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On the Physiology of Normal Swallowing as Revealed by Real-Time Magnetic Resonance Imaging

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Abstract
The purpose of this research was to evaluate the physiology of normal swallowing utilizing current developments in real-time magnetic resonance imaging (MRI). As a result, ten young healthy volunteers were subjected to real-time MRI and flexible endoscopic swallowing evaluations (FEES) with thickened pineapple juice as an oral contrast bolus. MRI movies were captured at approximately 25 frames per second in sagittal, coronal, and axial orientations during successive swallows. Inter-measurement variance was investigated, as well as comparisons between real-time MRI and FEES. Real-time MRI could detect twelve separate swallowing events (start time, end time, and duration). There were five valve functions: oro-velar opening, velo-pharyngeal closure, glottal closure, epiglottic retroflexion, and esophageal opening; three bolus transports: oro-velar transit, pharyngeal delay, pharyngeal transit; and four additional events: : laryngeal ascent, laryngeal descent, vallecular, and piriform sinus filling and pharyngeal constriction. Repetitive measurements confirmed the general reliability of the MRI method with only two significant differences for the start times of the velo-pharyngeal closure ($t(8) = -2.4$, $P \leq 0.046$) and laryngeal ascent ($t(8) = -2.6$, $P \leq 0.031$). The duration of the velo-pharyngeal closure was significantly longer in real-time MRI compared to FEES ($t(8) = -3.3$, $P \leq 0.011$). Real-time MRI emerges as a simple, robust, and reliable tool for obtaining comprehensive functional and anatomical information about the swallowing process.

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I. Introduction

Oropharyngeal dysphagia is a common complication of neuromuscular and neurological illnesses, as well as structural and organic abnormalities of the oropharyngeal tract in older patients [1, 2]. Deglutitive faults as a result include incorrect bolus direction with penetration and aspiration, insufficient bolus clearance with retentions in the vallecula and piriform sinuses, and extended or erratic timing of swallowing events during deglutition [3]. Because the succinct temporal succession of the various swallowing phases is crucial for bolus direction and clearance, it would be useful to have a diagnostic instrument capable of detecting and characterizing them with appropriate contrast and resolution. At the moment, videofluoroscopy is the gold standard for diagnosing deglutitive problems. It provides dynamic images in the sagittal plane that depict the entire course of deglutition, but it exposes patients to X-ray radiation. A coronal plane view is frequently required to rule out laryngeal penetration, but an axial plane view is not attainable.

Due to the limited visibility of soft tissues, timing evaluation of physiological processes during swallowing is solely based on bony anatomic landmarks. Flexible endoscopic evaluations of swallowing (FEES), on the other hand, provide an axial view and allow for pre- and post-deglutitive studies, which are useful for clinical diagnosis and therapy planning in swallowing disorders. However, the "white out" during swallowing makes it difficult to detect quiet intra-deglutitive aspiration and hence precludes timing investigations. High-resolution manometry has recently been demonstrated to be a reliable predictor of aspiration in the diagnosis of oropharyngeal dysphagia [4]. Preliminary research utilizing magnetic resonance imaging (MRI) showed potential for evaluating swallowing events and movements in the supine position [5-9].

However, such trials typically had poor spatial and temporal resolution. An axial plane was not generally considered, and event timing analysis was difficult due to rather poor image quality. Fortunately, recent developments in real-time MRI have achieved not only good picture quality, outstanding tissue contrast, and virtually no motion aberrations, but also spatiotemporal resolution equivalent to that of conventional videofluoroscopy [10, 11]. A preliminary investigation focused on technical factors effectively showed the movements of the oropharyngeal structures during normal swallowing and revealed considerable promise for providing noninvasive access to the deglutition process [12].

II. Materials And Methods

2.1. Subjects : Ten healthy volunteers (4 men, 6 women) were recruited from the local university, with a mean age of 28 ± 3 years (SD = standard deviation) and a range of 26 to 35 years. The selection criteria included no history of dyspnea, dysphonia, or dysphagia. They were met based on a personal medical history and a FEES examination of all participants performed by a competent otorhinolaryngologist (A. O.). The study was authorized by the Institutional Review Board, and all individuals provided written informed permission prior to evaluation. The same participants' MRI data were used in a prior paper describing the real-time approach [12].

2.2. FEES : In a sitting position, trans-nasal FEES was performed with an usual temporal resolution of 25 frames per second (fps). To ensure a distinct contrast to the tissues of the oropharyngeal tract, an oral bolus of one teaspoon (5 mL) greencolored pear pie was utilised. The flexible endoscope (Olympus ENF, Hamburg, Germany) was linked to a camera (Olympus visera OTVS-7, Hamburg, Germany), and the movies were saved on a hard disc (rpSzene, Rehder & Partner GmbH, Hamburg, Germany) for further analysis.

2.3. MRI in Real Time : A 3 Tesla MRI device was used to produce real-time dynamic MRI of deglutition (Tim Trio, Siemens Healthcare, Erlangen, Germany). The recently published real-time MRI approach [12] is based on radial fast low-angle shot (FLASH) collection [13] combined with image reconstruction by regularized nonlinear inversion [14]. Online reconstruction at about 17 frames per second was achieved by running a parallelized version of the method on a computer equipped with 8 graphics processing units, bypassing the commercial MRI system's conventional image reconstruction pipeline [15, 16]. array coil (NORAS MRI products, Hoechberg, Germany) centered to the thyroid prominence on both sides of the neck. Successive T1-weighted images (repetition time TR = 2.17 ms,
echo time TE = 1.44 ms, flip angle 5, field of view 192 ×192 mm2) were acquired with an in-plane resolution of 1.5 ×1.5 mm2 and a slice thickness of 10 mm in a midsagittal, oblique coronal, and oblique axial orientation. The total image acquisition time was 41.23 ms, which yielded a true temporal resolution of 24.3 fps without data interpolation or combination.

Because pineapple juice contains paramagnetic manganese, which produces a prominent signal in T1-weighted images, it was utilised as an oral contrast agent [17]. To improve the visibility of tissue activities and motions, the pineapple juice was thickened with starch (Quick & Dick, Pfrimmer Nutricia, Erlangen, Germany) before to the inspection. During the examination, an otorhinolaryngologist (A. O.) administered the thickened bolus (5 mL). After the dynamic image capture began, the individual was urged to swallow naturally and at a comfortable rate. Individual swallow movies were recorded twice in the same sagittal plane and 4 to 5 times in a coronal as well as numerous axial planes (5 mm shifts) to cover the full region of interest due to the complicated movements of the key anatomical components during deglutition. A previous article [12] provided further information on the imaging technology and examination procedure.

(2.4). Swallowing Events : The viewing software OsiriX (open-source software: http://www.osirix-viewer.com/) [18] and iMovie HD (version 6.0.3, Apple Computer Inc., USA) were used for real-time MRI movies and FEES recordings, respectively, to analyse swallowing events and quantitative timings. Both systems allowed for a "frame by frame" analysis of the data and were used by one otorhinolaryngologist to characterize and quantitatively assess various deglutition episodes, notably their start and end positions (A. O.). The notion of Logemann's "six-valve model" proposed from videofluoroscopic data [3] was used as a reference for the examination of valve functions and was compared to the current findings. To assess the visibility of each defined event, the timings of respective start and end points were classified in a dichotomic manner (yes or no). The results served to calculate a visibility ratio (in percentage) for each image orientation for all subjects. Only the orientation offering the highest visibility ratio was used for a determination of quantitative timings.

2.5. Quantitative Timings : Each event's absolute duration was estimated by subtracting the timings of its end and start point photos. A reference event had to be chosen for relative timings. Although prior research [12, 19] used esophageal opening, the uncertain appearance of the sphincter during bolus transport in the MRI movies hampered a firm description of the event. During deglutition, the oro-velar opening or velum elevation from the dorsum of the tongue could always be observed as a distinct landmark and thus functioned as a temporal reference for all subsequent events with its start time set to zero.

Table 1: Swallowing events revealed by real-time MRI and videofluoroscopy.

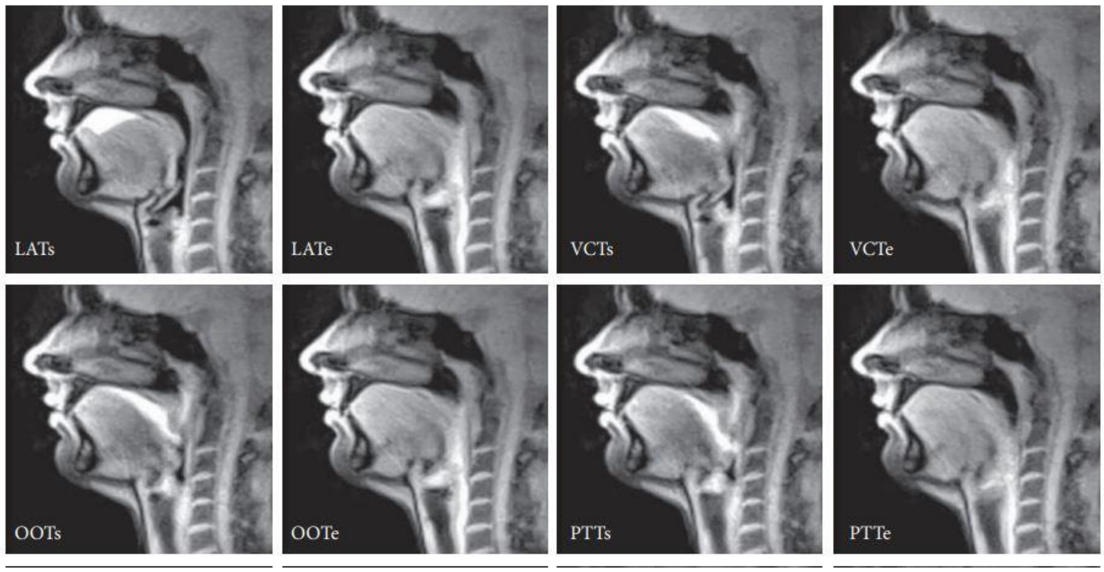
Deglutition events	Real-time MRI	Videofluoroscopy [3]
Valve function		
Oro-velar opening (OOT□, reference)	**Full rise of soft palate from dorsum**	**Not defined**
Velar-pharyngeal closure (VCT)	**Contact of soft palate and pharyngeal wall**	**Velopharyngeal sphincter (valve 3)**
Glottal closure (GCT)	**Closure of glottis and supraglottis**	**Larynx: vocal folds (valve 4c)**
Epiglottic retroflexion (ERT)	**Contact of epiglottis and supraglottis**	**Larynx: epiglottis and arytenoid to base of epiglottis (valve 4a/b)**
Esophageal opening (EOT)	**Separation of postcricoid and pharyngeal wall**	**Cricopharyngeal sphincter (valve 6)**
Bolus Transit		**Oral Transit**
Ore- velar transit (OTT)	s: OOTs e: OOTe	s: initiation of tongue movement e: bolus head reaches the cross of mandible and tongue base
Pharyngeal delay (PDT)	s: OTTs (OOTs) e: PTTs	s: bolus head reaches cross ofmandible andtongue base. e: start of laryngeal ascent
Pharyngeal transit (PTT)	s: bolus head passes oro-velar valve e: bolus tail passesesophageal sphincter	s: start of laryngeal ascent e: bolus tail passes cricopharyngeal region
Other		
Laryngeal ascent (LAT)	Ascendance of larynx	Upward and forward movement of hyoid and larynx
Laryngeal descent (LDT)	Descendance of larynx	Not defined
Vallecula and piriform sinus filling (SFT)	Bolus filling vallecula and piriform sinus	Not observed
Pharyngeal constriction (PCT)	Progressive contraction of pharyngeal constrictor	Tongue base and pharyngeal wall (valve 5). Not observed [3]

2.6. Statistics : Two-way repeated measures ANOVAs with the factors "measurements" and "events" were conducted to investigate possible differences for the start times, end times, and durations of defined events in two repetitive sagittal measurements. Post hoc paired t-tests between these measurements were conducted if applicable. For comparison between real-time MRI and FEES, the absolute timings of the same event were evaluated with a paired t-test.

III. Results

Real-time MRI movies were collected from all patients without difficulties or complaints, but one FEES examination failed due to the subject's noncompliance with the trans-nasal technique. In all individuals, MRI and FEES demonstrated normal deglutition and oromandibular function. The implementation of a standardised real-time MRI examination methodology, as well as a total in-room time of around 15 minutes, significantly reduced patient pain and streamlined the entire procedure.

3.1 Swallowing Incidents : Real-time MRI detected a total of 12 unique swallowing events. They are divided into five valve functions, three bolus transports, and four extra events. Table 1 contains a thorough description, whereas Figure 1 depicts a representative example of all distinct events. The observation of their oral and pharyngolaryngeal apertures (i.e., valves) that play a functional role in deglutition was used to define valve functions. They are the oro-velar opening (OOT), the velo-pharyngeal closure (VCT), the glottal closure (GCT), the epiglottic retroflexion (ERT), and the esophageal opening (EOT). The contact and separation of the respective valve tissues defined their start and end positions. For example, a large opening of the soft palate from the dorsum of the tongue signals the start of the OOT, whereas their subsequent touch identifies the conclusion of the OOT, which was discovered in this study. The oro-velar transit (OTT), pharyngeal delay (PDT), and pharyngeal transit (PT) are the three events that define the passage of the bolus rather than the behaviour of the valve (PTT). The OTT depicts bolus transport through the oro-velar valve, which began and ended at the same time as the OOT. The PTT was defined as the duration from the onset of the bolus head passing the oro-velar valve (start) to the point where the bolus tail passes the esophageal sphincter (end), while the PDT was the interval between the OOT start and the onset of the bolus head passing the orovelar valve. Additional events included the laryngeal ascent (LAT), laryngeal descent (LDT), vallecular and piriform sinus filling (SFT), and pharyngeal constriction (PCT). The latter two events were again newly detected by real-time MRI.



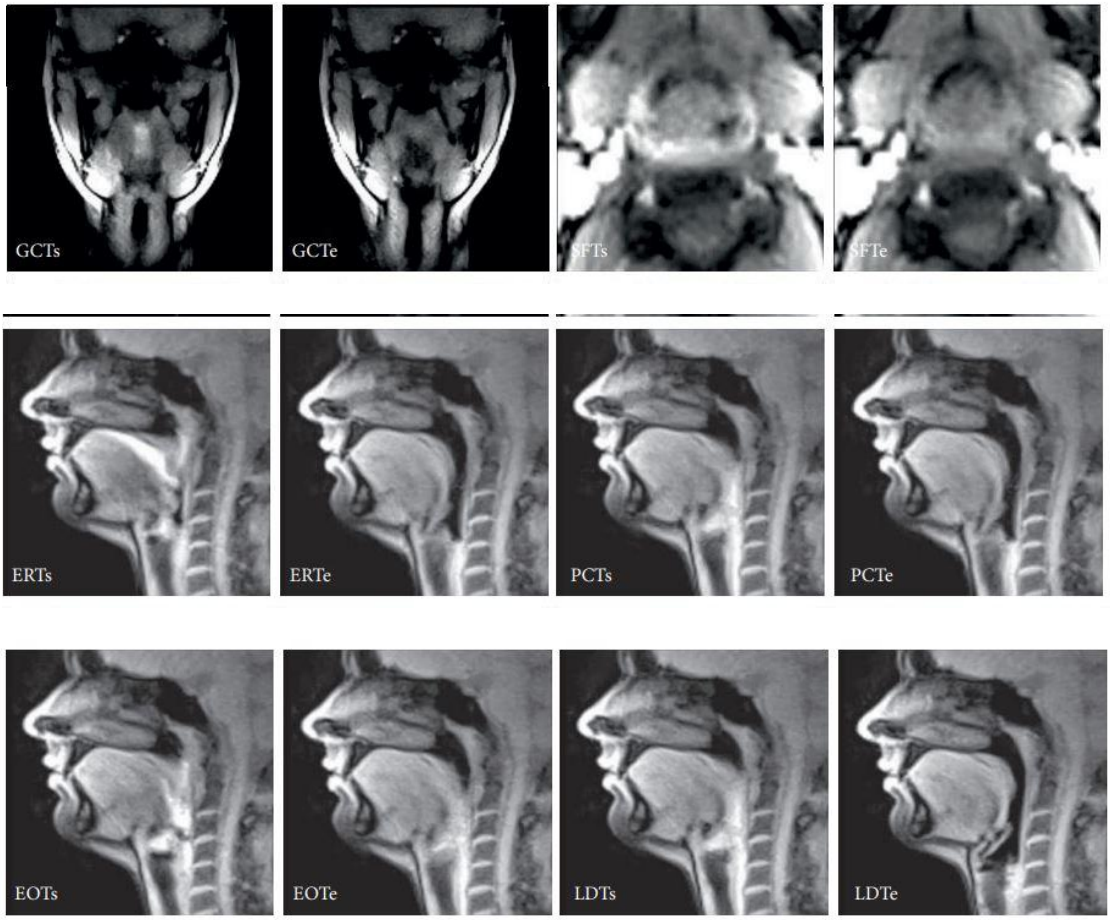


Figure 1: Physiological events of normal swallowing as seen by real-time MRI (27-year-old female). LAT: laryngeal ascent, VCT: velopharyngeal closure, OOT: oro-velar opening (start time defined as reference), PTT: pharyngeal transit, GCT: glottal closure, SFT: vallecular and piriform sinus filling, ERT: epiglottic retroflexion, PCT: pharyngeal constriction, EOT: esophageal opening, LDT: laryngeal descent ("s" and "e" refer to respective start and end times). The images are selected from respective movies.

Deglution events		**Real-time MRI**			**FEES**
		Sagittal	**Coronal**	**Axial**	**Axial**
Laryngeal ascent (LAT)	START END	**100 %** **100 %**	80 % 67 %	0 % 0%	89 %
Velo-pharyngeal closure (VCT)	START END	**100 %** **100 %**	93 % ***93%***	5 % 5%	**100 %** **100 %**
Oro-velar opening (OOT)	START END	**100 %** **100 %**	53 % 7 %	0 % 0 %	33 %
Pharyngeal transit (PTT)	START END	**100 %** **100 %**	93 % 20 %	0 % 0 %	
Glottal closure (GCT)	START END	0 % 0 %	**87 %** **87 %**	***86 %*** ***86 %***	22 %
Vallecular and piriform sinus filling (SFT)	START END	11 % 0 %	67 % 33 %	***95 %*** ***95 %***	
Epiglottic retroflexion (ERT)	START END	**100 %** **100 %**	0 % 0 %	5 % 0 %	89 %
Pharyngeal constriction (PCT)	START END	**100 %** **100 %**	***80 %*** ***80 %***	5 % 5 %	
Esophageal opening (EOT)	START END	**95 %** **95 %**	33 % 13 %	68 % 68 %	
Laryngeal descent (LDT)	START END	**100 %** **100 %**	47 % 53 %	0 % 0 %	11 %

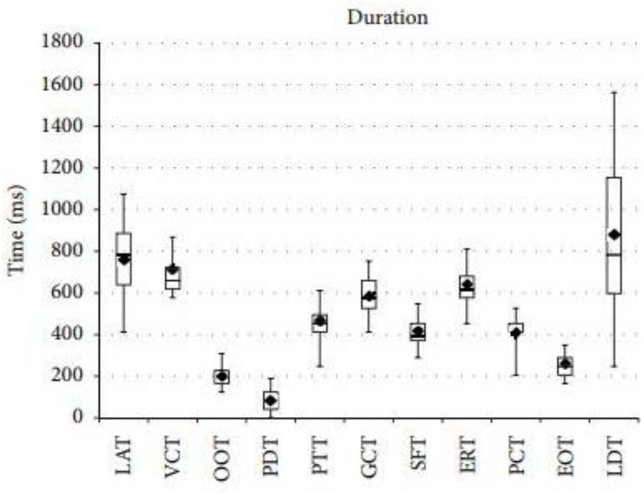
Table 2:Detectability of swallowing events by real-time MRI and FEES

Bold font: highest visibility rate.
Bold italic font: second highest visibility rate.

3.2. Recognizability : Table 2 outlines the optimum orientations for real-time MRI detection of individual events. The sagittal plane had the maximum detectability, with a visibility ratio of 95% for esophageal opening and 100% for all other events, excluding glottal closure and piriform sinus filling. Glottal closure was best visible in the coronal plane (87%), while vallecular and piriform sinus filling was best seen in the axial plane (95%, as indicated in bold font). The velo-pharyngeal closure, glottal closure, and pharyngeal constriction could all be seen in the coronal or axial planes, albeit at a somewhat lower but still acceptable visibility rate (>80%, as indicated in bold italic style). These additional picture orientations are intended to provide additional information in future clinical investigations.

3.3 Quantitative Timings : Figure 2 shows the durations of each swallowing episodes as measured by real-time MRI, as well as the start and end times (relative to OOT beginning). While individual temporal accuracy is limited to the acquisition time of a single frame, 41 ms, average durations across subjects were OOT = 200 ± 83 ms (mean ± SD), VCT = 714 ± 147 ms, GCT = 586 ± 93 ms, ERT = 642 ± 130 ms, EOT = 261 ± 62 ms, OTT = 200 ± 83 ms (same as OOT), PDT = 78 ± 66 ms, PTT = 467 ± 117 ms, LAT = 757 ±189 ms, LDT = 881 ± 410 ms, SFT = 413 ± 95 ms, and PCT = 410 ± 73 ms. The relative timings of most start and finish points were derived from data measured in the sagittal plane based on detectability. VCTs (detectable in both the sagittal and coronal planes) were used to determine GCT timings, while GCTs (detectable in both the coronal and axial planes) were used to calculate SFT timings. The significant correlation of the VTC durations for sagittal and coronal measurements ($r = 0.8$) and the GCT durations for coronal and axial measures ($r = 0.63$) confirmed this approach. Data from the two repetitive sagittal measurements were compared with ANOVAs for durations (Figure 3) as well as relative start and end times. A marginally significant difference between two measurements can only be shown for the start time across the events (main effect “measurement”: $F(1, 8) = 5.0$, $P \leq 0.055$), but not for the duration or end time. In particular, this discrepancy in start time differs between events (“event × measurement”: $F(7, 56) = 2.9$, $P \leq 0.011$) and is significant only for LATs ($t(8) = -2.6$, $P \leq 0.031$) and VCTs ($t(8) = -2.4$, $P \leq 0.046$) (Figure 4).

3.4. Real-Time MRI versus FEES : The duration of the velopharyngeal closure was compared between real-time MRI and FEES, as it is the only event detectable by the latter. Sagittal and coronal real-time MRI studies resulted in 724 ± 144 ms and 690 ± 112 ms, respectively, which strongly correlate ($r = 0.927$) and do not differ from each other ($t(8) = 1.8$, $P \leq 0.117$). However, these findings were significantly different from 591 ± 77 ms as detected by FEES for both sagittal ($t(8) = -3.3$, $P \leq 0.011$) and coronal MRI planes ($t(8) = -2.5$, $P \leq 0.036$).



(a)

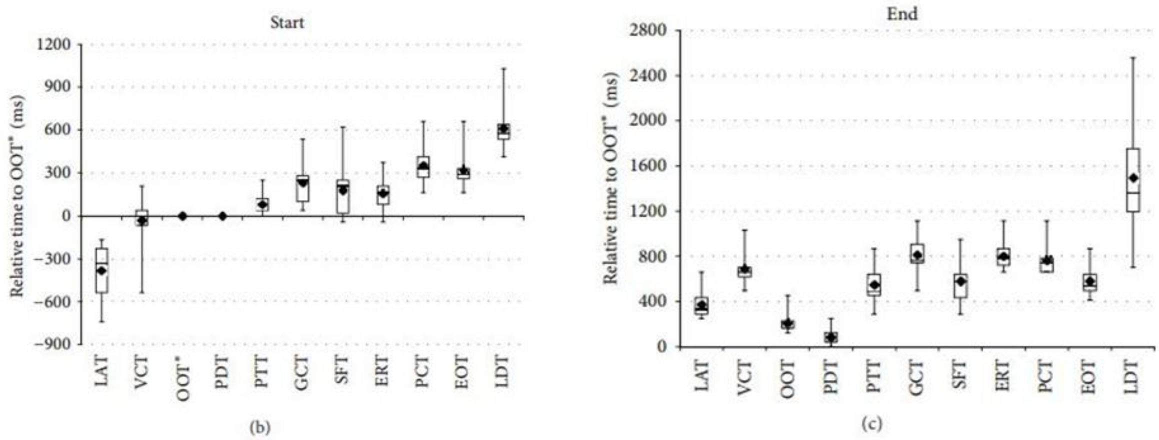


Figure 2: Durations, start times, and end times of distinct swallowing events as determined by real-time MRI (means and quartiles,10 subjects). LAT: laryngeal ascent, VCT: velo-pharyngeal closure, OOT: oro-velar opening (start time defined as reference), OTT: oro-velar transit, PDT: pharyngeal delay, PTT: pharyngeal transit, GCT: glottal closure, SFT: vallecular and piriform sinus filling, ERT: epiglottic retroflexion, PCT: pharyngeal constriction, EOT: esophageal opening, and LDT: laryngeal descent.

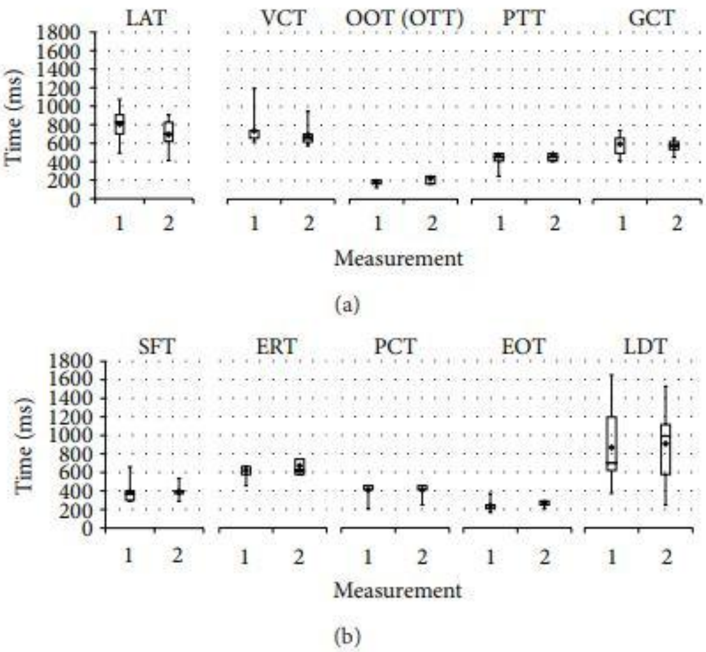


Figure 3: Durations of distinct swallowing events for two repetitive real-time MRI measurements (means and quartiles, 10 subjects). LAT: laryngeal ascent, VCT: velo-pharyngeal closure, OOT: orovelar opening (start time defined as reference), OTT: oro-velar transit, PTT: pharyngeal transit, GCT: glottal closure, SFT: vallecular and piriform sinus filling, ERT: epiglottic retroflexion, PCT: pharyngeal constriction, EOT: esophageal opening, and LDT: laryngeal descent.

IV. Discussion

This study shows that recent advancements in real-time MRI [11, 12, 20, 21] provide a straightforward, robust, and well-tolerated method of accessing the physiological features that characterize normal swallowing. The dynamic imaging method enables the thorough delineation of all deglutition events as well as the characterization of their temporal pattern at every imaging orientation. In reality, the approach adopted overcomes the long acquisition durations of traditional MRI exams and provides temporal resolution comparable to that of a standard videofluoroscopic or FEES deglutition measurement. As a result, more detailed representations of tissue activity and bolus transport are now achievable. When compared to Logemann's model [3,] the majority of valve function events detected by real-time MRI correspond well to earlier videofluoroscopy findings. There are some distinctions between oro-velar opening, vallecula and piriform sinus filling, and pharyngeal constriction. Furthermore, because the bolus was administered passively to the participant, the behaviour of the lips and tongue—previously classified as valve 1 [3]—was not taken into account in the current investigation. The oro-velar valve's opening and closing ensures safe bolus transport from the oral to pharyngeal area and also indicates its efficiency. As a result of the current observations, the event of OOT was redefined because vallecula and piriform sinus filling can only be detected in the axial plane, videofluoroscopy did not reveal it. As for pharyngeal constriction, Logemann stated that the pharyngeal wall is not observed as a “peristaltic wave” [19],Instead, the bolus is propelled forward by the movement of the tongue. In contrast, all ten participants had two confluent peristaltic waves. The first is passavant ridge, which is caused by superior pharyngeal constrictor contraction and occurs synchronously with velo-pharyngeal closure. The second wave is pharyngeal constriction, which might be interpreted as peristaltic lowering of the passavant ridge. It happens practically simultaneously with the cricopharyngeal sphincter opening and is followed by the esophageal peristaltic wave. This can be seen in both the sagittal and coronal planes, although it is best seen in dynamic movie recordings. Concurrent motions, such as those between the VCT and the passavant ridge, as well as between the EOT and the PCT, work in tandem with all temporally coordinated activities of individual valves to ensure thorough clearance of the bolus in the aerodigestive tract and firm airway protection. The creation of a landmark place appears to be a major problem for bolus transport events. There is currently no widely recognized standard. Previous definitions distinguish between oral transit, pharyngeal delay, and pharyngeal transit by referring to the "bolus head reaching the cross of the tongue base and posterior side of the mandibular ramus" and "start of laryngeal elevation" [3]. The "cross of tongue base and mandible" cannot be detected in the movie recordings because the MRI signal is generated from a cross-sectional slice rather than from overlapped structures in an X-ray projection image. At the same time, the tongue motion, which has been inconsistently defined in previous research [3, 11, 22, 23], fluctuates substantially during oral bolus delivery, making it unreliable as a landmark. As a result, the oro-velar transit was redefined as a distinct and plainly visible bolus moving through the oro-velar aperture. As the analogous valve function, its timing is identical to that of the oro-velar opening.

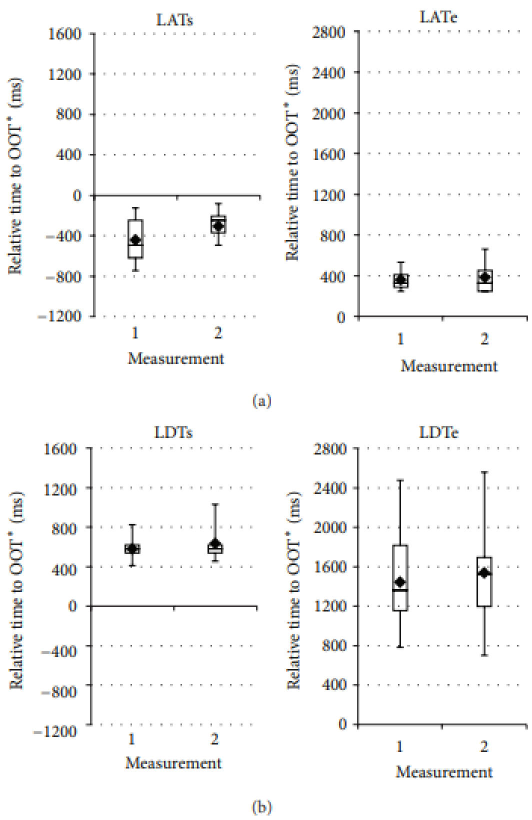


Figure 4: Start and end times of laryngeal ascent (LAT) and descent (LDT) for two repetitive real-time MRI measurements (means and quartiles, 10 subjects).

The laryngeal ascent, which was previously characterized as a landmark for the pharyngeal transit and its timings, raises similar concerns (PTT). According to the current data, the laryngeal ascent is one of only two events with a significant difference in start time between two repeated observations, showing that various laryngeal motions are engaged in the early phase of swallowing [12]. This is also evident in the sagittal view of

Supplementary Movie 1 and Figure 2, which show a wide range of LAT start timings and durations across patients. As a result, the well-visible and distinct bolus head passing through the oro-velar valve was chosen as a constant landmark describing the beginning of the pharyngeal transit. Based on these definitions, a delay ranging from zero to 200 ms (78 ± 66 ms) was observed between the wide opening of the oro-velar valve (OOTs) with the bolus ready to enter the pharyngeal cavity and the onset of the bolus head passing the oro-velar valve (PTTs)—here defined as pharyngeal delay (PDT). Although using a different landmark, its timing is in accordance with earlier videofluoroscopy findings [23]. Whether this new "PDT" observed by real-time MRI provides a more accurate, reliable, and meaningful standard for studying the related mechanism and eventually resolving the literature discrepancy [3, 23, 24] remains to be seen in future clinical investigations.Despite the small number of patients, our findings clearly show that the sagittal plane is the most useful orientation for assessing most physiological swallowing events. This also applies to conventional videofluoroscopy, and it may be possible to reduce clinical applications even more by restricting MRI examinations to the sagittal plane at even shorter scan intervals. This would be especially beneficial for patients suffering from dysphagia. The selection of a landmark or reference point is critical in the study of individual swallowing events. So far, the start of the esophageal opening (EOTs) has been used as a reference [12, 19]. However, because of the bolus' low concentration and complex fluid dynamics, MRI identification of the instant when the entire bolus tail passes past the upper esophageal sphincter is difficult. Furthermore, MRI signals from saliva or tissues arriving from surrounding locations (sections) during deglutition add to the ambiguity. The similar factor has contributed to EOT detectability being slightly lower (95%) in real-time MRI. As a result, the start time of the newly defined oro-velar transit (OTTs) in all subjects was utilised as a reference for calculating comparable timings (Figure 1).

While submental EMG recordings as an independent reference for a zero time point may be used in future therapeutic applications, such a technique was not considered in this pilot work. In this case, descriptive statistics revealed various amounts of variance associated with individual swallowing occurrences across subjects. LAT, VCT, and LDT have the greatest fluctuation in durations, but all other events had no difference in relative timings and durations from one measurement to the next. Figure 3 shows a better illustration of this by comparing the lengths of two recurrent real-time MRI sagittal measurements. Inspection of individual subject data reveals that the variation in VCT is primarily due to a single participant with an unusually earlier start time but no change in end time. The substantial difference in LAT arises from a difference in start time (LATs), notably a later start time in the second measurement in the majority of the individuals, as seen in Figure 4. A similar difference is seen at the end time of LDT but not its start time (LDTe in Figure 4), however it does not reach statistical significance due to the considerable variance. The higher variance associated with LAT and LDT could be due to variation in repeated swallowing habits rather than the measurement method. Indeed, this could imply that LATs and LDTe are volitional elements while other rest events are reflexive, implying that laryngeal movements are not a good and trustworthy marker to research swallows timings.

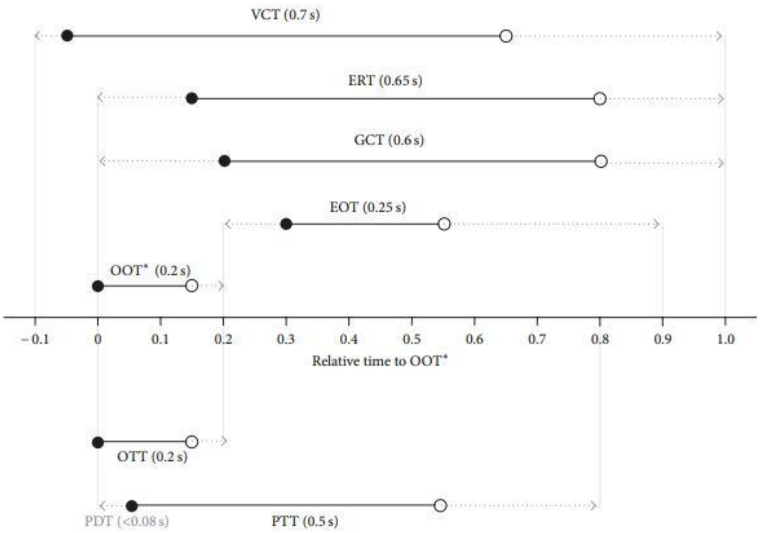


Figure 5: Temporal pattern of physiological events during normal swallowing. VCT: velo-pharyngeal closure, ERT: epiglottic retroflexion, GCT: glottal closure, EOT: esophageal opening, OOT: oro-velar opening (start time defined as reference), OTT: oro-velar transit, PDT: pharyngeal delay, and PTT: pharyngeal transit. Solid lines indicate durations with mean values in brackets (10 subjects), while circles represent respective start (solid) and end times (open). Arrows refer to maximal durations.

Taken together, the present real-time MRI findings unravel a well-orchestrated temporal pattern of physiological swallowing events during deglutition, as summarized in Figure 5. It includes 5 valve function events (VCT, OOT,ERT, GCT, and EOT) and three bolus transport events (OTT, PDT, and PTT), all of which are of particular diagnostic relevance in clinical practice. For example, VCTs happen shortly before OTTs (about 50 ms) and PTTs (about 100 ms), while VCTe happens after OTTe (about 500 ms) and PTTe (about 150 ms). In other words, the VCT covers OTT and PTT in order to fully protect the airway from aspiration by closing the velum and posterior pharyngeal wall. A similar behavior of GCT, namely, a coverage of EOT by closing the glottis and supraglottis could also be detected with GCTs about 80 ms ahead of EOTs and GCTe about 250 to 300 ms later than EOTe. The current durations for GCT (586 ± 93 ms) and PCT (410 ± 73 ms) agree well with previous data from videofluoroscopy, where GCT values have been reported to range between 500 ms [3] and 700 ms [25], and PCT values around 450 ms [26]. The largest deviation from previous studies with values of 400 ms [3] and 500 ms [26] was observed for the EOT duration (261 ± 62 ms). This deviation may be caused by an overestimation of the EOT duration in videofluoroscopy which might be due to a temporally less precise separation of the esophageal entrance from the hypo pharyngeal (postcricoid) region.

The upright body position for FEES versus the supine position for MRI is a significant difference. Because data based on VCT duration revealed a substantial difference between the two methods, it appears that the supine posture may have an effect on the precise time course of swallowing. This discovery calls for more research into the systematic impact of body posture on deglutitive timings. Any direct comparison, however, will be hampered by the small number of observable events in FEES and technical constraints that preclude a simultaneous dualmodality investigation. Patient investigations of swallowing in the supine position, on the other hand, have been described [2, 7], however special care should be made for patients with neurological abnormalities to avoid potential complications from aspiration.

V. Conclusion

In conclusion, the results of this preliminary real-time MRI study at 41 ms temporal resolution offer comprehensive information about the physiology of normal swallowing and the function of the dynamic events. Real-time MRI contributes to our understanding of swallowing by providing images in arbitrary orientations that cover the entire oropharyngolaryngeal region. It also allows for the establishment of new landmarks and standards and provides access to a detailed description of the temporospatial pattern of the swallowing process. The present reference values for normal swallowing in the supine position will serve as the basis for further investigations of pathological conditions as in an ongoing study of dysphagia patients. Other real-time MRI applications may address therapeutic interventions such as functional swallowing therapies. In general, clinical studies are now warranted to assess the real-time MRI potential for diagnosis and treatment monitoring of swallowing disorders.

ABBREVIATIONS

EOT: Eesophageal opening, **ERT:** Epiglottic retroflexion, **FEES:** Flexible endoscopic evaluations of swallowing, **FLASH:** Fast low-angle shot, **GCT:** Glottal closure, **LAT:** Laryngeal ascent, **LDT:** Laryngeal descent, **MRI:** Magnetic resonance imaging, **OOT:** Oro-velar opening, **OTT:** Oro-velar transit, **PCT:** Pharyngeal constriction, **PDT:** Pharyngeal delay, **PTT:** Pharyngeal transit, **SFT:** Vallecular and piriform sinus filling, **VCT:** Velo-pharyngeal closure.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

AUTHOR'S CONTRIBUTION

The first two authors have contributed equally to this study. Anil Tamang and Tshetiz Dahal designed the study, performed the examination and the analysis, interpreted the results, and drafted the paper. Manoj Kharka performed the statistical analysis and helped to interpret the results and to draft the paper. Aeleesha Rai conceived and supervised the study, interpreted the results, and revised the paper. All authors read and approved the final paper.

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