



Differential kinematic features of the hyoid bone during swallowing in patients with Parkinson's disease

Woo Hyung Lee^{a,1}, Min Hyuk Lim^{a,1}, Hyung Seok Nam^a, Yoon Jae Kim^c, Han Gil Seo^b,
Moon Suk Bang^b, Min Yong Seong^b, Byung-Mo Oh^{b,2,*}, Sungwan Kim^{a,c,2,*}

^a Department of Biomedical Engineering, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

^b Department of Rehabilitation Medicine, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

^c Institute of Medical and Biological Engineering, Medical Research Center, Seoul National University, 101 Daehak-ro, Jongno-gu, Seoul, 03080, Republic of Korea

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ABSTRACT

This study aimed to investigate spatiotemporal characteristics of the hyoid bone during swallowing in patients with Parkinson's disease (PD) and dysphagia. Spatiotemporal data of the hyoid bone was obtained from videofluoroscopic images of 69 subjects (23 patients with PD, 23 age- and sex-matched healthy elderly controls, and 23 healthy young controls). Normalized profiles of displacement/velocity were analyzed during different periods (percentile) of swallowing using functional regression analysis, and the maximal values were compared between the groups. Maximal horizontal displacement and velocity were significantly decreased during the initial backward ($P = 0.006$ and $P < 0.001$, respectively) and forward ($P = 0.008$ and $P < 0.001$, respectively) motions in PD patients compared to elderly controls. Maximal vertical velocity was significantly lower in PD patients than in elderly controls ($P = 0.001$). No significant difference was observed in maximal displacement and velocity in both horizontal and vertical planes between the healthy elderly and young controls, although horizontal displacement was significantly decreased during the forward motion (51st–57th percentiles) in the elderly controls. In conclusion, reduced horizontal displacement and velocity of the hyoid bone during the forward motion would be due to combined effects of disease and aging, whereas those over the initial backward motion may be considered specific to patients with PD.

1. Introduction

Dysphagia is a common complication in approximately 87% of patients with Parkinson's disease (PD) (Davie, 2008). It develops insidiously with a slowly progressive disease course (Bird et al., 1994; Suttrup and Warnecke, 2016). The resultant aspiration pneumonia has been described as one of the major causes of death in patients with PD (Schindler and Kelly, 2002). Notably, the oropharyngeal musculatures involved in the swallowing process can be impaired even in early-stage PD patients without subjective swallowing difficulty. This can be represented as reduced swallowing speed and decreased motions of lingual and palatal areas (Volonté et al., 2002). To achieve detailed diagnostic information and prevent silent aspiration, videofluoroscopic swallowing study (VFSS) is a valuable instrumental investigation,

contributing to assessment of the efficacy and safety of swallowing and characterization of impaired biomechanics (Rugiu, 2007). The VFSS enables visualization of dynamic motions of superficial and deep oropharyngeal structures, allowing quantitative measurements of swallowing kinematics with high accuracy in PD patients (Argolo et al., 2015; Lee et al., 2013).

In swallowing dynamics, hyoid excursion is one of the main physiological events during the pharyngeal phase of swallowing (Feng et al., 2014; Nam et al., 2015; Ragland et al., 2016). It is an important process to exert thyrohyoid approximation resulting in an epiglottic tilt and to actively open the upper esophageal sphincter, leading to protection of the airway from bolus aspiration (T. Lee et al., 2017; Taylor et al., 1990). In normal swallowing, the trajectory pattern of the hyoid bone is significantly influenced by sequential contractions of the hyoid

* Corresponding authors at: Department of Biomedical Engineering, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea (S. Kim).

E-mail addresses: keepwiz@gmail.com (B.-M. Oh), sungwan@snu.ac.kr (S. Kim).

¹ Co-first authors: these authors contributed equally to this work.

² Co-corresponding authors: these authors contributed equally to this work.

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muscles, including the stylohyoid, posterior digastric, and mylohyoid muscles, followed by the geniohyoid and anterior digastric muscles (Okada et al., 2013). Substantial impairment in hyoid excursion induces post-swallow pharyngeal residues and a greater risk of penetration-aspiration (Steele et al., 2011), which was also previously demonstrated in PD patients (Kim et al., 2015). Since the sequence of muscle activity is constant during the pharyngeal phase (Okada et al., 2013), any impairment of the swallow sequence by affecting the hyoid muscles can influence the trajectory of the hyoid bone and result in swallowing dysfunction (Dodrill and Gosa, 2015).

There is growing evidence of peripheral mechanisms affecting swallowing-associated peripheral nerves and muscles as well as reduced dopaminergic activity in the basal ganglia for the pathophysiology of PD-related dysphagia (Suttrup and Warnecke, 2016). Involvement of both central and peripheral nervous system can cause impaired control of the hyoid movement, which may result in abnormality of the motion of the muscle during swallowing. In a previous study, reduction of maximal displacement and mean velocity of the hyoid bone in the horizontal plane was reported in PD patients with dysphagia (Kim et al., 2015). However, this study ascertained the effects of disease on the motion of the hyoid by analyzing only specific variables such as maximum or mean values rather than the entire profile of movements over time. The conventional analyzing method may be limited to interpret changes in the shape of motion trajectory, since continuous position of the hyoid bone is time-series data that can vary during swallowing process (Durá et al., 2010). The methods analyzing continuous positional variation may necessitate complex analytical algorithms and heavy computation, which has impeded investigations of the distinguishing features of dysphagia.

Functional data analysis is a statistical method for evaluation of time-series data that are recorded at discrete time intervals (Wang et al., 2015). Discrete observations can be expressed in the form of a function that represent the entire measured function as a single observation using basis expansion and smoothing methods (Ullah and Finch, 2013). The method can be used to analyze hyoid motion data for accurate estimation of parameters with effective noise reduction and allows quantitative comparison of the motion curves between patients with PD and healthy controls. Functional regression analysis, which is the promising application in functional data analysis, may reveal the differential time interval during the swallowing process with respect to displacement/velocity (Morris, 2015).

Although reduced hyoid displacement and velocity were observed in the previous study, the kinematic features of the motion of the hyoid bone were not investigated as time-series data reflecting the process of swallowing (Kim et al., 2015). The functional linear regression model (FLR), which has not yet been applied in the analysis of swallowing motion, can demonstrate novel features of hyoid motion in patients with PD. Therefore, the aim of this study was to investigate spatio-temporal characteristics of the hyoid bone during swallowing in PD patients with dysphagia.

2. Materials and methods

2.1. Study design and population

Total 69 subjects (23 patients with PD, 23 age- and sex-matched healthy elderly controls, and 23 healthy young controls) were analyzed in this study. The PD patients were diagnosed by neurologists between January 1, 2015 and December 31, 2016, and had mild to moderate dysphagia corresponding to scores of 5–6 on the American Speech–Language–Hearing Association's National Outcome Measurement System (ASHA NOMS), as assessed with VFSS. Patients who had undergone tracheostomy; those suffering from diseases such as stroke, brain tumor, head and neck cancer, and those without any swallowing reflex during the examination were excluded. Demographic data, including sex, age, duration of disease, and duration of dysphagia

were collected. The data of healthy elderly and young controls were acquired from an anonymized VFSS data repository used in previous clinical studies (Leigh et al., 2015; Seong et al., 2018). The current study was approved by the relevant Institutional Review Board.

2.2. Swallowing assessment

Patients with PD presenting with swallowing difficulty were referred by neurologists to physiatrists. The physiatrists examined the patients clinically and evaluated swallowing function using VFSS, as described in detail in previous studies (Kim et al., 2015; Lee et al., 2016; Nam et al., 2013). VFSS was conducted by physiatrists with the assistance of radiologic technologists using a C-arm or fluoroscope. The patients were seated in an upright position and kept comfortable in a relaxed state. Before the VFSS, the PD patients were explained the overall process of examination and instructed to swallow the diluted barium solution in their usual manner after the verbal command. The volume of the administered liquid bolus was 2 mL of a 35% w/v diluted barium solution (Solutop Suspension, Tae Joon Pharm Corp., Ltd., Seoul, Korea) for all subjects. Based on the VFSS findings, the video-fluoroscopic dysphagia scale (VDS) (Kim et al., 2014) and ASHA NOMS swallowing scale were independently rated by two physiatrists.

2.3. Two-dimensional motion analysis

Displacement (HD) and velocity (HV) of the hyoid bone during swallowing were analyzed in this study. To obtain and calculate positional data of the hyoid bone, the swallowing motion analysis software, called spatio-temporal analyzer for motion and physiologic study (STAMPS; <https://github.com/cmookj/stamps>) was used in the present study (W. H. Lee et al., 2017). According to this software, the local coordinate system was defined for each image and the origin was set at the anteroinferior vertex of the fourth cervical vertebral body (C4) (Fig. 1). The vertical axis was the line connecting the origin to the anteroinferior vertex of the second vertebral body (C2), while the horizontal axis was perpendicular to the vertical axis. For clinical understanding, the horizontal axis was in the opposite direction to that of the conventional coordinate systems. The positional data of the hyoid bone, liquid bolus, C2 and C4 vertebrae, and a reference object were obtained by manually marking the target structures in each frame. To adjust for variation in the size of the structures involved in swallowing, the measurements were scaled using the ratio between the true and observed-in-image lengths of the reference object. In the present study, a coin with a diameter of 24 mm was used as the reference object to calculate the scale factor and the length between C2 and C4 was adjusted to 40 mm for spatial normalization. The starting points of the hyoid bone were set as the origin of the coordinate axes for comparison of trajectories. The time laps between the start- and endpoints of the swallowing process was interpolated to temporal values from 0 to 100 for temporal normalization (Chan et al., 2016). The start points were defined as the initiation of hyoid motion that resulted in a swallow (Kendall and Leonard, 2001).

2.4. Statistical analyses

Analyses for the demographic factors, VDS score, and maximal values of HD/HV were performed using the independent-samples *t*-test. The chi-squared test or Fisher's exact test was used to analyze proportions of subjects with abnormal VDS parameters: triggering of pharyngeal swallow, vallecular residue, laryngeal elevation, pyriform sinus residue, coating on the pharyngeal wall, pharyngeal transit time, and aspiration. Pearson or Spearman correlation coefficient was obtained to analyze the correlation between the VDS score and maximal values of HD/HV. The maximal values of HD/HV according to the VDS parameters and ASHA NOMS swallowing scale were analyzed using independent sample *t*-test or Mann-Whitney *U* test.

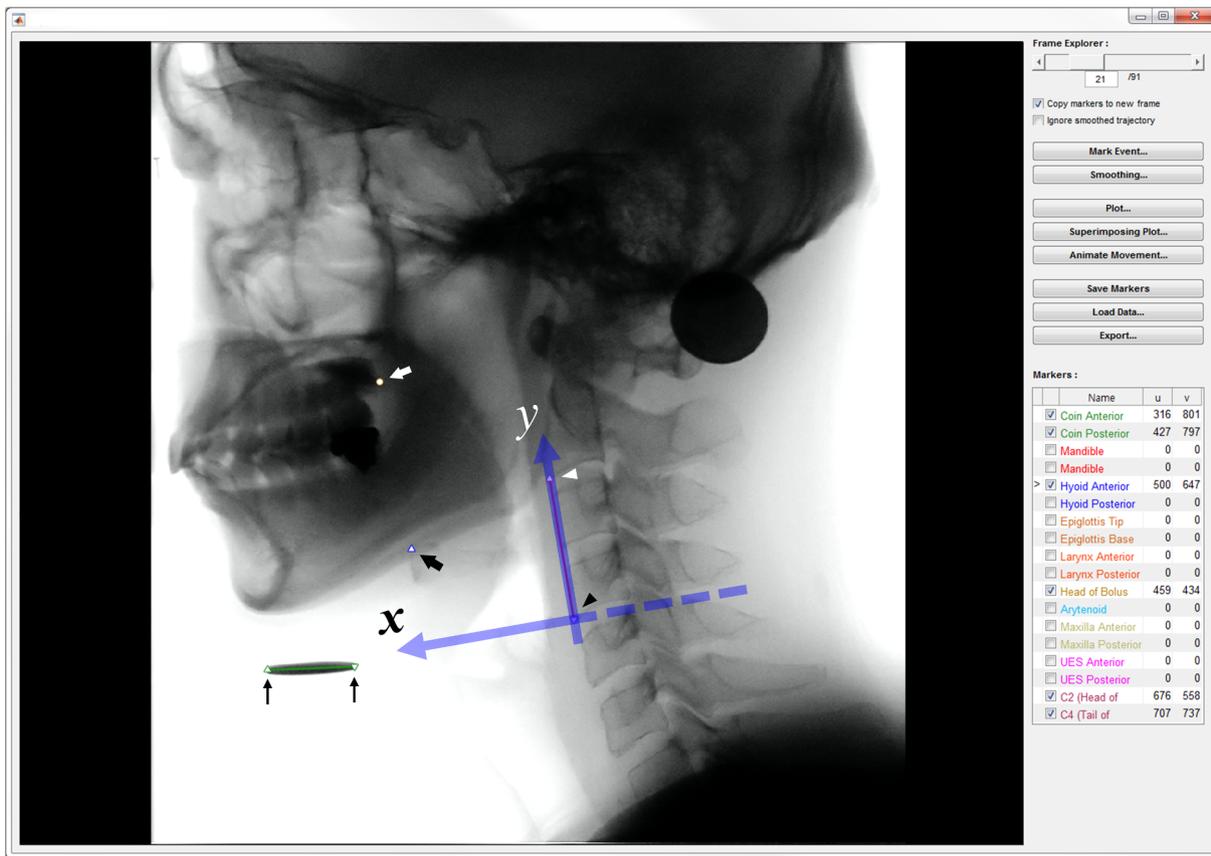


Fig. 1. The representation of a video fluoroscopic image and the coordinate systems using the swallowing motion analysis software. The horizontal axis is opposite in direction to that of the conventional coordinate systems for clinical understanding. The positional data of the hyoid bone (black solid arrow), liquid bolus (white solid arrow), second (white arrowhead) and fourth cervical vertebral bodies (black arrowhead), and a reference metal object (thin black arrow) were obtained by manually marking target structures in the software.

Positional data, obtained at discrete time points, can be mapped into sets of measurements along a continuum, called functional data, using a linear combination of basis functions, ϕ_k , which are B-spline functions (Levitin et al., 2007; Ramsay and Silverman, 2005). For the given true functions of $X_i(t)$ in the i -th subject, observation value with noise can be represented as $W_i(t) = X_i(t) + \epsilon_i(t)$ at time point t . $X_i(t)$ is estimated as $\hat{X}_i(t) = \sum_{k=1}^K \hat{c}_{ik} \phi_k(t)$. In general, this form can be expanded and represented as the concurrent regression model $y(t) = Z(t)\beta(t) + \epsilon(t)$, which consists of the functional matrix Z and regression coefficient function β for a given response function y .

In FLR, the response function y can be represented as

$$y_{ijk}(t) = \mu(t) + (-1)^i \alpha(t) + \beta_{ij}(t) + \epsilon_{ijk}(t), \quad (1)$$

where the output measure consists of a grand mean effect $\mu(t)$, mean difference $\alpha(t)$ between groups ($i = 1, 2$), effect of each subject $\beta_{ij}(t)$, and residual function $\epsilon_{ijk}(t)$. Smoothing for noise reduction and imposition of constraints on β_{ij} for identifiability of the model were also performed in the data analysis. Roughness penalties were used for regularization to prevent overfitting. To calculate regression coefficients, the penalized sum of squares (PENSSE $_{\lambda}$) was minimized with the least-squares approach. This step consisted of the two terms shown below.

$$\text{PENSSE}_{\lambda}(\alpha, \beta) = \sum [y_i - \alpha - \int x_i(t)\beta(t)dt]^2 + \lambda \int [L\beta(t)]^2 dt. \quad (2)$$

The PENSSE $_{\lambda}$ was minimized with penalty coefficient λ and operator L . Generalized cross-validation was adopted to identify the appropriate number of basis functions and the lambda value for penalization. Intergroup differences in hyoid displacement were fitted through FLR. Hyoid velocity was approximated using the symmetric

difference quotient as the sequence of the finite differences of the displacement. For all measures along time t , the difference in the hyoid motion was considered to be significant when the 95% confidence intervals of regression coefficients did not present with the value zero. Statistical significance was set at $P < 0.05$. This process was performed using R version 3.4.2 (The R Foundation, Vienna, Austria) with the *fd* package.

3. Results

Tables 1 and 2 summarize the demographics and VDS parameters in the patients with PD, healthy elderly controls, and healthy young controls included in the present study. The VDS score was significantly different between PD patients and healthy elderly controls (24.24 ± 12.41 vs 6.54 ± 7.28 , $P < 0.001$). The proportions of the subjects with abnormal VDS parameters were significantly different with respect to vallecular residue ($P = 0.011$), coating on the pharyngeal wall ($P < 0.001$), and aspiration ($P < 0.001$) between the two groups. No significant difference was observed between healthy elderly and young controls for both VDS score and proportions of each parameter.

The mean HDs in the horizontal and vertical planes for patients with PD, healthy elderly, and healthy young controls are shown in Fig. 2(A, D). The regression coefficient functions representing intergroup differences for the horizontal and vertical HDs over time between the PD patients and healthy elderly controls are shown in Fig. 2(B, E), and that between the healthy elderly and young controls in Fig. 2(C, F), respectively. Horizontal HD differed significantly between patients with PD and healthy elderly controls over the initial backward (9th–15th percentiles) and forward motions (33rd–69th percentiles). Vertical HD

Table 1
Demographics of patients with Parkinson's disease (PD), and healthy elderly and young controls.

	PD (n = 23)	Elderly (n = 23)	P (PD vs Elderly)	Young (n = 23)	P (Elderly vs Young)
Age (year)	70.8 ± 6.6	68.6 ± 5.0	0.213	36.0 ± 12.8	< 0.001
Sex (male)	12 (52.2)	12 (52.2)	1.000	11 (47.8)	1.000
ASHA-NOMS scale (5/6/7)	10/13/0	0/0/23	< 0.001	0/0/23	1.000
Disease duration (months)	111.7 ± 61.3	N/A	N/A	N/A	N/A
Dysphagia duration (months)	16.96 ± 28.4	N/A	N/A	N/A	N/A

Values are presented as mean ± standard deviation, or number (percent).

did not show any significant difference over time between the two groups. Between the healthy elderly and young controls, significant differences were observed in the horizontal and vertical HDs at the 51st–57th and 44th–62nd percentiles, respectively.

The mean HVs in the horizontal and vertical planes for patients with PD, healthy elderly, and healthy young controls are shown in Fig. 3(A, D). The regression coefficient functions representing intergroup differences for the horizontal and vertical HVs over time between patients with PD and healthy elderly controls are shown in Fig. 3(B, E), and that between the healthy elderly and healthy young controls in Fig. 3(C, F), respectively. The HV showed significant differences between patients with PD and healthy elderly controls at the 0–6th/27th–37th/47th–53rd/63rd–67th/93rd–97th percentiles in the horizontal plane, and the 0–3rd/83rd–87th percentiles in the vertical plane. Between the healthy elderly and young controls, the horizontal and vertical HVs were significantly different at the 19th–23rd/46th–51st percentiles, and 3rd–6th percentiles, respectively.

Table 3 shows the results of analysis for the maximal values of HD and HV. Both HD and HV of the horizontal plane differed significantly

in the initial backward ($P = 0.006$, $P < 0.001$, respectively), and forward motions ($P = 0.008$, $P < 0.001$, respectively) between patients with PD and healthy elderly controls. In the vertical plane, only HV showed significant difference between the two groups ($P = 0.001$). The HD and HV of the horizontal and vertical planes were not significantly different between the healthy elderly and young controls.

For the maximal values of HD and HV, the VDS score demonstrated a significant positive correlation with the horizontal HD/HV in the initial backward motion ($r = 0.353$, $P = 0.003$; $r = 0.481$, $P < 0.001$), and a significant negative correlation with the horizontal HD/HV in the forward motion ($r = -0.460$, $P < 0.001$; $r = -0.537$, $P < 0.001$). In the subgroup analysis for PD patients, the VDS score was significantly correlated with the horizontal HD ($\rho = -0.498$, $P = 0.016$) and HV ($\rho = -0.428$, $P = 0.042$) in the forward motion. Supplementary Materials 1–3 showed the significant associations between HD/HV and multiple VDS parameters in the PD patients and healthy controls. Among the PD patients, only vertical HV was significantly different between the groups with ASHA NOMS swallowing scale 5 and 6 ($n = 10$, 0.61 ± 0.17 vs $n = 13$, 0.79 ± 0.18 mm/%ile, $P = 0.022$).

Table 2

Parameters of pharyngeal swallowing based on the videofluoroscopic dysphagia scale in patients with Parkinson's disease (PD), and healthy elderly and young controls.

	PD (n = 23)	Elderly (n = 23)	P (PD vs Elderly)	Young (n = 23)	P (Elderly vs Young)
VDS score	24.24 ± 12.41	6.54 ± 7.28	< 0.001*	3.50 ± 5.25	0.111
Triggering of pharyngeal swallow			0.109		NA
Normal	19 (82.6)	23 (100.0)		23 (100.0)	
Delayed	4 (17.4)	0 (0.0)		0 (0.0)	
Vallecular residue			0.011*		0.134
None	2 (8.7)	7 (30.4)		12 (52.2)	
< 10%	13 (56.5)	16 (69.6)		11 (47.8)	
10–50%	5 (21.7)	0 (0.0)		0 (0.0)	
> 50%	3 (13.0)	0 (0.0)		0 (0.0)	
Laryngeal elevation			0.187		1.000
Normal	18 (78.3)	22 (95.7)		23 (100.0)	
Impaired	5 (21.7)	1 (4.3)		0 (0.0)	
Pyriform sinus residue			0.293		0.536
None	10 (43.5)	14 (60.9)		16 (69.6)	
< 10%	10 (43.5)	9 (39.1)		7 (30.4)	
10–50%	2 (8.7)	0 (0.0)		0 (0.0)	
> 50%	1 (4.3)	0 (0.0)		0 (0.0)	
Coating on the pharyngeal wall			0.001*		0.699
No	7 (30.4)	18 (78.3)		20 (87.0)	
Yes	16 (69.6)	5 (21.7)		3 (13.0)	
Pharyngeal transit time			0.109		NA
≤ 1.0 s	19 (82.6)	23 (100.0)		23 (100.0)	
> 1.0 s	4 (17.4)	0 (0.0)		0 (0.0)	
Aspiration			< 0.001*		0.233
None	3 (13.0)	20 (87.0)		23 (100.0)	
Supraglottic penetration	9 (39.1)	3 (13.0)		0 (0.0)	
Subglottic aspiration	11 (47.8)	0 (0.0)		0 (0.0)	

NA: Not available due to equal proportions between the two groups.

Values are presented as mean ± standard deviation, or number (percent).

* P value < 0.05.

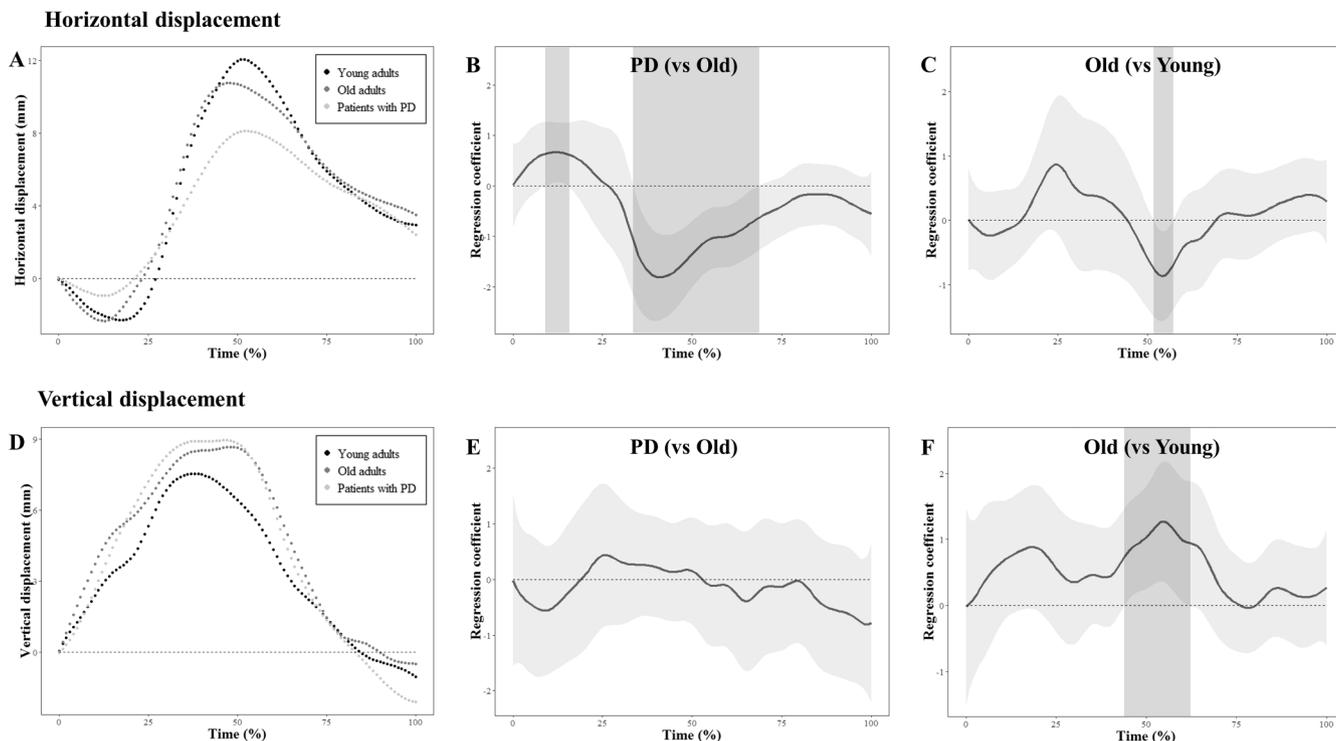


Fig. 2. Results of functional regression analysis for horizontal and vertical displacements of the hyoid bone. Mean trajectories of the horizontal (A) and vertical (D) displacements in patients with Parkinson’s disease, healthy elderly and young controls. Estimated regression coefficient functions with 95% confidence intervals for the horizontal and vertical displacements between patients with Parkinson’s disease and healthy elderly controls (B, E), and between healthy elderly and young controls (C, F). The light gray zones denote the time interval where the mean difference is significant between the groups.

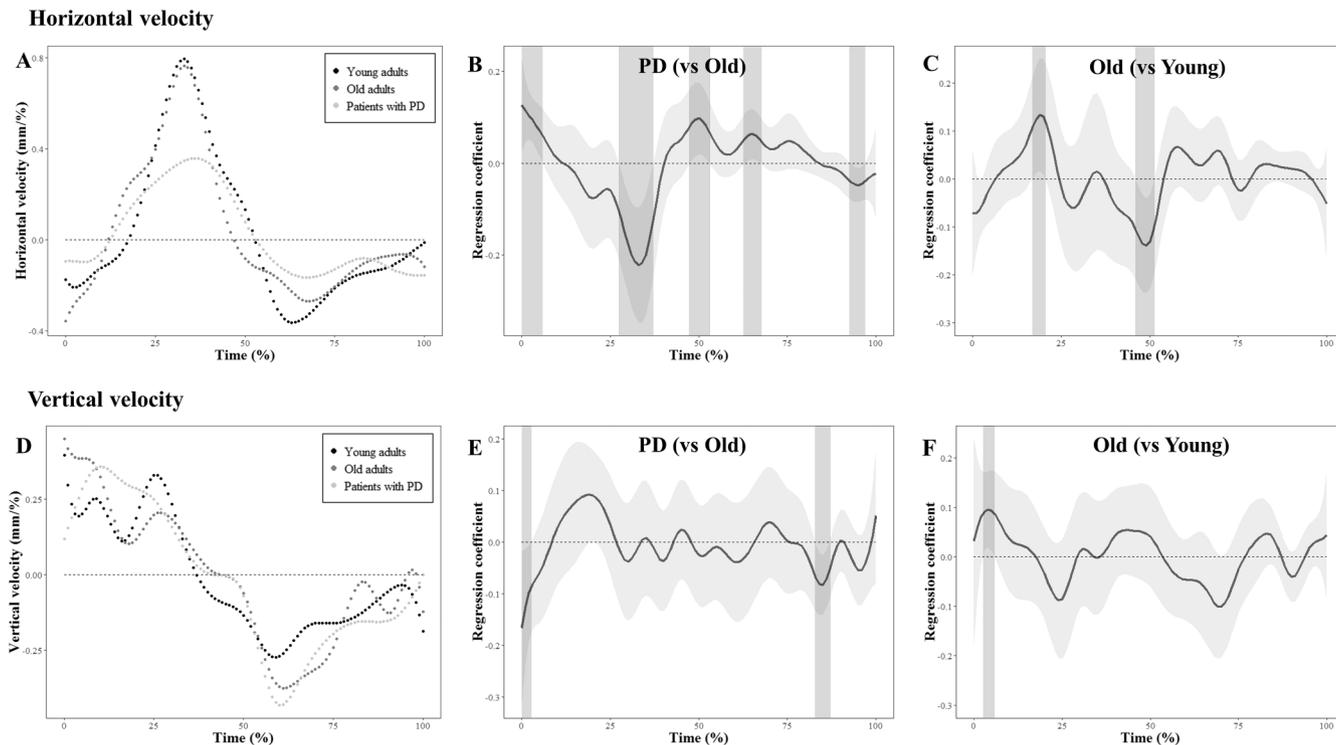


Fig. 3. Results of functional regression analysis for horizontal and vertical velocities of the hyoid bone. Mean trajectories of the horizontal (A) and vertical (D) velocities in patients with Parkinson’s disease, healthy elderly and young controls. Estimated regression coefficient functions with 95% confidence intervals for the horizontal and vertical velocities between patients with Parkinson’s disease and healthy elderly controls (B, E), and between healthy elderly and young controls (C, F). The light gray zones denote the time interval where the mean difference is significant between the groups.

Table 3

Results of analysis for the maximal displacement and velocity of the hyoid bone in patients with Parkinson's disease, and healthy elderly and young controls.

	PD (n = 23)	Elderly (n = 23)	P (PD vs Elderly)	Young (n = 23)	P (Elderly vs Young)
Maximal horizontal displacement (mm)					
Backward	-1.83 ± 1.21	-3.49 ± 2.14	0.006*	-3.46 ± 1.78	0.999
Forward	8.93 ± 3.00	12.30 ± 4.33	0.008*	13.5 ± 3.50	0.488
Maximal vertical displacement (mm)					
Upward	11.60 ± 5.12	10.50 ± 5.32	0.756	9.46 ± 5.31	0.763
Time to maximal displacement (%ile)					
Horizontal, backward	16.22 ± 9.30	14.97 ± 7.42	0.844	18.56 ± 5.87	0.258
Horizontal, forward	52.61 ± 11.55	51.07 ± 12.13	0.876	50.90 ± 7.84	0.998
Vertical, upward	38.40 ± 15.60	38.44 ± 11.95	0.999	41.23 ± 9.74	0.736
Maximal horizontal velocity (mm/%ile)					
Backward	-0.20 ± 0.03	-0.61 ± 0.32	< 0.001 [†]	-0.59 ± 0.31	0.972
Forward	0.63 ± 0.27	1.26 ± 0.47	< 0.001 [†]	1.38 ± 0.47	0.569
Maximal vertical velocity (mm/%ile)					
Upward	0.71 ± 0.20	1.23 ± 0.55	0.001*	1.00 ± 0.60	0.243
Time to maximal velocity (%ile)					
Horizontal, backward	7.29 ± 8.24	3.59 ± 6.14	0.139	5.98 ± 6.08	0.418
Horizontal, forward	32.26 ± 8.68	29.35 ± 7.30	0.426	33.67 ± 6.98	0.151
Vertical, upward	20.65 ± 13.08	12.11 ± 11.89	0.060	13.38 ± 12.52	0.936

Values are presented as mean ± standard deviation.

* P value < 0.05.

4. Discussion

The current study presents the kinematic features of swallowing in patients with PD using FLR. An analysis of the entire motion profiles of the hyoid bone during swallowing enabled sensitive detection of distinct features of swallowing in patients with PD: decreased horizontal HD and HV during the initial backward and forward motions. These findings were supported by the results of analysis of the maximal HD and HV between patients with PD and healthy elderly controls. The trajectories of the hyoid bone during swallowing in patients with PD could be distinguished from normal age-related changes by the comparison between the healthy elderly and young controls.

To the best of our knowledge, this is the first study to specifically assess pointwise differences in swallowing motion over time in patients with PD. Traditional approaches for the analysis of swallowing motion involve comparison of mean or maximal values over the time course of the observational data (Levitin et al., 2007). Maximal and mean values of HD and HV have been reported to be significant parameters for differentiation of patients with dysphagia from healthy controls, which was grossly consistent with the findings of the current study (Kim et al., 2015; Paik et al., 2008; Seo et al., 2016). The current study revealed several novel features of kinematics of the hyoid bone in patients with PD, by normalizing and transforming discrete data of hyoid motion to functional data, and describing reduced horizontal HD and HV over the period of each initial backward and forward motion. The analyses of maximal HD and HV between patients with PD and healthy elderly controls also showed consistent results with these findings. The VDS, which is the swallowing functional scale based on the VFSS, showed significant correlations with the horizontal HD/HV in the initial backward and forward motions. Patients with PD demonstrated significant reduction in maximal values of vertical HV despite preservation of vertical HD. Additionally, healthy elderly controls showed significantly decreased horizontal HD in forward motion, but increased vertical HD in upward motion compared to the healthy young controls in FLR, even though no significant difference was observed in the maximal values of HD. These results indicated that reduced horizontal displacement and velocity of the hyoid bone over the forward motion during swallowing could be attributed to the combined effects of disease and aging, whereas those over the initial backward motion may be considered specific to patients with PD.

The backward motion of the hyoid bone was preserved regardless of aging, which implies that reduced backward motion of the hyoid bone

during the early phase of swallowing may be one of the pathologic findings in PD patients with dysphagia. Previously, few studies have been published on the physiological role of initial backward hyoid motion on swallowing function. According to the literature, the suprahyoid muscles were sequentially recruited during swallowing by contractions of the stylohyoid, posterior digastric, and mylohyoid muscles, followed by those of the geniohyoid and anterior digastric muscles (Okada et al., 2013; Park et al., 2017). In the activation sequences, the stylohyoid and posterior digastric muscles with the force vector in the backward-upward direction can have the capacity to pull the hyoid bone backward simultaneously or prior to moving it in a forward-upward direction (Pearson et al., 2011). If the backward and forward motions of the hyoid bone are sequentially engaged in the initial swallowing process, it might be assumed that the backward motion helps generate strong forces for the forward/upward motion by increasing the length of the suprahyoid muscles in the early phase of swallowing (Rassier et al., 1999). The biomechanics of pulling the hyoid bone forward by the suprahyoid muscles, which behave with viscoelastic properties, can be possibly impaired in individuals with a reduced backward motion of the hyoid bone (Kim et al., 1999; Taylor et al., 1990). Primary motor manifestations including resting tremor, bradykinesia, incoordination, and rigidity that may affect the sequential activation of suprahyoid muscles can plausibly underlie the altered hyoid kinematics, resulting in impaired safety and efficacy of swallowing in PD patients. Multiple swallowing parameters rated by the VDS showed a significant association with the horizontal HD and/or HV of the initial backward motion, including triggering of pharyngeal swallow, vallecular residue, laryngeal elevation, coating on the pharyngeal wall, pharyngeal transit time, and aspiration (Supplementary Material 1). Further studies are necessary to elucidate detailed biomechanical properties and physiological role of the initial backward motion on swallowing function in PD patients.

Interestingly, vertical HD was highest in patients with PD, followed by healthy elderly and young controls, which was consistent with the results of previous studies (Kang et al., 2010; Kim et al., 2015). In contrast to the reduction in horizontal HD, vertical HD was preserved or even exaggerated in aging and neurodegenerative diseases. On the other hand, both horizontal and vertical HV were significantly decreased in patients with PD, which corresponds to the typical characteristics of such patients, namely bradykinesia and incoordination. The preserved HD with overall decline of HV implicated the possibility of a compensatory mechanisms to mask the effects of aging or

neurodegenerative diseases, which is more likely to occur at a greater vertical and not horizontal HD (Kang et al., 2010). One of the common natural compensatory mechanisms in swallowing impairment is effortful swallowing. Previous study revealed that effortful swallowing can increase every parameter of maximal displacement and velocity of the hyolaryngeal complex except the horizontal HD and HV, which is consistent with the results of the present study (Jang et al., 2015). Additional biomechanical study of the individual hyoid muscles is required to prove the compensatory mechanisms in aging and neurodegenerative diseases.

Functional data analysis is a statistical method for analyzing functional data and can be applied to noise reduction, derivative calculation, and fitting parameters of dynamic systems. The method can be a preliminary approach for more structured analyses and for providing novel insights into hidden mechanisms (Levitin et al., 2007). Functional data analysis extends the capabilities of conventional analysis to capture the temporal patterns of time-series data and facilitates clear interpretation of changes in the shape of the curve (Durá et al., 2010; Levitin et al., 2007). In the present study, FLR, which is a part of functional data analysis, was successfully applied for observation of swallowing motions. The displacement and velocity, which are the main parameters of swallowing motion, are continuous, smooth, interrelated, and change over time. These properties meet the assumptions of functional data analysis, making it a powerful tool for analysis of the kinematics of swallowing. The results of the present study clarified the aspects that are important for differentiating dysphagia from normal swallowing functions. Since swallowing is a complex activity involving sequential interactions among bone, cartilage, muscle, and other structures, these aspects would be critical to demonstrate differences in motions between healthy controls and patients with PD.

The present study has several limitations. First, the severity of impairment of the general physical function of patients with PD was not measured due to retrospective nature of the study. However, the severity of dysphagia of all patients with PD included in the present study was measured using the ASHA-NOMS swallowing scale, and only cases of mild to moderate dysphagia with ratings of 5–6 were included. Second, the sample size of the present study was relatively small. Further research should be supported by a large population of PD patients with mild to severe dysphagia. Third, the liquid bolus in this study was only 2 mL because of many missing data for large and viscous liquid. A previous study reported that a distinct pattern of changes in hyoid motion was not observed in PD patients with respect to bolus volume in contrast with healthy adults (Wintzen et al., 1994). This study interpreted that hypokinesia in PD patients was represented as lack of adaptation for the larger bolus. Further studies are necessary to investigate the volume effect on hyoid kinematics in PD patients.

5. Conclusion

The present study revealed that reduced horizontal HD and HV during the initial backward and forward motions are important kinematic features of swallowing in patients with PD. These kinematic parameters also showed a significant correlation with the swallowing functional scale. The reduced horizontal displacement and velocity of the hyoid bone over the forward motion could be attributed to the combined effects of disease and aging, whereas those over the initial backward motion may be considered specific to patients with PD. The results implicated that horizontal HD and HV during the initial backward and forward motions can have potential clinical usefulness to estimate the swallowing impairment in PD patients. Further studies will be needed to reveal the detailed biomechanical properties and physiological role of the initial backward motion of the hyoid bone in PD patients.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jelekin.2019.05.011>.

References

- Argolo, N., Sampaio, M., Pinho, P., Melo, A., Nóbrega, A.C., 2015. Videofluoroscopic predictors of penetration-aspiration in Parkinson's disease patients. *Dysphagia* 30, 751–758. <https://doi.org/10.1007/s00455-015-9653-y>.
- Bird, M.R., Woodward, M.C., Gibson, E.M., Phyland, D.J., Fonda, D., 1994. Asymptomatic swallowing disorders in elderly patients with Parkinson's disease. *Age Ageing* 23, 251–254.
- Chan, J., Gil, H., Hyung, W., Chan, H., 2016. Computer-assisted detection of swallowing. *Comput. Methods Programs Biomed.* 134, 79–88. <https://doi.org/10.1016/j.cmpb.2016.07.010>.
- Davie, C.A., 2008. A review of Parkinson's disease. *Br. Med. Bull.* 86, 109–127. <https://doi.org/10.1093/bmb/ldn013>.
- Dodrill, P., Gosa, M.M., 2015. Pediatric dysphagia: Physiology, assessment, and management. *Ann. Nutr. Metab.* 66, 24–31. <https://doi.org/10.1159/000381372>.
- Durá, J.V., Belda, J.M., Poveda, R., Page, Á., Laparra, J., Das, J., Prat, J., García, A.C., 2010. Comparison of functional regression and nonfunctional regression approaches to the study of the walking velocity effect in force platform measures. *J. Appl. Biomech.* 26, 234–239. <https://doi.org/10.1123/jab.26.2.234>.
- Feng, X., Todd, T., Hu, Y., Lintzenich, C.R., Carr, J.J., Browne, J.D., Kritchevsky, S.B., Butler, S.G., 2014. Age-related changes of hyoid bone position in healthy older adults with aspiration. *Laryngoscope* 124. <https://doi.org/10.1002/lary.24453>.
- Jang, H.J., Leigh, J.H., Seo, H.G., Han, T.R., Oh, B.M., 2015. Effortful swallow enhances vertical hyolaryngeal movement and prolongs duration after maximal excursion. *J. Oral Rehabil.* 42, 765–773. <https://doi.org/10.1111/joor.12312>.
- Kang, B.S., Oh, B.M., Kim, I.S., Chung, S.G., Kim, S.J., Han, T.R., 2010. Influence of aging on movement of the hyoid bone and epiglottis during normal swallowing: A motion analysis. *Gerontology* 56, 474–482. <https://doi.org/10.1159/000274517>.
- Kendall, K.A., Leonard, R.J., 2001. Hyoid movement during swallowing in older patients with dysphagia. *Arch. Otolaryngol. – Head Neck Surg.* 127, 1224–1229. <https://doi.org/10.1001/archotol.127.10.1224>.
- Kim, J., Oh, B.M., Kim, J.Y., Lee, G.J., Lee, S.A., Han, T.R., 2014. Validation of the videofluoroscopic dysphagia scale in various etiologies. *Dysphagia* 29, 438–443. <https://doi.org/10.1007/s00455-014-9524-y>.
- Kim, S.M., McCulloch, T.M., Rim, K., 1999. Comparison of viscoelastic properties of the pharyngeal tissue: Human and canine. *Dysphagia* 14, 8–16. <https://doi.org/10.1007/PL00009584>.
- Kim, Y.H., Oh, B.M., Jung, I.Y., Lee, J.C., Lee, G.J., Han, T.R., 2015. Spatiotemporal characteristics of swallowing in Parkinson's disease. *Laryngoscope* 125, 389–395. <https://doi.org/10.1002/lary.24869>.
- Lee, S.H., Oh, B.M., Chun, S.M., Lee, J.C., Min, Y., Bang, S.H., Kim, H.C., Han, T.R., 2013. The accuracy of the swallowing kinematic analysis at various movement velocities of the hyoid and epiglottis. *Ann. Rehabil. Med.* 37, 320–327. <https://doi.org/10.5535/arm.2013.37.3.320>.
- Lee, T., Park, J.H., Sohn, C., Yoon, K.J., Lee, Y.T., Park, J.H., Jung, I.S., 2017a. Failed deglutitive upper esophageal sphincter relaxation is a risk factor for aspiration in stroke patients with oropharyngeal dysphagia. *J. Neurogastroenterol. Motil.* 23, 34–40. <https://doi.org/10.5056/jnm16028>.
- Lee, W.H., Chun, C., Seo, H.G., Lee, S.H., Oh, B.M., 2017b. STAMPS: Development and verification of swallowing kinematic analysis software. *Biomed. Eng. Online* 16, 1–12. <https://doi.org/10.1186/s12938-017-0412-1>.
- Lee, W.H., Oh, B.M., Seo, H.G., Kim, S.K., Phi, J.H., Chong, S., Han, T.R., 2016. One-year outcome of postoperative swallowing impairment in pediatric patients with posterior fossa brain tumor. *J. Neurooncol.* 127, 73–81. <https://doi.org/10.1007/s11060-015-2010-z>.
- Leigh, J.H., Oh, B.M., Seo, H.G., Lee, G.J., Min, Y., Kim, K., Lee, J.C., Han, T.R., 2015. Influence of the chin-down and chin-tuck maneuver on the swallowing kinematics of healthy adults. *Dysphagia* 30, 89–98. <https://doi.org/10.1007/s00455-014-9580-3>.
- Levitin, D.J., Nuzzo, R.L., Vines, B.W., Ramsay, J.O., 2007. Introduction to functional data analysis. *Can. Psychol.* 48, 135–155. <https://doi.org/10.1037/cp2007014>.
- Morris, J.S., 2015. Functional regression. *Annu. Rev. Stat. Its Appl.* 2, 321–359. <https://doi.org/10.1146/annurev-statistics-010814-020413>.

- Nam, H.S., Beom, J., Oh, B.M., Han, T.R., 2013. Kinematic effects of hyolaryngeal electrical stimulation therapy on hyoid excursion and laryngeal elevation. *Dysphagia* 28, 548–556. <https://doi.org/10.1007/s00455-013-9465-x>.
- Nam, H.S., Oh, B.M., Han, T.R., 2015. Temporal characteristics of hyolaryngeal structural movements in normal swallowing. *Laryngoscope* 125, 2129–2133. <https://doi.org/10.1002/lary.25229>.
- Okada, T., Aoyagi, Y., Inamoto, Y., Saitoh, E., Kagaya, H., Shibata, S., Ota, K., Ueda, K., 2013. Dynamic change in hyoid muscle length associated with trajectory of hyoid bone during swallowing: analysis using 320-row area detector computed tomography. *J. Appl. Physiol.* 115, 1138–1145. <https://doi.org/10.1152/jappphysiol.00467.2013>.
- Paik, N.J., Kim, S.J., Lee, H.J., Jeon, J.Y., Lim, J.Y., Han, T.R., 2008. Movement of the hyoid bone and the epiglottis during swallowing in patients with dysphagia from different etiologies. *J. Electromyogr. Kinesiol.* 18, 329–335. <https://doi.org/10.1016/j.jelekin.2006.09.011>.
- Park, D., Lee, H.H., Lee, S.T., Oh, Y., Lee, J.C., Nam, K.W., Ryu, J.S., 2017. Normal contractile algorithm of swallowing related muscles revealed by needle EMG and its comparison to videofluoroscopic swallowing study and high resolution manometry studies: A preliminary study. *J. Electromyogr. Kinesiol.* 36, 81–89. <https://doi.org/10.1016/j.jelekin.2017.07.007>.
- Pearson, W.G., Langmore, S.E., Zumwalt, A.C., 2011. Evaluating the structural properties of suprahyoid muscles and their potential for moving the hyoid. *Dysphagia* 26, 345–351. <https://doi.org/10.1007/s00455-010-9315-z>.
- Ragland, M.C., Park, T., McCullough, G., Kim, Y., 2016. The speed of the hyoid excursion in normal swallowing. *Clin. Arch. Commun. Disord.* 1, 30–35. <https://doi.org/10.21849/cacd.2016.00010>.
- Ramsay, J.O., Silverman, B.W., 2005. *Functional Data Analysis, Second ed.* Springer-Verlag, New York.
- Rassier, D.E., Macintosh, B.R., Herzog, W., 1999. Length dependence of active force production in skeletal muscle. *J. Appl. Physiol.* 86, 1445–1457.
- Rugiu, M.G., 2007. Role of videofluoroscopy in evaluation of neurologic dysphagia. *Acta Otorhinolaryngol. Ital.* 27, 306–316. <https://doi.org/10.1088/1361-6641/aaae56>.
- Schindler, J.S., Kelly, J.H., 2002. Swallowing disorders in the elderly. *Laryngoscope* 112, 589–602. <https://doi.org/10.1097/00005537-200204000-00001>.
- Seo, H.G., Oh, B.M., Han, T.R., 2016. Swallowing kinematics and factors associated with laryngeal penetration and aspiration in stroke survivors with dysphagia. *Dysphagia* 31, 160–168. <https://doi.org/10.1007/s00455-015-9670-x>.
- Seong, M.Y., Oh, B.M., Seo, H.G., Han, T.R., 2018. Influence of supraglottic swallow on swallowing kinematics: comparison between the young and the elderly. *J. Korean Dysphagia Soc.* 101, 23–29.
- Steele, C.M., Bailey, G.L., Chau, T., Molfenter, S.M., Oshalla, M., Waito, A.A., Zoratto, D.C.B.H., 2011. The relationship between hyoid and laryngeal displacement and swallowing impairment. *Clin. Otolaryngol.* 36, 30–36. <https://doi.org/10.1111/j.1749-4486.2010.02219.x>.
- Suttrup, I., Warnecke, T., 2016. Dysphagia in Parkinson's disease. *Dysphagia* 31, 24–32. <https://doi.org/10.1007/s00455-015-9671-9>.
- Taylor, D.C., Dalton, J.D., Seaber, A.V., Garrett, W.E., 1990. Viscoelastic properties of muscle-tendon units: The biomechanical effects of stretching. *Am. J. Sports Med.* 18, 300–309. <https://doi.org/10.1177/036354659001800314>.
- Ullah, S., Finch, C.F., 2013. Applications of functional data analysis: A systematic review. *BMC Med. Res. Methodol.* 13, 43. <https://doi.org/10.1186/1471-2288-13-43>.
- Volonté, M.A., Porta, M., Comi, G., 2002. Clinical assessment of dysphagia in early phases of Parkinson's disease. *Neurol. Sci.* 23, S121–S122. <https://doi.org/10.1007/s100720200099>.
- Wang, J.-L., Chiou, J.-M., Müller, H.-G., 2015. Review of functional data analysis. *Annu. Rev. Stat. Its Appl.* 3, 257–295. <https://doi.org/10.1146/annurev-statistics-041715-033624>.
- Wintzen, A.R., Badrising, U.A., Roos, R.A., Vielvoye, J., Liauw, L., 1994. Influence of bolus volume on hyoid movements in normal individuals and patients with Parkinson's disease. *Can. J. Neurol. Sci.* 21, 57–59.