarettes. This dose corresponds to a very rare risk of developing a radiation-induced stochastic effect from the videofluoroscopic swallowing study (<0.0001%).

All the equipment that is used in this study is manufactured according to safety standards for hospital settings. There are no known risks associated with the equipment.
If you have food allergies, please report this to us so that we can discuss any concerns you might have about these issues. We may advise you not to participate on this basis.

In the unlikely event that an unexpected abnormal finding is noted on your x-ray, a licensed speech language pathologist will consult with the on-call radiologist and generate a clinical report documenting the finding. You will be informed that an abnormality was detected and advised to consult their family doctor regarding further investigation of these unanticipated findings.

There are no risks involved in the acoustic pharyngometry measurement of the dimensions of your throat.

**Benefits**
There are no direct benefits to you.

**Compensation**
You will be provided with a $25 gift card for participating in the videofluoroscopy portion of this experiment. A receipt will be provided. If you wish to have a copy of your swallowing x-ray, you may request a DVD copy of it. If you also agree to complete the acoustic pharyngometry session, you will receive a second $25 gift card for participating.

**Confidentiality**
Any information learned about you during the study will be kept confidential. Neither your name nor any other identifying information will be made available to anyone other than the investigators. All records will be kept secure under the supervision of Catriona M. Steele, Ph.D. Paper records will be kept stored in a secure locked filing cabinet in the Dr. Steele’s office or the Swallowing Rehabilitation Research Laboratory at Toronto Rehabilitation Institute. Computer records will be kept in a secure, password-protected drive on the Toronto Rehab research server, and on an encrypted back-up hard drive. Access to the data will be restricted to Dr. Steele and to research personnel working under her direct supervision. All records will be destroyed after a period of ten years.

Should you choose to participate in this study, you will be asked if your swallowing x-ray can be used for future educational purposes. You will be given a separate consent form for this. Your decision will not influence participation in the current study.

**Participant’s rights**
You are encouraged to ask any questions that you may have about the study and all your inquiries will be answered. You can withdraw from this study at any time without further consequences or limitations regarding your current or future access to and use of services at Toronto Rehab.
If you have questions about your rights as a research participant, or about any ethical issues relating to this study, you can contact someone who is independent of the research team. Please call the Research Ethics Board Office at (416) 597-3422 x 3081.

Thank you for your consideration.

Please contact research coordinator Tasnim Shariff (tel: 416-597-3422, ext 7810; e-mail shariff.tasnim@torontorehab.on.ca) or Principle Investigator Dr. Catriona Steele (tel: 416-597-3422, ext 7603; e-mail steele.catriona@torontorehab.on.ca) with any concerns or questions you may have about this study.

Sincerely,
Catriona M. Steele, Ph.D.
Title of research project: Investigating variability in healthy swallowing using videofluoroscopy

I, __________________________, agree to participate in this study that is testing swallowing physiology in healthy individuals in videofluoroscopy. The study is conducted by Dr. Catriona Steele, Research Scientist at the Toronto Rehabilitation Institute.

The purpose, procedures and risks of this study have been fully explained and I understand them. I have been given the opportunity to ask questions about the study, and they have been answered.

I understand that I am required to participate in one 15-minute data collection session where I will swallow 15 different items of varying volumes, thicknesses and densities. I understand that there risks associated with the radiation exposure and barium sulfate ingestion and they have been explained to me.

I understand that I have the option to also participate in a second 15-minute data collection session to measure the shape of my mouth and throat using acoustic pharyngometry.

I understand that I am under no obligation to agree to participate in this study. I understand that I may refuse to answer any questions, stop the data collection procedures, or withdraw from the study without any consequences at any time. If I am or will be receiving services from the Toronto Rehabilitation Institute in the future, I understand that my decision to participate, decline or withdraw will not affect my treatment.

I understand that if abnormal findings are observed on my x-ray, I will receive a report from the Speech Language Pathologist on the research team. I understand that it will be my responsibility to follow-up with my family physician regarding these findings.

I understand that the information I provide will be kept confidential. I understand that my name will not be identified in any report or presentation that may arise from the study. I understand that only the principal investigator and her research
assistants will have access to the information collected during the study. I understand that while I will not benefit directly from the study, the study results may advance current knowledge regarding swallowing and swallowing difficulties.

I understand that one decision to participate or not in the study will not affect future care, relations or employment with Toronto Rehabilitation Institute.

I understand what this study involves, and I agree to participate. I have been given a copy of this consent form.

Participant Name (PRINT) ___________________________ Date: ____________

Participant Signature ___________________________ Date: ____________

Person obtaining consent ___________________________ Date: ____________

Signature principal investigator ___________________________ Date: ____________

If there are any questions or concerns about this study, please contact the Research Coordinator Tasnim Shariff at 416-597-3422 (ext 7810) or Dr. Catriona Steele, Ph.D. at 416-597-3422 (ext 7603).

If you have questions about your rights as a research participant, or about any ethical issues relating to this study, you can contact someone who is independent of the research team. Please call the Research Ethics Board Office at (416) 597 3422 x 3081.
Retrospective VF in Patients Ethics protocol

**Title:** Investigating variability in videofluoroscopic swallow study ratings

**Principal investigator:** Catriona M. Steele, Ph.D. (Toronto Rehabilitation Institute)

**Co-investigators:** Sonja M. Molfenter, M.H.Sc. (Toronto Rehabilitation Institute)
1. Background, Purpose, Objectives

**Background**
The Videofluoroscopic Swallow Study (VFSS) is a procedure whereby food and liquid is mixed with barium and swallowed under fluoroscopy allowing direct visualization of swallowing function. This tool is considered the current instrumental 'Gold Standard' for diagnostic evaluation, treatment planning and outcome measurement of dysphagia (swallowing disorders). Due to the radiographic nature of this tool, VFSS assessments tend to be relatively short in duration, for example between 3 and 10 swallows (Perlman, Booth, & Grayhack 1994) and represent a mere ‘snapshot’ view of swallowing. Clinicians are faced with the challenge of recommending optimal diet texture, compensatory manoeuvres, and therapeutic intervention based on this brief set of swallows. Pilot work (Molfenter et al., 2009) suggests that there is a discrepancy between clinical judgement of swallow safety and actual physiological performance when single swallows are analysed at random on ordinal scales by blinded raters. Molfenter et al. (2009) suggest that this discrepancy may be explained by a) inherent variation in swallow physiology on VFSS or b) that the presence/absence of contextual information influences the clinical interpretation. The proposed study seeks to understand the contribution of these variables to clinical decision making and dysphagia management.

**Purpose**
This study is part of the co-applicant’s (Molfenter) doctoral research. The ultimate purpose of the doctoral research is to provide clinicians with concrete evidence regarding swallow variability to inform the clinical decision making process in VFSS. This ethics application outlines Experiment 1 (of 2) within the overall program of doctoral research and specifically seeks to determine the extent of within- and across-subject variability on various quantitative and physiological measures across repeated VFSS assessments. This will allow the candidate to determine which measures are robust, and to calculate the magnitude of physiological differences that can be interpreted as clinically and statistically meaningful versus those attributable to inherent variability.

**Objectives**
To quantify swallow performance on previously recorded VFSS. We will focus on extracting within- and across-subject variability on several quantitative variables (see Appendix A) across repeated VFSS measures.

It is hypothesized that some (or all) of the physiological variables will present as variable over repeated measures, both within- and across-subjects.

2. Research Methodology and Data Collection
An existing archive of 250 VFSS collected by Toronto Rehabilitation Institute (Toronto Rehab) Speech-Language Pathologists (SLP) between January 2007 and December 2009 will be searched for patients who have had more than one VFSS during their time as a
patient at Toronto Rehab. These files will be rendered anonymous and de-identified by a trained research staff person. A unique alphanumeric code will be assigned to each file prior to secondary analysis by the investigators. Analysis will consist of frame by frame investigation of:

a) **Ordinal measures** such as bolus location at swallow onset, depth of airway invasion, airway closure [perceived] and bolus clearance; and

b) **Objective timing and distance measures** such as stage transition duration, pharyngeal transit time, airway closure [measured], pharyngeal constrictor ratio, and distance of hyoid and laryngeal excursion.

For detailed descriptions of the rating scales and associated literature references, please see Appendix A.

Results from the retrospective analysis of the repeated measures VFSS (n~100 assessments from approximately 50 patients) will be compiled. Statistical analysis will be performed on all the variables rated in Appendix A. This analysis of physiological results across repeated measures data will allow the investigators to determine which (if any) features of swallowing exhibit inherent variability and which remain more stable. This information will inform clinical practice by providing clinicians with evidence regarding those features of swallow that are robust, and therefore provide a solid foundation on which to base clinical decisions regarding treatment and management of swallowing disorders.

### 3. Procedures

**Data Processing and Analysis**

A research assistant will search the existing repository of VFSS exams (dating back to Sept 2007) that is stored on Toronto Rehab’s terraserver to identify patients who have had more than one VFSS exam conducted. The research assistant will then take a copy of each of these video files, de-identify them and re-label them with a unique study code. The research assistant will also record the corresponding age (in years, not DOB) and sex for each study. These are visible on the top left-hand corner of each file. Please see an example of this in Appendix B. The name and DOB of the patient is not visible. The physician’s name is the same on all of the files (Dr. Jaffer). Dr. Jaffer is the senior radiologist at Mt. Sinai Hospital where the VFSS are conducted. The number below Dr. Jaffer’s name is a procedural number that is not associated with the patient’s health record.

A master key of the study codes will be maintained to enable the researchers to determine which videos were collected from the same participants across repeated assessments. The research assistant will then go through each VFSS exam and extract spliced partial-videos for all swallows of thin liquid (2-4 swallows per study) and all swallows for thick liquids (2-4 swallows per study). These de-identified video clips will then be placed in random order for the co-applicant (Molfenter) and SRL speech pathologist (Oshalla) to analyze for the variables listed in Appendix A. Results for each rating on each swallow will be entered into an excel spreadsheet.
Ten percent of the sample will be randomly selected and presented in duplicate for inter-rater reliability measures.

Outcome measures will include inter- and intra-rater agreement and measures of within participant change on the variables in Appendix A.

4. Participants and Recruitment
Analysis will commence in January 2010. All analysis will be retrospective, therefore no active recruitment of participants is required. All patients who have undergone more than one VFSS at Toronto Rehab between September, 2007 and December, 2009 will be included. However, those patients for whom a tracheostomy and/or spinal cord hardware are visible on the VFSS will be excluded.

A sample size calculation reveals that 46 patients with more than one VFSS assessment will be required in order to achieve 80% power to detect a difference of 5 mm in hyoid excursion in a repeated measures ANOVA. A difference of 5 mm is just slightly larger than the currently reported standard deviations for hyoid excursion in healthy adults (Kim & McCullough, 2008), and therefore constitutes a meaningful degree of within-participant variation to identify in our dataset. As of June 1st, 2009, recordings of more than one VFSS assessment are available for 36 patients on the terraserver. It is anticipated that by December 31st, 2009 a total of 50 patients will have completed more than one VFSS assessment.

5. Risks and benefits
Risks
There are no known risks associated with this experiment.

Benefits
There is no direct benefit to the patients in this experiment.

6. Privacy and confidentiality
All data will be stored on a computer for offline analysis on a password protected, onsite Toronto Rehab computer. Information gathered from participants will be kept confidential and identified using a set of unique alphanumeric identification codes. All hard copy data will be stored in a secure locked area in the Swallowing Rehabilitation Research Laboratory at the Toronto Rehabilitation Institute. Access to participant information and experimental raw data will be restricted to the investigators named in this proposal. All records will be destroyed after 10 years under the supervision of Dr. Steele.

7. Compensation
There will be no compensation for this experiment.

8. Conflicts of interest
There are no known conflicts of interest in this study.
9. Informed Consent Process
The five criteria for a study that waives written consent appear in the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (Section 2.1c). Experiment 1 of the proposed project meets three of five criteria: the research involves no risk to the subjects (i), the waiving of consent is unlikely to adversely affect the rights and welfare of the subjects (ii), and that the waived consent does not involve a therapeutic intervention (v). Due to its retrospective nature, Experiment 1 cannot meet the criteria to provide the participant with information after participation (iv). Finally, while it is theoretically possible to conduct this experiment with a waiver of consent (iii), it would not be feasible or efficient given the large number of VFSS that would need to be prospectively collected, and the time and cost associated with doing so. We request, therefore, that specific informed consent not be required for the proposed secondary analysis of these pre-recorded assessments.

10. Scholarly review
This study was reviewed in funding competition for the NSERC Create: CARE (Create Academic Rehabilitation Engineering). The applicant (Sonja Molfenter) was successful in obtaining the funding.

11. Additional ethics reviews
Not applicable.

12. Contracts
Not applicable.

13. Clinical Trials
Not applicable.

REFERENCES


Appendix A:

a) VFSS Rating Scales: Ordinal measures

**Bolus Location At Swallow Onset** (Martin-Harris, 2008)
(Note: this feature will be rated at first frame showing upward hyoid excursion)
0 = Bolus head at posterior angle of ramus
1 = Bolus head at vallecular pit
2 = Bolus head at posterior laryngeal surface of epiglottis
3 = Bolus head at pit of pyriforms
4 = No appreciable initiation at any location

**Airway Closure [perceived]** (Kahrilas et al., 1997)
(Note: this feature will be rated based on the frame illustrating the maximum degree of laryngeal closure observed during the swallow sequence, compared to a rest frame taken before the swallow)
0 = Structural movement results in complete closure of the laryngeal additus (100% of the original arytenoid-vallecular height distance at rest), including contact between the arytenoid cartilages and the underside of the epiglottis, and complete disappearance of white air space in the laryngeal additus
1 = Partial structural movement to close the laryngeal additus is observed (25-75% of the original arytenoid-vallecular height distance at rest), such that an air space remains visible
2 = There is minimal to non-existent structural movement to close the laryngeal additus, which remains open throughout the entire swallow (≤ 25% of the original arytenoid-vallecular height distance at rest)

**Penetration-Aspiration Scale** (Rosenbek et al., 1996)
1 = Material does not enter the airway
2 = Material enters the supraglottic space, remains above the true vocal folds, and is then ejected
3 = Material enters the supraglottic space, remains above the true vocal folds, but is not ejected (residue remains visible)
4 = Material enters the supraglottic space, contacts the true vocal folds, but is then ejected
5 = Material enters the supraglottic space, contacts the true vocal folds, but is not ejected (residue remains visible)
6 = Material enters the airway, falling beneath the true vocal folds, but is then ejected to a position above the true vocal folds
7 = Material enters the airway, falling beneath the true vocal folds, but is not ejected despite volitional clearance attempts
8 = Material enters the airway, falling beneath the true vocal folds, and there is no attempt to clear
Bolus Clearance: Vallesculae (Eisenhuber, et al., 2002)
(Note: This feature will be rated following a single discrete swallow of the desired bolus consistency. A maximum of ONE spontaneous or cued dry swallow will be permitted prior to noting the degree of residual that is present.)

0 = No evidence of residual  
1 = A thin coating of residual material (≤ 25% of the available space)  
2 = Residual material sufficient to be obvious, but not to fill the available space to capacity (25-50% of the available space)  
3 = Substantial residual material either filling a space to near-capacity (>50%) or overflowing the available space

Bolus Clearance: Pyriform Sinuses (Eisenhuber, et al., 2002)
(Note: This feature will be rated following a single discrete swallow of the desired bolus consistency. A maximum of ONE spontaneous or cued dry swallow will be permitted prior to noting the degree of residual that is present.)

0 = No evidence of residual  
1 = A thin coating of residual material (≤ 25% of the available space)  
2 = Residual material sufficient to be obvious, but not to fill the available space to capacity (25-50% of the available space)  
3 = Substantial residual material either filling a space to near-capacity (>50%) or overflowing the available space

Total possible ordinal score (greatest severity): 20
b) VFSS Ratings: Objective timing and distance measures

**Stage Transition Duration** (Robbins et al. 1992)
The interval (in milliseconds) between arrival of the head of the bolus at the lower margin of the shadow of the ramus of mandible and the onset of the first hyolaryngeal excursion associated with UES opening.

**Pharyngeal Transit Time** (Robbins et al. 1992)
The interval (in milliseconds) between the first frame showing the arrival of the bolus head at the hypopharynx (i.e., beyond the shadow of the lower margin of the ramus of the mandible) to the last frame showing the tail of the bolus passing through the mid-margin of the upper esophageal sphincter.

The ratio of pharyngeal area measured in lateral fluoroscopic view at the point of maximum pharyngeal constriction during the swallow to the pharyngeal area measured with the bolus held in the oral cavity.

**Airway Closure** (Kahrilas et al., 1997)
Arytenoid-vallecular height difference (in mm) on the frame of maximum laryngeal closure divided by the arytenoid-vallecular height difference (in mm) from a rest frame taken prior to the swallow, with the bolus held in the oral cavity. These measures will be calculated relative to a vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae.

**Upward Hyoid Movement** *
The maximum distance (in mm) that the hyoid moves in the vertical direction, with the vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae.

**Forward Hyoid Movement** *
The maximum distance (in mm) that the hyoid moves in the anterior direction, i.e. at 90 degrees to a vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae.

**Upward Laryngeal Movement** *
The maximum distance (in mm) that a point at the posterior aspect of the vocal cords (the top of the laryngeal air column) moves in the vertical direction, with the vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae.

**Forward Laryngeal Movement** *
The maximum distance (in mm) that a point at the posterior aspect of the vocal cords (the top of the laryngeal air column) moves in the anterior direction, i.e. at 90 degrees to a vertical axis defined by a line running through the lower anterior corner of the C2 and C4 vertebrae.

* These are direct measurements of the physiological parameters, not scales. These direct measures do not require validation and have been accepted in the peer-reviewed literature. (See for example Leonard et al 2000, Kim & McCullough 2008, Kim & McCullough 2009)
Appendix B

Figure 1 – A typical still-image taken from a VFSS exam, depicting age (in years) and sex in the top left-hand corner of the screen. The name of the patient is not visible. The physician’s name is the same on all of the files (Dr. Jaffer). Dr. Jaffer is the senior radiologist at Mt. Sinai Hospital where the VFSS are conducted. The number below Dr. Jaffer's name is a procedural number that is not associated with the patient’s health record.