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Functional Outcomes of Pharyngeal Stimulation in Patients with Dysphagia after Surgical Treatment for Head and Neck Cancer

by

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Abstract

Purpose: Head and neck cancer patients often experience swallowing disorders placing them at risk for aspiration and malnutrition. This study examined the effects of electrical stimulation to the pharyngeal wall on swallowing function in post-surgical head and neck cancer patients. Methods: Swallowing of liquid, pudding, and cookie consistencies was examined using videofluoroscopy before, and 30 minutes after, a ten minute application of electrical stimulation (pulse width 0.2 ms, 5 Hz, 1.0 m amp) to the pharyngeal wall in 5 male patients (52 to 75 years of age) experiencing moderate-severe dysphagia. A total of ten measures of swallowing function were obtained from pre- and post-videofluoroscopy studies. Results: Changes were observed post-stimulation in *duration of posterior pharyngeal wall to base of tongue contact*, *total number of swallows*, *cricopharyngeal opening durations*, and *pharyngeal transit time*. Conclusions: Preliminary findings indicate that electrical stimulation of the pharynx may impact certain features of swallowing in head and neck cancer patients who experience dysphagia. However, further studies are required to confirm the present findings, explore the mechanisms responsible for these changes, and investigate the effect on swallowing function as a result of manipulating stimulus frequencies, intensities and durations.

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Introduction

Background

Introduction to head and neck cancer. Each year, over 4550 Canadians will be diagnosed with head and neck cancer (Canadian Cancer Society/National Cancer Institute of Canada: Canadian Cancer Statistics 2009). Head and neck cancer refers to a group of cancers originating in the lips, tongue, oral and nasal cavities, paranasal sinuses, pharynx and larynx. The majority of head and neck cancers are squamous cell carcinomas, that is, malignant tumors of squamous epithelium (mucosal lining) of the aforementioned regions. The primary risk factors associated with head and neck cancer include tobacco, heavy alcohol consumption, mechanical irritation and poor oral hygiene (Crary & Groher, 2003).

Primary treatment interventions for head and neck cancer may include the surgical removal of affected tissues, radiation, chemotherapy or some combination of these. The treatment that is specific to the present research includes surgical resection followed by either radiation or chemoradiation. Surgical treatment can include the removal of part or all of the mandible, maxilla, the tongue, hard palate, soft palate, base of the tongue, larynx and pharyngeal wall. External beam radiation would be targeted at the affected regions. These oncologic interventions put patients at risk of developing dysphagia as these structures are essential for normal swallowing function. Dysphagia is a delay in the transport, or

misdirection of a food bolus as it passes from the mouth to the esophagus. Problems can include difficulties with oral transport and containment of the bolus, stasis in the oral or pharyngeal cavities, a lack of contact between the posterior pharyngeal wall and the base of tongue, inadequate elevation of the larynx, inadequate closure of the epiglottis over the laryngeal vestibule, and insufficient opening of the upper esophageal sphincter. Damage to swallowing function can present a significant challenge in terms of maintaining adequate nutrition.

Malnutrition is a common problem among people with dysphagia with rate estimations ranging from 30% to 50% (Crary & Groher, 2003). More than half of patients experiencing swallowing problems report eating less because of discomfort, and one-third say they are still hungry and/or thirsty after meals (Ekberg, Hamdy, Woisard, Wuttge-Hannig, & Ortega, 2002). Patients may be placed on thickened liquid-type diets or may have to resort to nutrition delivered via a feeding tube. Altered deglutition also can place patients at risk for aspiration pneumonia if food or oral secretions are misdirected into the lungs. Aspiration pneumonia is a lung infection resulting from the entrance of foreign materials into the bronchial tree and lower airways. In addition to these medical complications, dysphagia can have serious social implications. People with feeding and swallowing difficulties often limit their participation in social activities where eating is central (Ekberg et al., 2002). Modified diets not only negatively impact the quality of life for these patients (Ekberg et al., 2002) but also

place a heavy financial burden on the healthcare system. Taken together, functional outcomes following oncologic intervention of head and neck cancer can have significant consequences related to health and nutrition as well as social function and overall quality of life for these patients.

Anatomy and physiology of swallowing. Swallowing is a very complex sensorimotor activity involving both voluntary and reflexive elements to move the bolus from the mouth to the esophagus. Historically, swallowing was viewed as purely reflexive but is presently classified as a *modifiable patterned response* (Robbins et al., 2008). The physiology of swallowing has been described largely by dividing the entire process into four stages: (1) oral-preparatory, (2) oral, (3) pharyngeal, and (4) esophageal. However, it is important to note that these stages are substantially interrelated and overlapping (Martin-Harris, Michel, & Castell, 2005). Movement of the bolus through all of these phases requires the coordinated movement of structures via prescribed patterns of muscle contractions appropriately timed to produce a series of low and high pressure gradients. For example, the movement of the bolus out of the hypopharynx and into the esophagus requires that there is a zone of high pressure above the bolus (in the hypopharynx) and a zone of low pressure below the bolus (in the esophagus).

The oral-preparatory stage uses the tongue, jaw, and teeth for mastication of the bolus, which reduces it in size, mixes it with saliva, and forms it into a cohesive form. Mastication must be initiated voluntarily but

continues reflexively, although this movement pattern can be overridden cortically (Crary & Groher, 2003; Dellow & Lund, 1971). While the bolus is being prepared, important sensory information (temperature, texture, size of the bolus) is being collected by the teeth, tongue, gums and palate to be sent to the brainstem via the trigeminal (V), facial (VII), and glossopharyngeal (IX) nerves.

The oral stage of swallowing begins as the bolus is propelled backwards into the oropharynx. The oropharynx is comprised of the soft palate, the base of the tongue, anterior and posterior faucial pillars, tonsillar fossae, palatine tonsils, and lateral and posterior oropharyngeal walls (Ridley, 1999). The swallow begins as the tongue tip elevates and the bolus is held against the hard palate. The extrinsic muscles of the tongue (mainly the anterior belly of the digastric, mylohyoid, and geniohyoid) then contract to propel the bolus posteriorly. There are several important events that co-occur with this movement. First, the hyoid bone is elevated which aids in airway protection. Second, the velum is raised to close of the nasopharynx. Not only is this important to prevent food from entering the nasal cavity, but velar position also plays an important role in generating and maintaining the pressure needed to move the bolus past the oropharynx.

The goal of the pharyngeal phase is to safely transport the bolus from the oropharynx, past the opening of the airway, and through the cricopharyngeus, the sphincter that separates the pharynx and the

esophagus. This is accomplished by carefully timed contractions and relaxation of the superior, middle and inferior constrictors, palatopharyngeus, stylopharyngeus muscles, and the muscles of the cricopharyngeus. The cricopharyngeus remains contracted most of the time via autonomic system efferents, which prevents reflux of stomach acids into the pharynx. However, to allow the bolus to pass into the esophagus the cricopharyngeus must relax temporarily. When relaxed, the cricopharyngeus is pulled open by anterior and superior movement of the larynx. The larynx is anchored to the hyoid bone which is connected to the tongue; therefore when the mylohyoid, geniohyoid, and the anterior belly of the digastric contract the larynx is moved anteriorly to pull open the cricopharyngeus.

The pharyngeal swallowing reflex is triggered as the bolus passes into the oropharynx, although the exact point at which the reflex is triggered has been found to have high inter-subject variability during normal swallows (Dua, Ren, Bardan, Xie, & Shaker, 1997; Linden, Tippett, Johnston, Siebens, & French, 1989). Sensory information from the oropharynx is sent to the brainstem and the pharyngeal swallowing reflex is triggered once the afferent threshold has been met (Miller, 2002). The reflex is composed of a neuromuscular response in the following sequence: (1) the elevation of the velum, (2) the elevation and closure of the larynx, (3) contraction of the pharyngeal constrictors, and (4) relaxation of the cricopharyngeus.

The fourth and final stage of swallowing, the esophageal stage, is entirely involuntary (Crary & Groher, 2003). During this phase the bolus is transported to the stomach by peristaltic contractions which are triggered by the passage of the bolus into the esophagus.

As stated previously, the motor control system for swallowing has both voluntary and reflexive elements. The swallowing control center is located in the reticular formation of the medulla and houses two critical components for swallowing control including the Nucleus Tractus Solitarius (NTS) and the Nucleus Ambiguous (NA). Most sensory information from the pharynx synapses first in the nuclei of the trigeminal system and secondarily in the NTS. The NTS receives information from sensors in the swallowing and respiratory systems, via the trigeminal (V), facial (VII), glossopharyngeal (IX), and vagus (X) nerves. Some sensory information, regarding taste, temperature and texture of the bolus, as well as information about respiratory status, synapses at the NTS. The information is integrated in the NTS before being relayed to the NA and other neighboring areas in the brainstem including the nucleus reticulus parvocellularis and nucleus reticulus gigantocellularis (Miller, 1999). The NTS also relays some taste information to the thalamus. The NA receives a highly patterned pre-motor plan from the NTS and then incorporates cortical input before sending out the final orchestration of the motor response to the swallowing muscles via the trigeminal, facial, glossopharyngeal, vagus, and hypoglossal (XII) nerves.

Treatment and management of dysphagia. Historically, treatment and management of swallowing disorders has included a number of interventions. In the most severe cases of dysphagia, management may include the use of enteral (tube) feeding. Traditional interventions that can be trialed in an effort to circumvent the need for enteral feeding include: (a) diet modification, where thickening liquids and restricting textures are commonly used; (b) behavioural modifications and maneuvers such as postural techniques (e.g, chin tuck, head turn, head tilt) or the *Mendelsohn Maneuver*; (c) swallowing exercises to reduce swallowing difficulties by strengthening the muscles involved (e.g., the *Effortful Swallow*); and (d) surface electromyography (sEMG) designed to provide external feedback to patients while they are performing swallowing exercises. Surface electrodes are placed on the head and/or neck, most often over the suprahyoid musculature, to record the activation signal of the swallowing muscles and relay this information to the patient through an auditory or visual signal (Crary & Groher, 2003; Yoshida, Groher, Crary, Carnaby Mann, & Akagawa, 2007). These signals provide immediate feedback related to muscular effort exerted along with the duration of the swallow event (Crary & Groher, 2003; Yoshida et al., 2007).

Another widely-recognized, but fairly controversial treatment, involves the use of surface electrical stimulation (such as the patented *Vitalstim* therapy) to the submental and laryngeal regions. It is thought that

stimulation in this manner targets the mylohyoid and thyrohyoid muscles resulting in improved hyoid and laryngeal elevation. Whereas positive results have been found (Shaw et al., 2007), treatment efficacy has not been established. A study conducted by Ludlow et al. (2006) and colleagues found that surface electrical stimulation actually resulted in laryngeal depression. Surprisingly, the lowering of laryngeal structures did not seem to be associated with a functional disturbance in swallowing. Moreover, the patients who showed the most dramatic laryngeal depression demonstrated the greatest reduction in aspiration and pooling (Ludlow et al., 2006).

Other studies have explored possible therapeutic effects by electrically stimulating the pharynx (Fraser et al., 2002; Hamdy et al., 1998). Hamdy and colleagues applied electrical stimulation to the pharyngeal muscles of healthy participants and found associated changes in the CNS, as measured by transcranial magnetic stimulation (TMS) (Hamdy et al., 1998). Specifically, they noted an increase in motor cortex excitability and area of representation devoted to the pharynx in tandem with a simultaneous decrease in esophageal representation (Hamdy et al., 1998). The same paradigms have been applied to dysphagic hemiplegic patients and were correlated with an improvement in swallowing function (Fraser et al., 2002). The findings from this work have led to further questions about potential applications of the stimulation protocol to other populations with dysphagia.

Theoretical and clinical implications of electrical stimulation for head and neck cancer. The original work completed by Fraser et al., 2002 has opened the door to clinical research designed to assess functional outcomes following electrical stimulation of the pharyngeal wall in other populations with dysphagia. The clinical implications of their findings are significant for patients with head and neck cancer who are experiencing dysphagia. Whereas with stroke patients the neural deficit is central in nature, head and neck cancer patients who are treated with surgical intervention will be in a situation where the peripheral system is affected. The surgical intervention for head and neck cancer patients involves removing epithelial and muscular tissue in the oropharyngeal area. Resection of these tissues leads to a loss of sensory and motor function in the pharynx. The defect is then reconstructed using tissue from another area of the body such as the radial forearm. This free flap, consisting of dermal and fascial tissue, is intended to correct the anatomical or structural defect in the area. However, the free flap does not have the capacity to correct any functional deficits associated with the loss of muscles and/or motor conduits in the lateral and posterior pharyngeal walls. Sensory nerve reconstruction procedures are not usually employed when reconstructing the oropharyngeal area leaving transferred tissue without sensory innervation. This significantly impacts the sensation and motor function of both the affected and surrounding native tissues.

Theoretically, electrical stimulation of the remaining native tissues of the pharyngeal wall post surgery could induce changes in connections between the PNS and the CNS. It is thought that the electrical stimulation will provoke neuroplastic changes resulting in increased sensory input from the pharynx to the CNS. It is possible that electrical stimulation will modify sensory reception of the pharynx. If this is true, the CNS should receive more accurate information about the nature of the bolus. Sensory information is critical for a safe swallow as it allows for modification of the swallowing reflex to suit the size and nature of the bolus. Support for the modification of sensorimotor loops has been demonstrated in studies showing that changes in sensation can modify swallowing threshold and alter the level of swallowing muscle recruitment (Miller, Vargervik, & Phillips, 1985; Mistry & Hamdy, 2008). It is possible to postulate that by improving the sensory input from the remaining native tissue of the pharyngeal wall increased motor output of the remaining native tissue might be observed. Moreover, it has been demonstrated that changes in sensory input can produce changes in the cortical representation of swallowing (Fraser et al., 2002). Fraser et al. (2002) compared the time course of the motor cortex changes they saw to those established in other studies on human motor cortex (Stefan et al., 2000) and therefore speculated that long-term potentiation and long-term depression may be the neuroplastic mechanisms responsible for changes induced by peripheral nerve stimulation.

Hypothetically, with stimulation, a greater number of motor units associated with remaining native tissue will be recruited by one of two mechanisms. First, a peripheral mechanism will recruit motor units by depolarizing the motor axons that are beneath the stimulating electrode (Collins, 2007; Dean, Yates, & Collins, 2008). This mechanism is an acute effect and would only have influence during the stimulation; therefore, it is unlikely that this mechanism would account for any changes seen half an hour post-stimulation. A study by Thompson, Doran, & Stein (2006) has suggested that a central mechanism, rather than peripheral, is more likely to account for changes seen post-functional electrical stimulation. A proposed central mechanism suggests that sensory axons are stimulated that will recruit spinal motoneurons through a reflex pathway (Collins, 2007; Dean et al., 2008). Either of these mechanisms (peripheral or central) may result in a greater number of muscles fibres contracting during the swallow but the central mechanism would likely account for changes seen *after* stimulation.

If these changes are occurring in the PNS and the CNS, then accompanying changes in the functional aspects of swallowing may be observed. In the current study, movements associated with swallowing were quantified using videofluoroscopy. Videofluoroscopy is an imaging technique that is sensitive in detecting subtle changes in different phases of the nutritive swallow. The modified barium swallow (MBS) procedure (Martin-Harris, Logemann, McMahon, Schleicher, and Sandidge, 2000)

involves having the patient swallow different consistencies of liquid and food (mixed with barium sulfate) while they undergo videofluoroscopy. This provides objective data about bolus flow and structural movement throughout the swallow. The MBS is appropriate for functional outcomes research as a number of variables reflecting the flow of the bolus, level of protection of the airway and the risk of aspiration or penetration can be taken from the fluoroscopic footage.

Purpose

The purpose of the present study was to determine whether functional improvement in the swallowing ability of patients with head and neck cancer could be observed following a standardized protocol of pharyngeal stimulation. It was predicted that improvement in swallowing function would be noted following the stimulation as a result of improved pharyngeal sensitivity, recruitment of motoneurons in the remaining native tissue, or a combination of both. Changes in selected swallowing behaviors post-stimulation would infer changes in sensation and/or motor activity.

When evaluating a swallow, clinicians observe characteristics that indicate: (a) the efficiency of bolus transport as measured through durational events, (b) the efficiency of bolus clearance as measured through management of residue and (c) physiological markers related to safe and effective clearance of a bolus. These characteristics were hypothesized to be reflected in the anticipated changes in several

dependent variables chosen to represent these swallowing characteristics. Questions that were addressed in this study included:

- Is electrical stimulation of the pharynx effective in improving the efficiency of bolus transport in the swallows of post-surgical head and neck cancer patients?
- Is electrical stimulation of the pharynx effective in increasing the efficiency of bolus clearance in the swallows of post-surgical head and neck cancer patients?
- Is electrical stimulation of the pharynx effective in improving the physiological markers of a safe and effective clearance of a bolus in post-surgical head and neck cancer patients?

Methods

Participants

Approval was obtained from the Health Research Ethics Board at the University of Alberta, prior to contacting potential participants. Participants were recruited by mail through the Institute for Reconstructive Sciences in Medicine (iRSM) and were sent information about the study (Appendices A and B). Participants who agreed to participate were contacted by phone to arrange a date and time for study. Upon arrival, the Transcranial Magnetic Stimulation Adult Safety Screen (TASS) (Keel et al., 2000) was administered (Appendix C), study information was reviewed and participants had the opportunity to ask any questions before signing consent forms (Appendix B).

A convenience sample of five subjects was recruited for this study. Demographic information for all participants can be found in Table 1. Participants were all male, ranging in age from 52 to 75 with a mean age of 61. Participants had all received surgical treatment for oropharyngeal cancer as well as adjunctive radiation (S4) or chemoradiation (S1, S2, S3, and S5). Surgery involved the structures of the oropharynx, including the base of tongue, soft palate, and lateral and posterior pharyngeal walls. Due to the individuality of each patient's surgery, sensory deficits may have existed in the oral as well as the pharyngeal cavities. To be included, participants must have received a diagnosis of chronic dysphagia involving the pharyngeal stage of the swallow. Additionally, there must have been an indication within the operative report that some native tissue remained in the posterior pharyngeal wall of the oropharynx. Finally, for participant data to be included in the analysis, a motor evoked potential (MEP) must have been elicited during the TMS procedure inferring native sensory tissue was remaining. Patients who had undergone surgery and or radiation treatment within six months of the study were excluded in order to ensure their comfort with the catheter.

Table 1

Demographic Information for All Subjects

Partici-pant	Age*	Cancer Dx	Surgery (resected tissue)	Time post Sx (mnths)*	Postoperative Radiation	Postoperative Chemo-therapy	Postoperative Alternative to oral feeds	Oral diet*
S1	70	T2 SCC	SP, 75%; R LPW to level of PS; PPW, 50%	23	✓	✓	✓	Jell-O
S2	55	T3 SCC	R BOT, 75%; R tonsil; R LPW; R oral tongue, 50%	19	✓	✓	✓	Liquids Apple sauce
S3	52	T3 SCC	BOT, 50%; SP, 100%; LPW	24	✓	-	-	Solids Thin liquids
S4	55	T2 SCC	BOT, 25%; SP, 1/3; L LPW; L & R submandibular glands	12	✓	✓	-	Soft solids Thin liquids
S5	75	T3 SCC	BOT, 100%; R LPW; R tonsil; SP, 25%	32	✓	✓	✓	Pudding consistency

*at time of study

SCC = squamous cell carcinoma; SP = soft palate; PS = piriform sinus; LPW = lateral pharyngeal wall

PPW = posterior pharyngeal wall; L = left; R = right; BOT = base of tongue

Instrumentation

Videofluoroscopy. A standard videofluoroscopic unit was used to acquire pre- and post-stimulation swallowing studies. These studies were recorded to super-VHS video-recording media. The pre- and post-stimulation swallowing assessments were then transferred from analogue videotape to the KayPENTAX Digital Swallowing Workstation (KayPENTAX, Lincoln Park, NJ, U.S.A.) for analyses of swallowing events. A Panasonic Omnivision VCR (S-VHS, 4-head Hi-Fi stereo; Panasonic North America, Secaucus, NJ, U.S.A.) was used to convert the footage from S-VHS format into digital format.

Transcranial magnetic stimulation & electromyographic measurements. A TMS protocol was employed to elicit MEPs pre- and post-stimulation as part of a secondary protocol which will not be described in the present results. Transcranial magnetic stimulation of the cortex was delivered via a circular coil (outer diameter = 70mm) with a maximum output of 2.2 Tesla. This was connected to a magnetic stimulator that was set at single monophasic pulse stimulation (Magstim 200², The Magstim Company Ltd., Whitland, Carmarthenshire, Wales).

Motor evoked potentials elicited by the TMS were recorded at the pharyngeal muscles via a transnasal catheter (Gaeltec Ltd, Dunvegan, Isle of Skye, Scotland). The catheter was 3mm in diameter and housed two biopolar platinum ring electrodes built into a 3mm, intraluminal catheter (Gaeltec, Dunvegan, Scotland). The electrode pairs were

positioned 5 cm and 12 cm from the tip of the catheter with an interelectrode distance (within each electrode pair) of 1 cm. Midway between the electrode pairs was a solid-state strain-gauge transducer used to assess pressure at the level of the upper esophageal sphincter; pressure and EMG signals were used to detect proper positioning of the electrodes along the lateral and posterior aspects of the pharyngeal wall. The secondary TMS protocol used the thenar muscle as a control. Therefore, two skin electrodes also were placed on the thenar eminence, 1 cm apart (Fraser et al., 2002). A ground electrode was placed on the clavicle for both catheter and thenar muscle stimulation.

As described in the protocol used by Fraser et al. (2002), the electrodes were then connected to a preamplifier with filter settings at 5 Hz - 2 kHz (CED 1902, Cambridge Electronic Design, Cambridge, England, United Kingdom). A laboratory interface (Micro 1401 plus) was used to collect pharyngeal MEPs at a sampling rate of 4 - 8 kHz. To remove any electrical interference, response signals were processed through a 50/60 Hz noise eliminator (‘HumBug’; Quest Scientific, North Vancouver, Canada), as reported in Mistry, Rothwell, Thompson, & Hamdy, (2006). Finally, pharyngeal response data were recorded on a desktop computer using the "hot spot" program (SPIKE 2 software, version 6.0, Cambridge Electronic Design, Cambridge, England, United Kingdom).

Pharyngeal stimulation. Electrical stimulation of the posterior pharyngeal wall was administered using the same trans-nasal catheter described above. The catheter was connected to an electrical stimulator (Digitimer DS7A Constant Current Stimulator, Digitimer Ltd., Welwyn Garden City, Hertfordshire, England). The stimulation parameters (5Hz, pulse duration 0.2 ms) were set using the "peripheral stim" program (SPIKE 2 software, version 6.0, Cambridge Electronic Design, Cambridge, England, United Kingdom).

Procedures

Laboratory preparation. The catheter was soaked in 0.9% saline solution for 3-5 hours prior to use. It was then marked with indelible black ink at 15, 16, 17, 18, 19, and 20 cm from the pressure transducer. The instrumentation was set up for TMS and pharyngeal stimulation as described above, with the catheter arranged for measuring MEPs first. The laboratory was arranged so that the participant's chair was facing a window with all the equipment placed behind them. The SPIKE 2 program was then activated and "hot spot" was loaded in preparation for data display and collection.

Pre-stimulation. Prior to stimulation, a videofluoroscopic swallowing study was administered using the MBS procedure. The swallowing assessment was completed in the radiology department at the University of Alberta Hospital. With a radiologist present, two recordings of the patient’s swallows were attempted for three consistencies: liquid

(water mixed with liquid barium), pudding (mixed with barium paste), and cookie (with barium paste). It should be noted that not all consistencies were trialed with every participant due to clinician concern for patient safety and participant comfort level. The liquid bolus was presented to the participants in a cup and they were instructed to take a normal mouthful and swallow. The pudding bolus was offered to the participants on a teaspoon and they were instructed to clear the whole bolus from the teaspoon. One quarter of the cookie was presented to the participants and they were instructed to try to take the entire piece, chew and swallow. If the participant was unable to clear the cookie bolus from the oral cavity, they were offered water to help clear the bolus. No data were gathered from footage taken during or after a liquid wash.

The participants were then taken to the gastro-motility laboratory at the University of Alberta Hospital. The pharyngeal catheter was inserted trans-nasally, preferably on the side with least resection, using lidocaine gel as an anesthetic and lubricant if desired by the participant. The catheter was then left in-situ for five to ten minutes before starting the stimulation protocol to allow for habituation.

The cranial vertex was marked on the scalp using a measuring tape and marker (½ distance from bridge of nose [nasion] to occipital notch [inion] and ½ distance between the right and left tragi), (Jasper, 1958). The approximate area of pharyngeal cortex was also marked over both hemispheres (7.5 cm ± 2 cm lateral and 4 cm ± 2 cm anterior to the vertex

in the left hemisphere and 7 cm ± 2 cm lateral and 5 cm ± 2 cm anterior to the vertex in the right hemisphere), as outlined in Hamdy et al., 1996.

The "swallow2" program was then loaded on the desktop computer and the catheter was connected to the preamplifier. The catheter position was adjusted to the optimum position by observing real-time EMG responses to wet swallows and the catheter was taped in place on the nose.

The "hotspot" program was loaded to begin the TMS protocol. First, the cortical site evoking the largest MEPs was determined and marked, starting with the hemisphere contralateral to the side of the pharynx with the most damage. A stimulus response curve was then obtained for each hemisphere at the site found to evoke the largest MEPs. This was done beginning with the stimulator output that evoked the largest MEPs then decreasing by 5% increments until a threshold (an MEP less than 20 μV on two out of five trials) was reached. A similar protocol was repeated to determine the cortical site and stimulus response curve for the thenar muscle of the dominant hand (in contralateral hemisphere only).

Pharyngeal stimulation. The "pharyngeal stim" program was loaded and the stimulation parameters (5Hz, pulse duration 0.2 ms) were set. Electrical stimulation was administered to the pharyngeal native tissue following a standardized stimulation protocol (Fraser et al., 2002). First, the participant's pharyngeal sensory threshold was determined by averaging the intensity at which the stimulation was first perceived over

five trials (Gow, Hobson, Furlong, & Hamdy, 2004). Each of the trials began with 1.0 m amps and increased by 0.1 m amp intervals until the participant signaled that the stimulation was felt. The intensity was continually increased until the participant reported the maximum intensity tolerable. These maximums were recorded to determine the average of maximum intensities (Gow et al., 2004). In one case, a maximum was not achieved; in this instance, stimulation was determined from the maximum deliverable intensity. The stimulation was then decreased back to 1.0 m amps and the protocol was repeated four times. The intensity used for electrical stimulation was calculated using the following formula: intensity = AveSTmin + 0.75 (AveSTmax – AveSTmin) (adapted from Gow et al., 2004). In the event that the participant could not tolerate the stimulation intensity, the amplitude was dropped to: AveSTmin + 0.50 (AveSTmin – AveSTmin). During stimulation the participant was instructed to relax and avoid talking. Examiners did not interact with the participant during the stimulation phase.

Post-stimulation. Post-stimulation MEP response curves for pharynx and thenar muscle were assessed from the same cortical site immediately following stimulation.

The participant was then taken back to the radiology department and a videofluoroscopic swallowing study was administered. The post-stimulation swallowing assessment included the same consistencies trialed pre-stimulation. As maximum facilitation effects with 5Hz

stimulation have been found to be 30 minutes and 60 minutes post-stimulation in previous studies (Fraser et al., 2002), a similar time-line was attempted with this protocol, and all videofluoroscopic exams were completed within 30 minutes of stimulation.

Data Measurement and Analysis

All of the dependent swallowing variables were acquired from the videofluoroscopy footage recorded before and after stimulation. The footage was converted from S-VHS to digital so that it could be analyzed using the KayPENTAX Digital Swallowing Workstation. Videofluoroscopic footage was analyzed frame-by-frame and timed recordings of specific physiological events were made by a clinician who was blinded to the condition (i.e., pre- or post- stimulation). The first bolus of each consistency was used for analysis unless the radiological image was unclear or cut-off; in these cases, the second bolus was analyzed. Swallowing outcome variables were derived in the following manner, which is consistent with the definitions used clinically at the Institute for Reconstructive Sciences in Medicine:

1. *Pharyngeal transit time* was determined by calculating the time between the point where the bolus head passed the intersection place of the ramus and the base of tongue and the point at which the cricopharyngeus closed after the bolus had passed into the esophagus.

2. *Swallowing response time* was determined by calculating the time between the frame that showed the bolus head passing the trigger point (where the ramus crosses the base of tongue) and the first frame that showed superior movement of the hyoid.
3. *Cricopharyngeal opening duration* was determined by calculating the time between the first frame that showed the opening of the cricopharyngeus to allow the bolus into the esophagus and the frame that showed the point at which the cricopharyngeus closed after the bolus had passed into the esophagus.
4. *Oral transit time* was determined by calculating the time between the first frame that showed the backward propulsion of the bolus (via superior-posterior movement of the tip of the tongue) and the first frame that showed the bolus head passing the point where the ramus crosses the base of the tongue.
5. *Pharyngeal residue* was determined by assessing the amount of residue left in the pharynx after the first swallow on one bolus was completed. The residue was rated on a three point scale: 1=none or mild, 2=moderate without threat to airway, 3=severe with threat to airway.
6. *Total number of swallows* was determined by counting the total number of swallows completed before the patient indicated that they feel they were done swallowing. Swallows that occurred before the participant had attempted to propel the bolus posteriorly through the

oral cavity (as indicated by a “stripping motion” of the tongue) were not counted.

7. *Penetration/aspiration score* was evaluated using the eight point scale developed by Rosenbek, Robbins, Roeker, Coyle, and Wood (1996) which assesses the degree of aspiration or penetration and the level of airway compromise before, during, and after a swallow. *Penetration* is defined as passage of material into the larynx that does not pass below the vocal folds. *Aspiration* is defined as passage of material below the level of the vocal folds. *Penetration/aspiration scores* were assessed before, during and after all swallows of the bolus.
8. *Epiglottic inversion* was determined by evaluating whether or not epiglottic inversion occurred to cover the laryngeal vestibule when the pharyngeal swallow was initiated; swallows were coded dichotomously as “yes” or “no”. *Epiglottic inversion* was marked “yes” for a particular bolus if inversion was noted on any of the swallows of that bolus.
9. *BOT-PPW contact* was determined by evaluating whether or not the base of tongue base made contact with the posterior pharyngeal wall during the pharyngeal swallow; swallows were coded dichotomously as “yes” or “no”. *BOT-PPW contact* was marked “yes” for a particular bolus if contact was noted on any of the swallows of that bolus.
10. *Duration of BOT-PPW contact* was determined by calculating the time between the first- and last- frames showing contact between the base of tongue and the posterior pharyngeal wall. *Duration of BOT-PPW*

contact only was calculated in the event that base of tongue contact was observed both pre- and post-stimulation.

The videofluoroscopic footage was tagged at particular points of interest in the swallow in order to calculate the durational variables (*pharyngeal transit time*, *swallowing response time*, *cricopharyngeal opening duration*, *oral transit time, duration of BOT-PPW contact*). The durational variables were not calculated for the liquid boluses as these were not calibrated and therefore could not be reliably compared between swallows. The following time tags were made to the pudding and cookie boluses:

1. *Onset of posterior movement of the bolus*: defined as the point at which the head of the bolus was propelled toward the back of the oral cavity; this was often associated with movement of the tip of the tongue in a posterior direction within the oral cavity.
2. *Onset superior movement of hyoid*: defined as the point at which the hyoid bone began to move upward and forward. This tag was only marked when the hyoid could be visualized.
3. *Head of bolus passes ramus*: defined as the point at which the leading edge of the bolus passed the intersection of the ramus and the base-of-tongue. In cases where the rami were out of line, the anterior ramus was used as a landmark.

4. *Cricopharyngeal opening*: defined as the point at which the upper esophageal sphincter opens to allow the bolus into the esophagus.
5. *Cricopharyngeal closing*: defined as the point at which the upper esophageal sphincter closed after the bolus passed through it.
6. *Start BOT-PPW contact*: defined as the first frame in which the base of tongue made contact with the posterior pharyngeal wall.
7. *End BOT-PPW wall contact*: defined as the last frame in which the base of tongue made contact with the posterior pharyngeal wall.

Pharyngeal transit time, *swallowing response time*, *cricopharyngeal opening duration*, and *oral transit time* were used to assess efficiency of bolus transport.

The efficiency of bolus clearance was assessed by judging *pharyngeal residue* and counting the *total number of swallows.* Finally, the safety and effectiveness of bolus clearance was evaluated by grading *penetration/aspiration*, *BOT-PPW contact*, *duration of BOT-PPW contact with the posterior pharyngeal wall*, and *epiglottic inversion*. An additional qualitative clinical judgment of the swallow that exhibited the most characteristics of a safe, effective and efficient swallow was made based on blind paired comparisons of the pre-stimulation and post-stimulation swallows.

In order to establish inter-rater reliability, twenty percent of the videofluoroscopic data were evaluated by another rater and a two-way

mixed effects model was run. The intraclass correlation coefficient was 0.977 indicating strong inter-rater reliability.

Design and Statistical Analyses

The current study incorporated a within-subjects design. The independent variable was the stimulation treatment with two levels: pre-stimulation and post-stimulation. There were ten dependent variables. The first four dependent variables (*pharyngeal transit time*, *swallowing response time*, *cricopharyngeal opening duration*, and *oral transit time*) were related to efficiency and were based on durational events. Non-durational variables included *pharyngeal residue ratings* and *total number of swallows* which related to pharyngeal residue and clearance of that residue. The last four variables (*penetration/aspiration scores, epiglottic inversion, BOT-PPW contact,* and *duration of BOT-PPW contact*) were used to analyze the safety and effectiveness of bolus clearance. The last variable, *duration of BOT-PPW contact*, only was assessed if *BOT-PPW contact* was found both before and after stimulation.

Descriptive and inferential analyses were completed on all ten variables. For the continuous variables (*pharyngeal transit time*, *swallowing response time*, *cricopharyngeal opening duration*, *oral transit time*, *duration of BOT-PPW contact*, and *total number of swallows)*, an exploratory analysis including a Shapiro-Wilk test was completed to determine whether the variables were normally distributed. As shown in Table 2, inferential statistical analysis included paired-samples t-test for

the continuous variables that were found to be normally distributed. The Wilcoxon paired-samples rank test was used to analyze the discrete variables and any continuous variables that were not found to be normally distributed. The dichotomous variables were assessed using the McNemar Test for nominal variables.

Due to the exploratory nature of this study, a familywise error rate was not applied to the statistical analysis. Any changes in the values of interest are believed to be of importance to the investigative nature of this study. A more conservative *p*-value may miss crucial changes in these values.

Table 2

Inferential Statistical Analysis of Dependent Variables

Variable	Parametric / Nonpara.[a]	Statistical Test	Result	
			Liquid	Pudding
Pharyngeal Transit Time	NP	Wilcoxon paired-samples rank test		(z = -0.730, p = 0.465, two-tailed)
Swallowing Response Time	P	Paired-samples t-test		(t = 0.004, df = 1, p = 0.998, two-tailed)
Cricopharyngeal Opening Duration	NP	Wilcoxon paired-samples rank test		(z = -0.365, p = 0.715, two-tailed)
Oral Transit Time	NP	Wilcoxon paired-samples rank test		(z = -0.535, p = 0.593, two-tailed)
Pharyngeal Residue	NP	Wilcoxon paired-samples rank test	(z = -1.000, p = 0.317, two-tailed)	(z = 0.000, p = 1.000, two-tailed)
Total Number of Swallows	P	Paired-samples t-test	(t = -0.878; df = 3; p = 0.444, two-tailed)	(t = 2.402; df = 3; p=0.096, two-tailed)
Penetration/Aspiration Score	NP	Wilcoxon paired-samples rank test	(z = 0.816, p = 0.414, two-tailed)	(z = 0.000, p = 1.000, two-tailed)
Epiglottic Inversion	NP	McNemar test	(N = 4, exact p = 1.000)	(N = 4, exact p = 1.000)
BOT-PPW Contact	NP	McNemar test	(N = 4, exact p = 1.000)	(N = 4, exact p = 1.000)
Duration of BOT-PPW Contact	P	Paired-samples t-test		(t = -6.119; df = 2; p = 0.026, two-tailed)

[a] P = parametric; NP = nonparametric
Statistical analysis not completed on cookie bolus (n=1)

To determine if the magnitude of change seen pre- to post-stimulation was greater than the expected variability between two swallows, pilot work was completed on archived videofluoroscopic footage collected from patients with oropharyngeal cancer who had undergone surgery and associated oncological treatments for their disease. These archived data consisted of two swallows of pudding that were captured in succession at one clinical visit to iRSM. Analyses of liquid or cookie boluses were not completed. Pilot work consisted of determining the normal variance between two swallows in the same patient to derive a set of data, hereto forward referred to as *comparison data*. The comparison data were used to determine whether potential differences found in the present study were clinically relevant as opposed to a reflection of normal variance. A value of 70% was used as a "bench-mark" to represent the majority of values derived from the comparison data (henceforth *majority* will refer to 70% or more of the comparison data). This method was selected because absolute values were taken with the comparison data; therefore, mean difference was not considered an accurate meaningful indicator of central tendency. The 70% criterion was selected because it reflects approximately a 1.5 standard deviation bandwidth.

Analysis of the results also included visual inspection of the swallowing outcomes profiles of the cases to look for general trends in the data, similarities and differences between cases, and the relationships between variables.

Results

Bolus Transport Efficiency

The first research question, “Is electrical stimulation of the pharynx effective in improving the efficiency of bolus transport in the swallows of post-surgical head and neck cancer patients?” was addressed by analyzing *oral transit time, swallowing response time, pharyngeal transit time,* and *cricopharyngeal opening duration* with pudding. Findings are presented as averaged group data in Table 3 and individual performance pre- and post-stimulation in Figure 1-Figure 6.

Table 3

Group Descriptive Statistics for Efficiency of Bolus Transport Pre- and Post-Stimulation Outcome Measures

	Pudding			
Variable	Pre		Post	
	Mean (SD)	Median	Mean (SD)	Median
Oral transit time (s)	1.01 (1.19)	0.53	1.69 (2.88)	0.27
Swallowing response time (s)	1.07 (0.76)	1.06	1.07 (0.94)	1.07
Pharyngeal transit time (s)	9.34 (15.40)	1.84	3.88 (3.94)	2.49
Cricopharyngeal opening duration (s)	0.49 (0.13)	0.55	0.53 (0.19)	0.45

Oral transit time. Values from the comparison data derived from patients in the pilot study with oropharyngeal cancer indicated a mean *oral transit time* of 0.89 (sd = 1.09) seconds. In the present study, *oral transit time* for pudding was calculated for four participants. Mean pre- and post-stimulation oral transit times did not differ significantly (z = -0.535, p =

0.593, two-tailed). However, as can be see in Figure 1 and 2, all of the participants showed some change post-stimulation. S4 and S5 showed a slight increase (0.13 and 0.23 seconds, respectively) post-stimulation, whereas S3 showed a decrease (0.27 seconds) in *oral transit time* bringing it to within the range of swallows in the comparison data. Moreover, S1 showed a large increase of 3.64 seconds in *oral transit time* post-stimulation (6.01 seconds). It should be noted that the change seen in S3, S4, and S5 are within the swallow-to-swallow variability seen in the majority of the comparison data (0.33 seconds) whereas S1 showed a change well outside of this range.

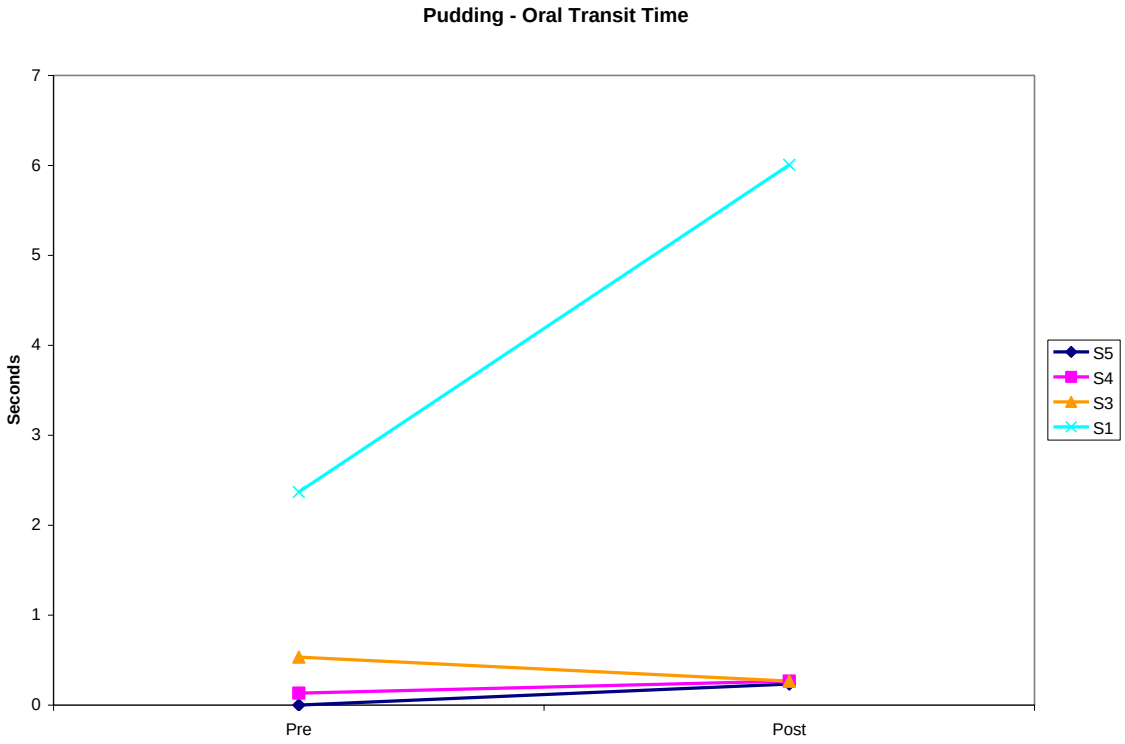

Figure 1. Oral transit times in seconds are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

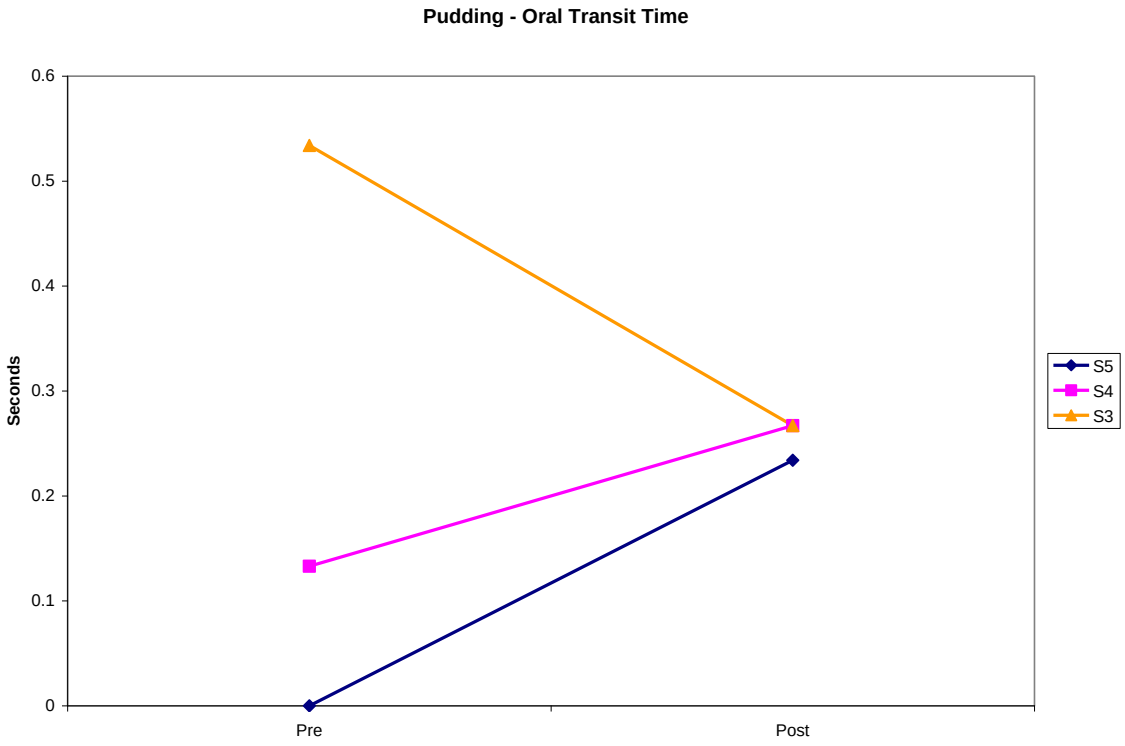

Figure 2. Oral transit times in seconds are depicted for each participant pre- and post-stimulation, excluding outliers. Each line color represents a different participant.

Swallowing response time. Typical swallows in normal healthy yield a mean *swallowing response time* with a 1mL pudding bolus of -0.01 (sd = 0.08) seconds (Lazarus et al., 1993); the negative value indicates that the onset of laryngeal elevation occurred *before* the bolus passed the point at which the ramus crosses the tongue base. The oropharyngeal comparison data revealed a mean *swallowing response time* of 0.36 (sd = 0.77) seconds. In the present study, *swallowing response time* only could be determined pre- and post-stimulation for two participants; S1 did not have any visible hyoid movement, S2 did not do pudding swallows, and S5's hyoid bone could not be visualized. Mean pre-and post swallow

response times did not differ significantly (t = 0.004, df = 1, p = 0.998, two-tailed). As can be seen in Figure 3, S4 showed a slight increase in *swallowing response time* (0.13 seconds) following stimulation and S3 showed a slight decrease (0.13 seconds) post-stimulation. It should be noted, however that neither of these changes was outside of the difference between swallows (0.38 seconds) observed in the majority of the comparison group.

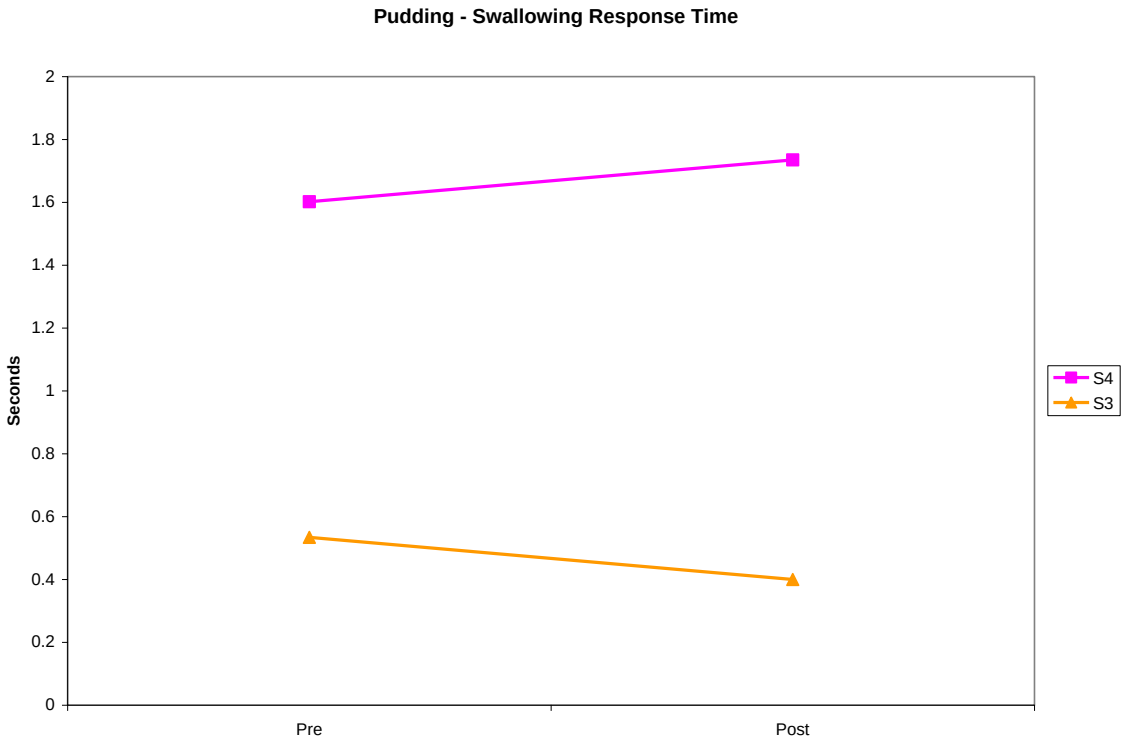

Figure 3. Swallowing response times in seconds are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

Pharyngeal transit time. The oropharyngeal comparison data indicated a mean *pharyngeal transit time* of 1.62 (sd = 1.12) seconds. *Pharyngeal transit time* was calculated for four participants pre- and post-stimulation and mean pre- and post times did not differ significantly (z = -

0.730, p = 0.465, two-tailed). As can be seen in Figure 4 and 5, post-stimulation two of the participants (S3 and S4) showed slight decreases (0.30 and 0.43 seconds, respectively), S5 showed an increase (1.73 seconds), and S1 showed a dramatic decrease (22.82 seconds). It should be noted that the decreases seen in S3 and S4 are not outside of the difference found between swallows in the majority of the comparison data (0.60 seconds). The distribution of values for *pharyngeal transit times* indicated that S1 fell outside the upper and was considered an extreme outlier for both pre- and post-stimulation with times of 32.4 and 9.62 seconds, respectively.

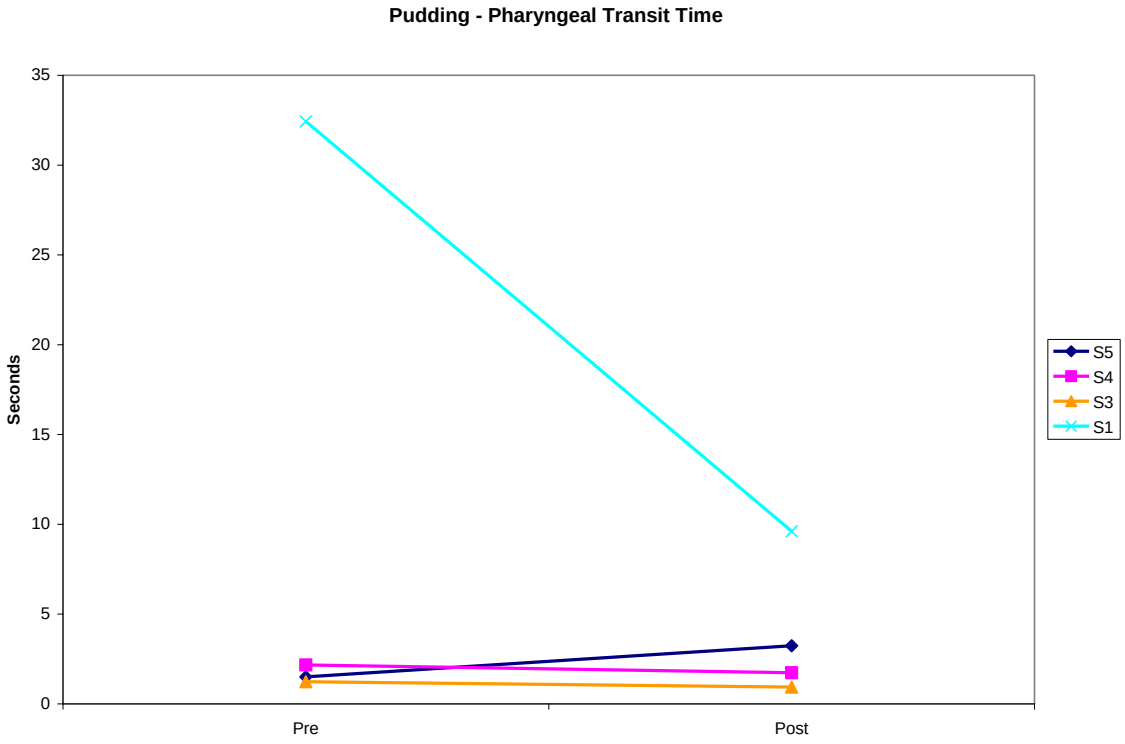

Figure 4. Pharyngeal transit time in seconds are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

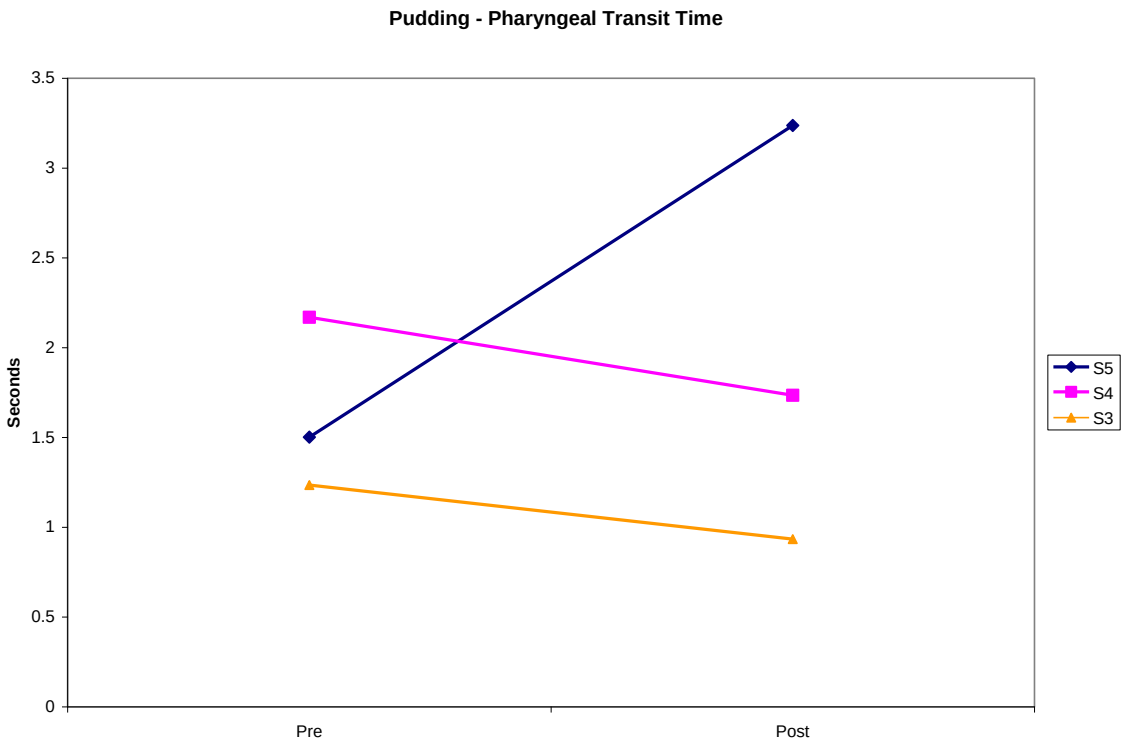

Figure 5. Pharyngeal transit time in seconds are depicted for each participant pre- and post-stimulation, excluding outliers. Each line color represents a different participant.

Cricopharyngeal opening duration. The mean *cricopharyngeal opening duration* with a 1mL pudding bolus in healthy individuals is 0.50 (sd = 0.01) seconds (Lazarus et al., 1993). Values from the oropharyngeal comparison data indicated a mean of 0.43 (sd = 0.11) seconds. *Cricopharyngeal opening duration* was calculated for four participants in the present study. Mean pre-and post cricopharyngeal opening durations did not differ significantly (z = -0.365, p = 0.715, two-tailed). However, visual inspection of Figure 6 reveals a downward trend in three of the four participants suggesting shorter opening durations post-stimulation. It should be noted that the decrease observed in S3, S4 and S5 (0.13, 0.10,

and 0.23 seconds, respectively) was equal to or greater than the swallow-to-swallow variability observed in the majority of the oropharyngeal comparison data (0.10 seconds).

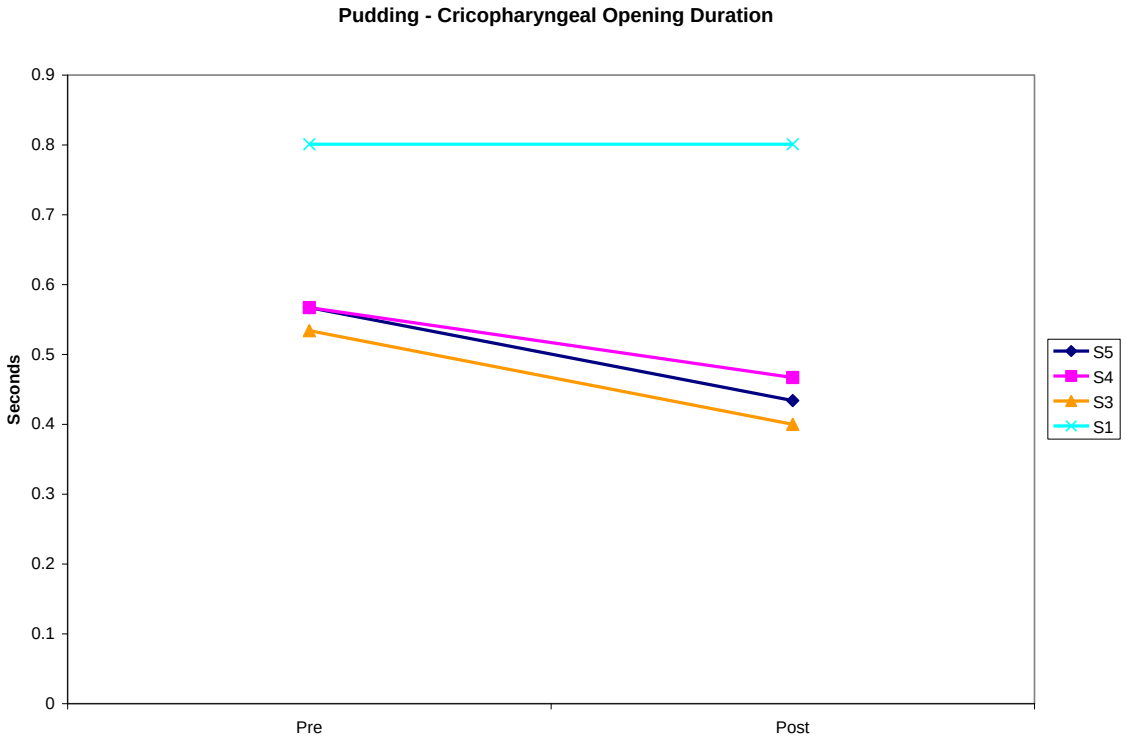

Figure 6. Cricopharyngeal opening durations are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

Bolus Clearance Efficiency

The second research question, "Is electrical stimulation of the pharynx effective in increasing the efficiency of bolus clearance in the swallows of post-surgical head and neck cancer patients?" was addressed by analyzing *pharyngeal residue* and *total number of swallows*. Findings are presented as averaged group data and individual performance pre- and post-stimulation for both liquid and pudding boluses. Table 4 shows the group means, standard deviations and medians for pharyngeal residue

and total number of swallows. Individual performances are illustrated in Figure 7-Figure ***10***.

Table 4

Descriptive Statistics for Efficiency of Bolus Clearance Pre- and Post-Stimulation Outcome Measures

	Liquid				Pudding			
	Pre		Post		Pre		Post	
Variable	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
Pharyngeal residue [a]	2.75 (0.50)	3.00	2.50 (1.00)	3.00	2.50 (1.00)	3.00	2.50 (1.00)	3.00
Total number of swallows	4.00 (2.16)	3.50	4.75 (2.22)	5.00	8.50 (6.81)	7.00	6.00 (4.97)	4.50

[a] scored out of 3

Pharyngeal residue. Pharyngeal residue with liquids was determined for four participants. Mean pre-and post comparisons did not differ significantly on this measure (z = -1.000, p = 0.317, two-tailed). As seen in Figure 7, in three of the cases, *pharyngeal residue* remained unchanged pre- to post-stimulation. In one case, S4, *pharyngeal residue* changed by one point, indicating an improvement from moderate to trace residue.

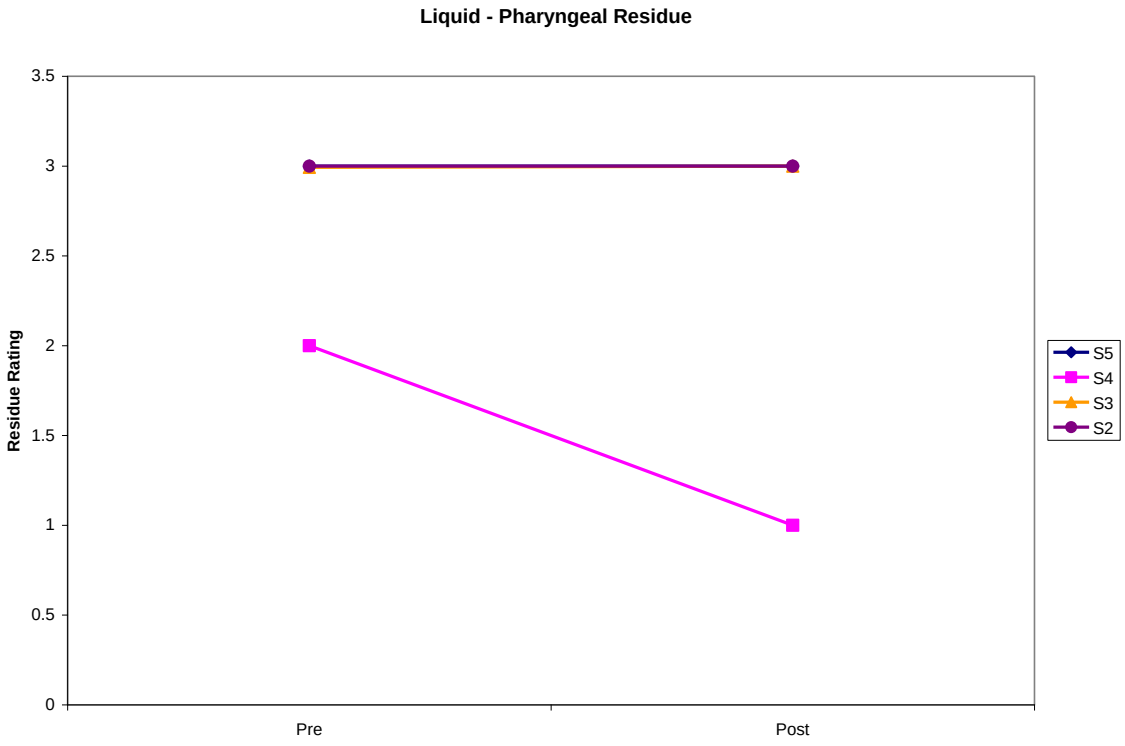

Figure 7. Pharyngeal residue ratings with liquids are depicted for each participant pre- and post-stimulation. Each line color represents a different participant. For this variable, values for several participants overlap.

Pharyngeal residue with the pudding bolus was calculated for four participants. The oropharyngeal comparison data indicated a mean *pharyngeal residue* rating of 2.34 (sd = 0.83) and a median of 3 for pudding; a rating of 3 suggests a significant amount of pharyngeal residue that threatens the airway. All participants of the present study maintained the same *pharyngeal residue* rating pre- to post- stimulation, therefore mean pre-and post comparisons did not differ significantly on this measure ($z = 0.000$, $p = 1.000$, two-tailed). As can be seen in Figure 8, S4 had a *pharyngeal residue* rating of 1, indicating only trace residue whereas S1,

S3, and S5 had ratings of 3, indicating a substantial amount of residue that could threaten the airway.

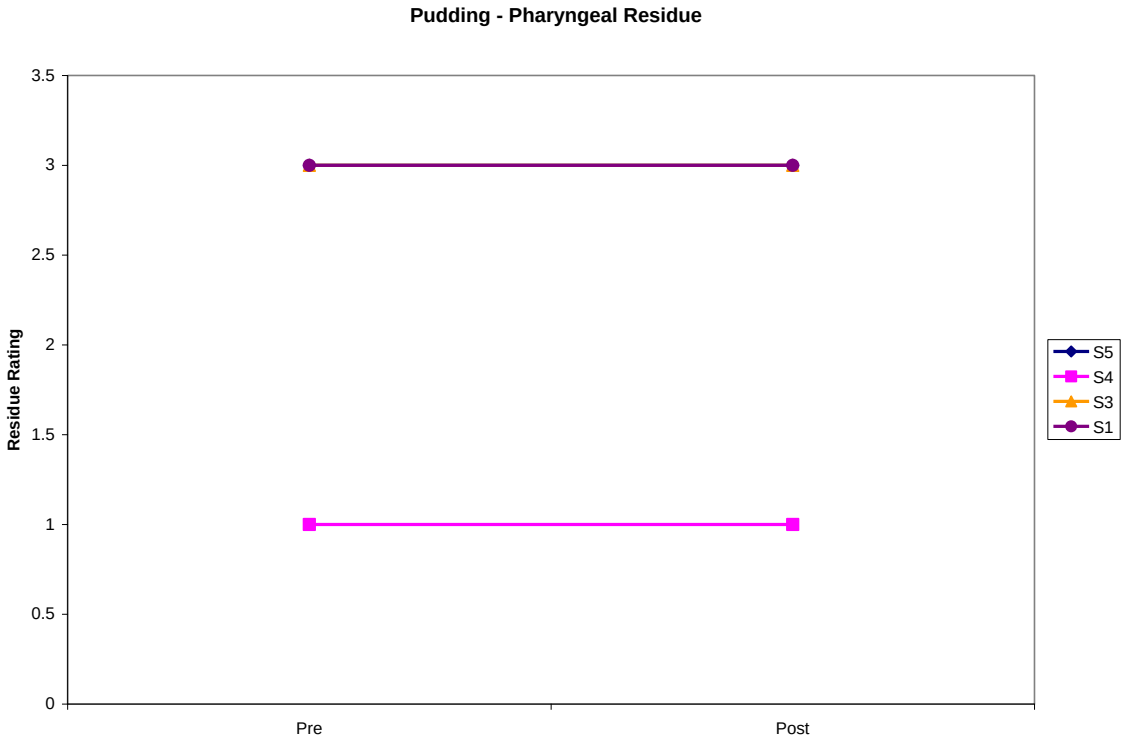

Figure 8. Pharyngeal residue ratings for pudding are depicted for each participant pre- and post-stimulation. Each line color represents a different participant. For this variable, values for several participants overlap.

Total number of swallows. The mean *total number of swallows* derived from healthy adults using a 10mL liquid bolus is 1.40 (sd = 0.25) swallows (Stachler et al., 1994). *Total number of swallows* was determined for four participants. Mean pre-and post comparisons did not differ significantly on this measure for liquid boluses (t = -0.878; df = 3; p = 0.444, two-tailed). As can be seen in Figure 9, two participants (S3 & S5) increased the total number of swallows, S2 decreased and S4 stayed the same.

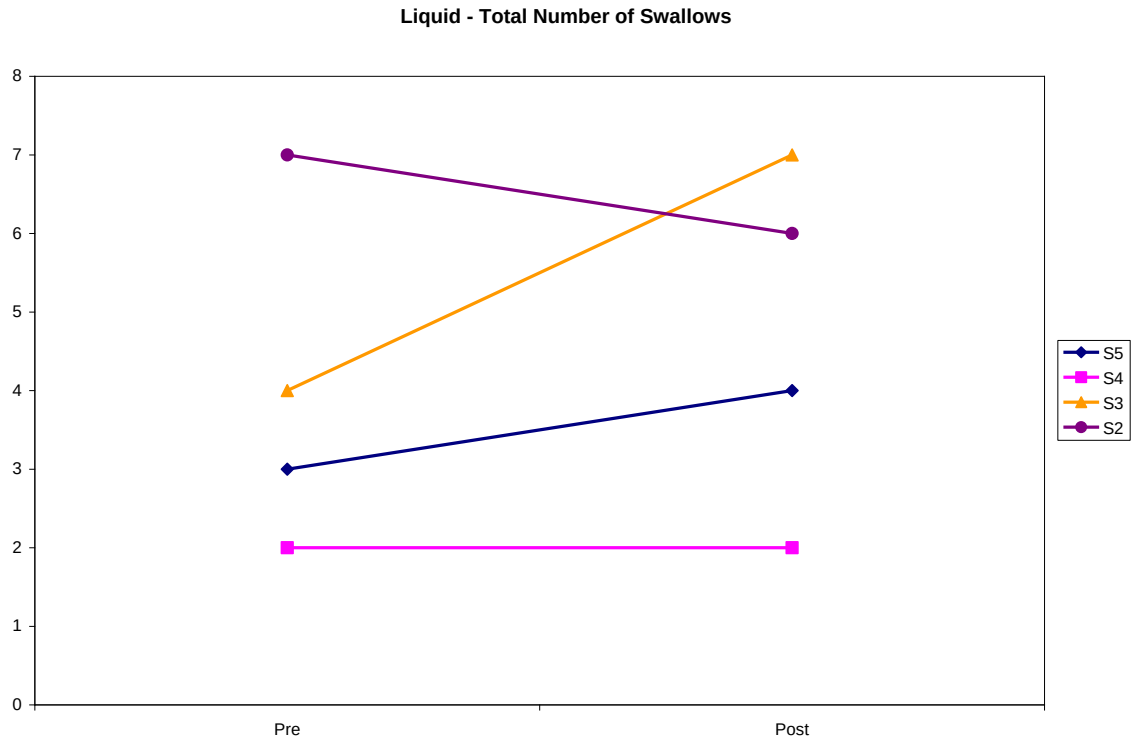

Figure 9. Total number of swallows for liquid are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

The mean *total number of swallows* derived from healthy adults using a 1/2 tsp paste bolus is 2.00 (sd = 0.55) swallows (Stachler et al., 1994). The *total number of swallows* was determined for four participants in the present study. The oropharyngeal comparison data indicated a median *total number of swallows* of 4 swallows for a pudding bolus. Mean pre-and post comparisons did not indicate a significant difference for the total number of swallows (t = 2.402; df = 3; p = 0.096, two-tailed). However, as seen in Figure 10, three of four participants (S1, S3, and S5) decreased the *total number of swallows* post-stimulation, whereas S4 stayed the same. It should be noted that the decreases observed in S1 (2 swallows), S3 (5 swallows), and S5 (3 swallows) are outside of the

swallow-to-swallow variability observed in the majority of the oropharyngeal comparison data (1 swallow).

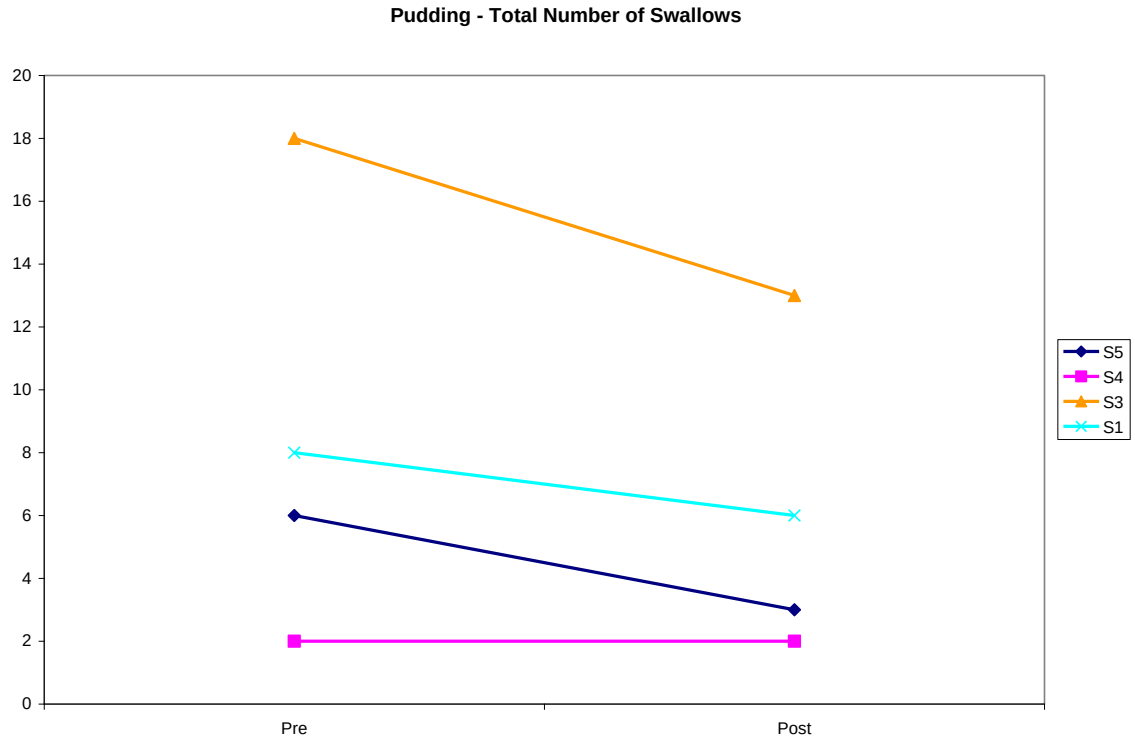

Figure 10. Total number of swallows for pudding are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

Safety and Effectiveness of Bolus Clearance

The third research question, "Is electrical stimulation of the pharynx effective in improving the physiological markers of safe and effective clearance of a bolus in post-surgical head and neck cancer patients?" was addressed by analyzing *penetration/aspiration score, epiglottic inversion, BOT-PPW contact* and *duration of BOT-PPW contact.* The group descriptive data are presented in Table 5 and individual performance is presented in Figure 11-Figure ***13***.

Table 5

Descriptive Statistics for the Physiological Markers of Safe and Effective Bolus Clearance Pre- and Post-Stimulation.

Variable	Liquid						Pudding					
	Pre			Post			Pre			Post		
	Mean (SD)	Med.	Freq	Mean (SD)	Med.	Freq	Mean (SD)	Med.	Freq	Mean (SD)	Med.	Freq
Penetration/ aspiration score	4.25 (2.50)	3.00	-	4.75 (1.71)	4.50	-	4.50 (2.89)	4.50	-	3.75 (2.87)	2.50	-
Duration of BOT-PPW contact	-	-	-	-	-	-	0.58 (0.32)	0.75	-	0.83 (0.28)	0.92	-
BOT-PPW contact	-	-	y – 2 n - 2	-	-	y – 2 n - 2	-	-	y – 3 n - 1	-	-	y – 3 n - 1
Epiglottic inversion	-	-	y - 0 n - 4	-	-	y – 1 n - 3	-	-	y -1 n - 3	-	-	y – 1 n - 3

Note. Blank cells, indicated by " – " represent statistics not applicable for that variable or consistency.

Med. = median; Freq = frequency; y=yes; n=no

Penetration/aspiration scale. Penetration/aspiration scores were determined for the four participants who completed liquid boluses. Mean pre-and post comparisons did not differ significantly on this measure (z = 0.816, p = 0.414, two-tailed). As can be seen in Figure 11, S2 and S4 increased by one and two points, respectively. S5 decreased by 1 point and S3 stayed the same. These scores indicated a decrease, increase, and maintenance of swallowing safety, respectively.

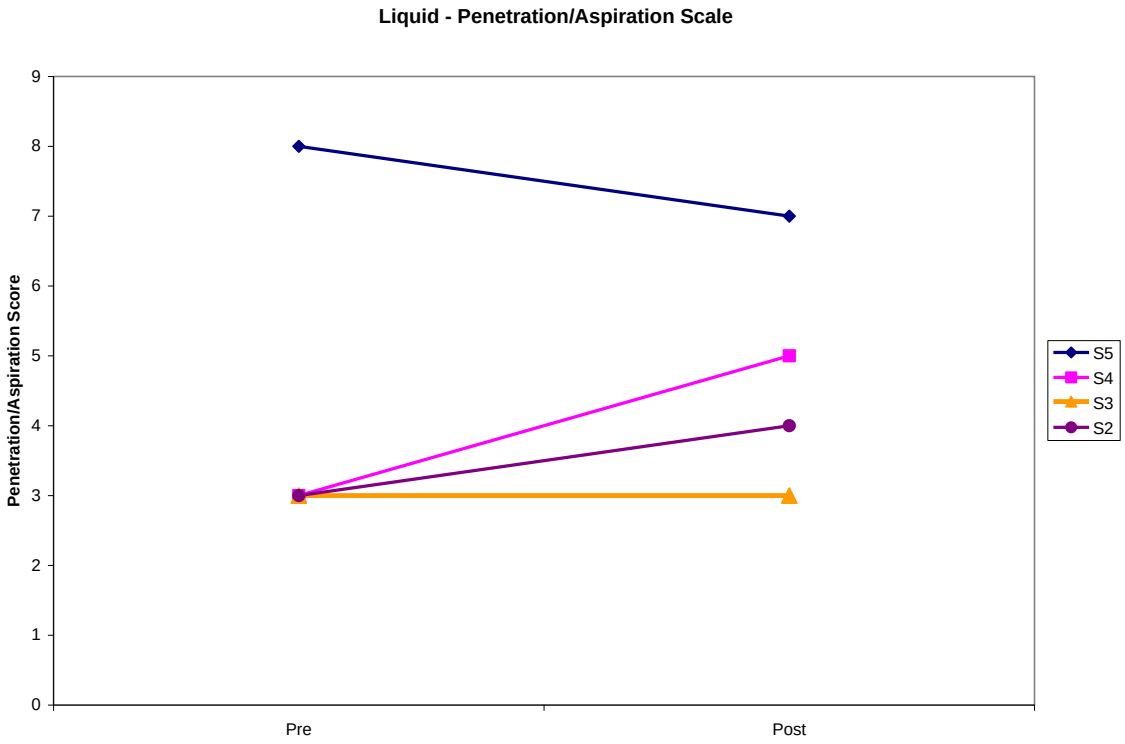

Figure 11. Penetration/aspiration scores for liquid are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

The oropharyngeal comparison for pudding data indicated a mean *penetration /aspiration* score of 1.47 (sd = 1.30) with a median score of 1, on an 8 point scale. In the experimental trials *penetration/aspiration score* with pudding was determined for four participants. Mean pre-and post

comparisons did not differ significantly on this measure (z = 0.000, p = 1.000, two-tailed). As shown in Figure 12, two of the participants increased by one (S1 and S3), one participant (S5) decreased by five, and one participant (S4) stayed the same; indicating a decrease, increase and maintenance of swallowing safety, respectively. The changes seen with S1, S3, and S5 are outside of the swallow-to-swallow variability (0 points) observed with the majority of the comparison data.

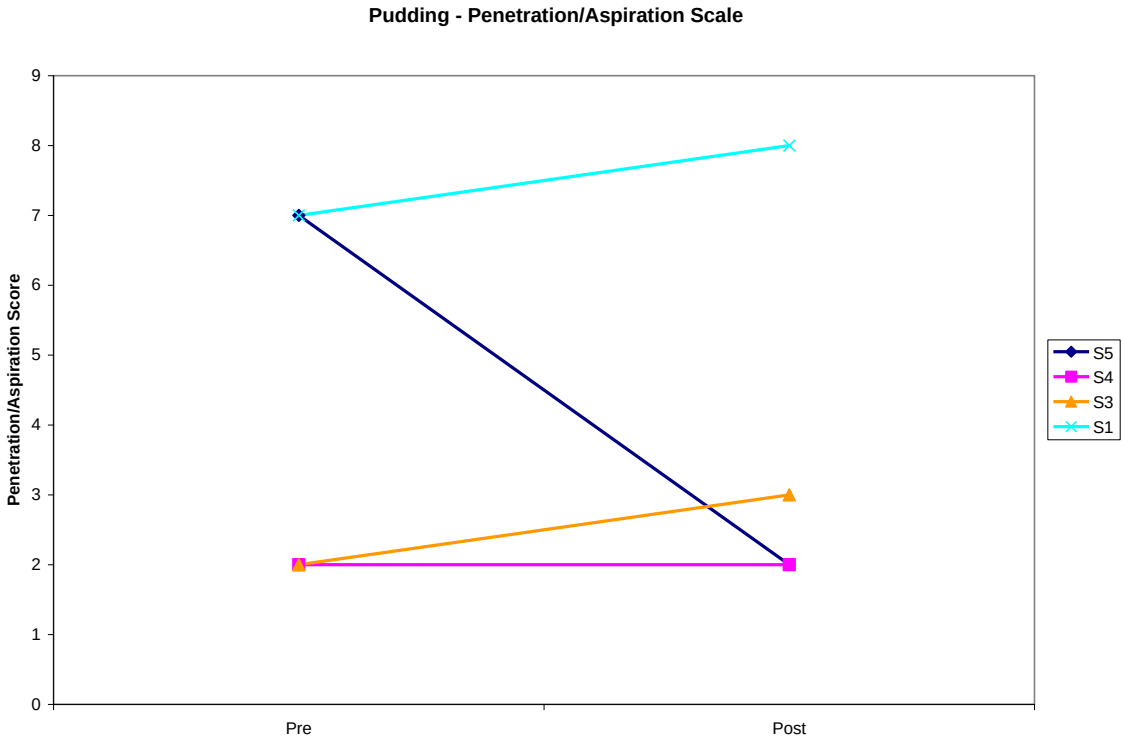

Figure 12. Penetration/aspiration scores are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

BOT-PPW contact. *BOT-PPW contact* with liquids was determined for four participants and remained unchanged for all participants post-stimulation. Consequently, mean pre- and post comparisons did not differ

significantly on this measure (*N* = 4, exact *p* = 1.000). Two participants (S3 and S4) had *BOT-PPW contact* prior to stimulation and maintained this contact post-stimulation; two participants (S2 and S5) did not have BOT-PPW contact pre- or post-stimulation.

For *BOT-PPW contact* with the pudding bolus, the oropharyngeal comparison data indicated 100% agreement between pre- and post-stimulation swallows. The participant data were collected for four participants, none of which showed a change in *BOT-PPW contact* post-stimulation. Accordingly, mean pre- and post comparisons did not differ significantly on this measure (*N* = 4, exact *p* = 1.000). Three of the participants (S1, S3, and S4) had contact pre-stimulation and they maintained it post-stimulation; one participant (S5) did not have contact pre-stimulation and he still did not have contact post-stimulation.

In the experimental trials, only one participant was comfortable trying a cookie bolus. S3 had *BOT-PPW contact* both pre- and post-stimulation with this consistency, which is consistent with normal swallowing function.

Duration of BOT-PPW contact. The mean *duration of BOT-PPW contact* in healthy adults using a 1mL pudding bolus is 0.27 (sd = 0.02) seconds (Lazarus et al., 1993). The oropharyngeal comparison data indicated a mean *duration of BOT-PPW contact* of 0.47 (sd = 0.23) seconds. In the experimental trials *duration of BOT-PPW contact* was determined for the three participants who had BOT-PPW contact both pre-

and post-stimulation. The mean comparison found *duration of BOT-PPW* to be significantly longer post-stimulation (t = -6.119; df = 2; p = 0.026, two-tailed). As can be seen in Figure 13, all of the participants exhibited increased *duration of BOT-PPW contact* post-stimulation. It should be noted that the changes seen in S1 (0.27 seconds) and S4 (0.30 seconds) are greater than the swallow-to-swallow variability seen with the majority of the oropharyngeal comparison data (0.17 seconds). The increase seen in S3 (0.17 seconds), however, was within the swallow-to-swallow variability observed with the majority of the comparison data.

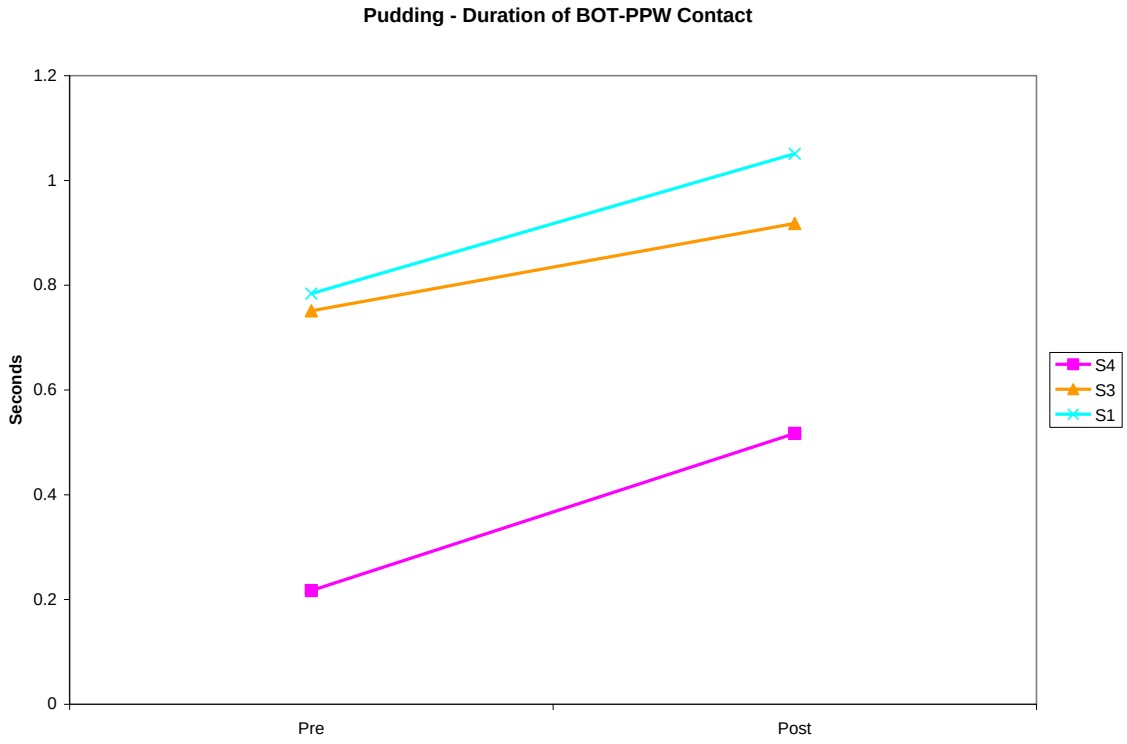

Figure 13. Durations of BOT-PPW contact are depicted for each participant pre- and post-stimulation. Each line color represents a different participant.

Epiglottic inversion. *Epiglottic inversion* for liquids was determined for four participants. Mean pre-and post comparisons did not differ significantly on this measure (N = 4, exact p = 1.000). None of the participants showed *epiglottic inversion* pre-stimulation and one, S4, showed inversion post-stimulation, indicating a positive change in swallowing safety.

For pudding, the comparison data indicated 94% agreement for *epiglottic inversion* between pre- and post-stimulation swallows. *Epiglottic inversion* was found 91% of the time in the oropharyngeal comparison data of pudding swallows. In the experimental trials, *epiglottic inversion* with pudding was observed in four participants. No change after stimulation was observed in any of the participants (N = 4, exact p = 1.000); three participants did not have *epiglottic inversion* pre- or post-stimulation and one participant did have *epiglottic inversion* pre- and post-stimulation.

Epiglottic inversion with cookie was only applicable for one participant. In this case epiglottic inversion was not found either pre- or post-stimulation.

Case Report S1

Case Information and History. S1 was a 70-year-old male diagnosed with severe oropharyngeal dysphagia secondary to treatment for T2 squamous cell carcinoma of the right tonsil. Treatment included surgical resection of 75% of the soft palate, the right lateral pharyngeal

wall to the level of the piriform sinus, and 50% of the posterior pharyngeal wall. This was followed by chemotherapy and radiation. At the time of the study, S1 was 23 months post-surgery and he was receiving his nutrition via enteral feeding and only eating Jell-O by mouth.

S1 trialed the pudding but not liquid and cookie consistencies. Summary information regarding variable changes for S1 can be found in Table 6. He had severely dyphagic pudding swallows both pre- and post-stimulation. However, he made *BOT-PPW contact* both pre- and post-stimulation and the *duration of BOT-PPW contact* increased post-stimulation. The *total number of swallows* and *pharyngeal transit time* both decreased, suggesting more efficient bolus transport and clearance post-stimulation. It should be noted, however, that minimal hyolaryngeal excursion along with discoordination and “fluttering” movements of the cricopharyngeus made swallow counts difficult. *Epiglottic inversion* was not seen pre- or post-stimulation, leaving the airway vulnerable during swallowing. An increase in *penetration/aspiration score* from 7 to 8 post-stimulation indicated that aspiration occurred both pre- and post-stimulation, but that a cough response only was observed pre-stimulation. Side-by-side comparisons were run in which the clinician was blinded to which videos were pre- and post-stimulation. These comparisons suggested a longer oral preparatory stage post-stimulation. Additionally, pre-stimulation S1 lifted his chin, assumedly in an attempt to help propel the bolus posteriorly, which was not seen post-stimulation.

Table 6

Change Post-Stimulation of Variables for S1 as Compared to Oropharyngeal Comparison Data

Variables	Pudding
Oral Transit Time	↑
Swallowing Response Time	--
Pharyngeal Transit Time	↓
Cricopharyngeal Opening Duration	→
Pharyngeal Residue Rating	→
Total Number of Swallows	↓
Penetration/Aspiration Score	↑
Duration of BOT-PPW Contact	↑

↑	increase greater than difference found between swallow 1 and 2 in 70% of comparison data
⇡	increase less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
↓	decrease greater than difference found between swallow 1 and 2 in 70% of comparison data
⇣	decrease less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
→	no change
--	not applicable

Case Report S2

Case Information and History. S2 was a 55-year-old male diagnosed with severe oropharyngeal dysphagia secondary to treatment for T3 squamous cell carcinoma of the right tongue base. Treatment included surgical resection of 75% of the right base of tongue, the right tonsil & lateral pharyngeal wall, and 50% of the right oral tongue. This was followed by chemotherapy and radiation. At the time of the study, S2 was 19 months post-surgery and was receiving nutrition via enteral feeding. At home he was taking liquids using the *Mendelsohn maneuver* and having teaspoons of applesauce with meals.

S2 did not trial the cookie or pudding boluses, therefore no durational measures were available. Summary information regarding variable changes for S2 can be found in Table 7. This participant had a significant amount of difficulty clearing pharyngeal residue from the liquid bolus, both pre- and post-stimulation. This resulted in large amounts of residue pooling in the vallecula and piriform sinuses. No *epiglottic inversion* was noted pre- or post-stimulation indicating little airway protection. The *penetration/aspiration score* increased from a 3 to a 4 indicating deeper penetration post-stimulation. This was congruent with the side-by-side, blind comparisons which suggested that the pre-stimulation stimulation swallow appeared slightly safer. It was concerning that while the *pharyngeal residue* remained at a score of 3, the *total number of swallows* decreased by one.

Table 7

Change Post-Stimulation of Variables for S2 as Compared to Comparison Data

Variables	Liquid
Oral Transit Time	--
Swallowing Response Time	--
Pharyngeal Transit Time	--
Cricopharyngeal Opening Duration	--
Pharyngeal Residue Rating	→
Total Number of Swallows	⇣
Penetration/Aspiration Score	↑
Duration of BOT-PPW Contact	--

↑ increase greater than difference found between swallow 1 and 2 in 70% of comparison data
⇡ increase less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
↓ decrease greater than difference found between swallow 1 and 2 in 70% of comparison data
⇣ decrease less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
→ no change
-- not applicable

Case Report S3

Case Information and History. S3 was a 52-year-old male diagnosed with mild-moderate oropharyngeal dysphagia secondary to treatment for T3 squamous cell carcinoma of the right tonsilar fossa. Treatment included surgical resection of 50% of the base of tongue, 100% of the soft palate, and lateral pharyngeal wall. The soft palate was reconstructed with a soft palate insufficiency repair (SPIR) and the base of tongue defect was reconstructed with a radial forearm free flap (RFFF) with a beavertail modification. Surgery was followed by radiation. At the

time of the study, S3 was 24 months post-surgery and was eating solid foods and thin liquids at home.

S3 trialed all three consistencies. Summary information regarding variable changes for S3 can be found in Table 8. While liquid swallows were generally well-managed both pre- and post-stimulation, they appeared very risky in side-by-side, blind comparisons due to a delay before initiation of the swallow and a large amount of *pharyngeal residue* after the first swallow. Additionally, *epiglottic inversion* was not seen pre- or post-stimulation. All factors considered, the swallows appeared generally well managed with the *penetration/aspiration score* (3) indicating penetration above the vocal folds pre- and post-stimulation. *BOT-PPW contact* also remained unchanged and was present in pre- and post-stimulation conditions. Although the *total number of swallows* increased from 4 to 7 post-stimulation, side-by-side, blind comparisons revealed two confounding factors that should be considered during interpretation. Firstly, S3 appeared to take a larger bolus post-stimulation. Secondly, both videos appeared to be cut off once only trace amounts of residue remained despite that fact that patient looked as though he was about to initiate additional swallows. It also was noted in the side-by-side, blind comparisons that the majority of the pharyngeal residue had cleared after all swallows in both the pre- and post-stimulation conditions.

S3 demonstrated significant difficulty moving the pudding boluses below the oropharyngeal level. Consequently, when the pharyngeal

swallow was initiated, the bolus was too high to be moved by the BOT-PPW contact (seen both pre- and post-stimulation). When the boluses were eventually mobilized to the hypopharyngeal level, an open airway (with no *epiglottic inversion)* left this participant vulnerable to aspiration. *Penetration/aspiration scores* increased from 2 to 3 post-stimulation indicating penetration to the same level with visible residue only observed post-stimulation. A liquid wash was given with both pudding swallows which appeared to help move the large amount of vallecular residue; a number of swallows were still needed to reduce the residue to a safe amount. Post-stimulation aspiration was seen after the liquid wash, followed immediately by a successful cough response. Side-by-side, blind comparisons suggested that the pre-stimulation pudding swallows appeared to be more discoordinated resulting in greater difficulty mobilizing the bolus from the oropharynx. This discoordination was consistent with the observation that all of the durational measures were slightly longer pre-stimulation.

S3 was the only participant to trial the cookie bolus. He showed a long oral-preparatory stage both pre- and post-stimulation with difficulty propelling the bolus into the pharynx in both conditions. Xerostomia is hypothesized to have been a significant, but constant factor with the cookie swallows. In both pre- and post-stimulation conditions, S3 was unable to move the bolus past the vallecula without the assistance of a liquid wash. Pre-stimulation, after the liquid he was able to clear the

pharyngeal residue with a number of subsequent swallows. Post-stimulation he appeared to have greater difficulty clearing the vallecular residue even with a liquid wash; however, he was eventually successful in doing so. An increase in *total number of swallows* was seen post-stimulation; however, it should be noted that swallows were only counted prior to the liquid wash. The swallow count, therefore, reflected the point at which he took this wash more so than the actual *total number of swallows*.

Table 8

Change Post-Stimulation of Variables for S3 as Compared to Comparison Data

Variables	Liquid	Pudding	Cookie
Oral Transit Time	--	⇣	--
Swallowing Response Time	--	⇣	--
Pharyngeal Transit Time	--	⇣	--
Cricopharyngeal Opening Duration	--	↓	--
Pharyngeal Residue Rating	→	→	--
Total Number of Swallows	↑	↓	↑
Penetration/Aspiration Score	→	↑	--
Duration of BOT-PPW Contact	--	⇡	--

↑	increase greater than difference found between swallow 1 and 2 in 70% of comparison data
⇡	increase less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
↓	decrease greater than difference found between swallow 1 and 2 in 70% of comparison data
⇣	decrease less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
→	no change
--	not applicable

Case Report S4

Case Information and History. S4 was a 55-year-old male diagnosed with minimal oral stage and mild-moderate pharyngeal stage dysphagia secondary to treatment for T2 squamous cell carcinoma of the left tonsil and neck. Treatment included surgical resection of 25% of the base of tongue, 1/3 of the soft palate, the left lateral pharyngeal wall, and bilateral submandibular glands. This was followed by chemotherapy and radiation. At the time of the study, S4 was 12 months post-surgery. S4 was receiving enteral feeds until approximately 4 months prior to the study date. S4 reported that he has trouble chewing and that he eats soft solids and regular liquids at home.

S4 trialed liquid and pudding boluses. Summary information regarding variable changes for S4 can be found in Table 9. Overall, with liquids he showed controlled and safe swallows both pre- and post-stimulation; epiglottic *inversion,* however, only was seen pre-stimulation. A decrease in *penetration/aspiration score* was seen from 3 to 5 indicates deeper penetration post-stimulation. In contrast, this was accompanied by a reduction in *pharyngeal residue* rating from 2 (moderate) pre-stimulation to 1 (trace) post-stimulation. It is interesting to note, however, that the moderate *pharyngeal residue* noted pre-stimulation was only present after the first swallow and was reduced to only trace amount post all swallows. It was surprising to see that *penetration/aspiration scores* became worse post-stimulation in light of the improvement in *pharyngeal residue scores*

and *epiglottic inversion*. While *swallowing response time* was not determined for liquid boluses, side-by-side, blind comparisons revealed a significantly longer delay in swallow initiation post-stimulation, perhaps contributing to the deeper penetration.

For pudding, side-by-side, blind comparisons suggested that both pre- and post-stimulation swallows were delayed but generally well managed. This was congruent with the fact that most of the variables (*penetration/aspiration score, pharyngeal residue, total number of swallows, epiglottic inversion, and BOT-PPW contact)* were the best possible on the first pudding swallow. This was important to note as no change would be expected in these measures post-stimulation. A significant increase in *duration of BOT-PPW contact* was seen post-stimulation. This was accompanied by a slight decrease in *pharyngeal transit time* and *cricopharyngeal opening duration,* and a slight increase in *oral transit time* and *swallowing response time.*

It should be noted that S4 made significant function gains (as indicated in his most recent clinical swallowing study) between the time when participants were recruited and when he was seen for the study. His swallowing performance was therefore stronger than the other participants.

Table 9

Change Post-Stimulation of Variables for S4 as Compared to Comparison Data

Variables	Liquid	Pudding
Oral Transit Time	--	⇡
Swallowing Response Time	--	⇡
Pharyngeal Transit Time	--	⇣
Cricopharyngeal Opening Duration	--	⇣
Pharyngeal Residue Rating	↓	→
Total Number of Swallows	→	→
Penetration/Aspiration Score	↑	→
Duration of BOT-PPW Contact	--	↑

↑	increase greater than difference found between swallow 1 and 2 in 70% of comparison data
⇡	increase less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
↓	decrease greater than difference found between swallow 1 and 2 in 70% of comparison data
⇣	decrease less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
→	no change
--	not applicable

Case Report S5

Case Information and History. S5 was a 75-year-old male diagnosed with mild oral stage and moderate-severe pharyngeal stage dysphagia secondary to treatment for T3 squamous cell carcinoma of the tongue base. Treatment included surgical resection of 100% of the base of tongue, the right lateral pharyngeal wall, right tonsil, and 25% of the soft palate. This was followed by chemotherapy and radiation. At the time of the present study, S5 was 32 months post-surgery and was receiving all

his nutrition via enteral feeding and only eating pudding consistency at home.

S5 trialed liquid and pudding boluses. Summary information regarding variable changes for S5 can be found in Table 10. Overall impressions from the side-by-side, blind comparisons suggested that liquid swallows were not safely managed pre- or post-stimulation. This was illustrated in the *penetration/aspiration scores* which were 8 pre-stimulation and 7 post-stimulation indicating aspiration below the glottis with a cough response seen only post-stimulation. It should be noted that a S5 appeared to take a larger liquid bolus post-stimulation which may have resulted in a larger amount of aspirated material, thus triggering the cough response.

S5 showed a decrease in *penetration/aspiration score* with pudding post-stimulation from 7 to 2 indicating a significant improvement from full aspiration to shallow penetration. However, a substantial amount of *pharyngeal residue* remained after all swallows which posed a significant threat of being aspirated after fluoroscopy was stopped. The *total number of swallows* also decreased with pudding post-stimulation from 6 to 3. While the outcomes measures seemed to indicate positive changes post-stimulation, side-by-side blind comparisons did not clearly illustrate improvements based on overall clinical impression. Interestingly, *oral* and *pharyngeal transit times* increased post-stimulation while *cricopharyngeal opening duration* decreased. It is possible that the increased oral and

pharyngeal durations resulted in increased sensory input and processing time to coordinate the appropriate swallowing movements. This could have resulted in a more effective swallow with a greater portion of the bolus being pushed through the cricopharyngeus with each swallow/opening.

Table 10

Change Post-Stimulation of Variables for S5 as Compared to Comparison Data

Variables	Liquid	Pudding
Oral Transit Time	--	↟
Swallowing Response Time	--	--
Pharyngeal Transit Time	--	↑
Cricopharyngeal Opening Duration	--	↓
Pharyngeal Residue Rating	→	→
Total Number of Swallows	↟	↓
Penetration/Aspiration Score	↓	↓
Duration of BOT-PPW Contact	--	--

↑	increase greater than difference found between swallow 1 and 2 in 70% of comparison data
↟	increase less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
↓	decrease greater than difference found between swallow 1 and 2 in 70% of comparison data
↡	decrease less than or equal to difference found between swallow 1 and 2 in 70% of comparison data
→	no change
--	not applicable

Discussion

The purpose of the present study was to determine whether functional improvement in the swallowing ability of patients with head and neck cancer could be observed following a standardized protocol of pharyngeal stimulation. Functional improvement was defined as an improvement in (i) the efficiency of bolus transport, (ii) the efficiency of bolus clearance, and (iii) the physiological markers of the safe and effective clearance of a bolus. It was predicted that improvement in swallowing function would be noted following stimulation as a result of improved pharyngeal sensitivity, recruitment of motoneurons in the remaining native tissue, or a combination of both. Changes in selected swallowing behaviors post-stimulation would infer changes in sensorimotor pathways.

Descriptive and inferential analyses were completed on ten variables of interest that related to swallowing outcome. Comparison data were used in order to determine if the magnitude of change seen pre- to post-stimulation was greater than the expected variability between two swallows in a similar patient population. In addition, the swallowing profiles for each participant provided a visual inspection of pre- to post-stimulation differences among swallowing variables. Whereas the number of participants in the current study was small, the preliminary data provide initial evidence that some aspects of swallowing function might have changed, following a dose of peripheral electrical stimulation. Specifically,

a downward trend was seen in *total number of swallows, pharyngeal residue ratings,* and *cricopharyngeal opening duration* with a corresponding increase in *duration of BOT-PPW contact.*

One variable, *duration of BOT-PPW contact* met the criteria for a statistically significant change from pre- to post-stimulation. The *duration of BOT-PPW contact* was significantly longer post-stimulation and, for two of the three participants, changes were greater than the swallow-to-swallow variability observed in the comparison data. Lengthening the duration of contact of the tongue base to the posterior pharyngeal wall is related to effective pharyngeal clearance (Pauloski & Logemann, 1999). Moreover, achieving sufficient *duration of BOT-PPW contact* is necessary for establishing adequate driving pressure to move the bolus through the pharynx (Pauloski & Logemann, 1999). A longer *duration of BOT-PPW contact* therefore suggests a stronger, more effective mechanism to propel the bolus into the cricoesophagus.

Effective bolus propulsion is characterized by a swallow that results in little pharyngeal residue. Unfortunately, in the present study, changes in *pharyngeal residue* after stimulation were not observed with pudding despite increases in observed BOT-PPW contact. There are several possible explanations for this finding. Whereas contact between the tongue base and posterior pharyngeal wall is necessary, it is not sufficient to ensure effective pharyngeal clearance. BOT-PPW contact will only facilitate a more effective swallow if the majority of the bolus has passed

into the hypopharynx, and if there is sufficient contact in that area to push the bolus into the upper esophageal sphincter. If, however, the level of BOT-PPW contact is higher in the oropharynx, retrograde flow of the bolus into the nasopharynx or pharyngeal stasis can occur. In the present study, although no retrograde flow into the nasopharynx was noted, there was often pharyngeal stasis possibly because of the lack of BOT-PPW contact lower in the oropharynx.

Another factor that could explain the lack of change in *pharyngeal residue* was the 3-point scale that was used. This scale may not have been sensitive enough to identify subtle changes in a large volume of residue, resulting in a ceiling effect in cases where severe residue was observed. Whereas subtle changes in large volumes of residue may not be enough to alter decisions clinically, they could be very meaningful in detecting small changes experimentally. Further research using three-dimensional imaging techniques would be useful in clarifying questions around changes in the amount of residue that exist after a swallow.

In addition to the statistically-robust finding, there were several other trends that, while not statistically significant, may be clinically meaningful. For example, *pharyngeal transit time* was found to decrease in three of four participants. Furthermore, effect size calculations suggested stimulation had a moderate effect on *pharyngeal transit time* (*d* = 0.469). This could be clinically meaningful as an accumulation of shorter transit times might result in overall shorter meal durations. The negative

implications of long meal durations are significant for dysphagic patients; dysphagic patients frequently cite long meal durations as a contributing factor to decreased intake due to fatigue and social discomfort with eating long after others have finished. Consequently, many people experiencing dysphagia report significant weight loss (Ekberg et al., 2002). It should be noted that one participant, S5, showed an increase in *pharyngeal transit time* that was outside of the swallow-to-swallow variability seen in the comparison data. It is meaningful to note that this participant had resection of 100% of the tongue base, whereas all participants who showed decreased *pharyngeal transit* time had 50% or less of the tongue base resected. As the base of tongue is needed to generate pharyngeal bolus driving pressure, it is reasonable to propose that a more limited amount of native tongue base tissue restricts base of tongue retraction. Additionally, stimulation may have affected the suprahyoid muscles (mylohyoid, geniohyoid, and the anterior belly of the digastric) in an inhibitory manner. This could result in decreased hyolaryngeal excursion and therefore impact cricopharyngeal opening. If the cricopharyngeal opening is shorter, then *pharyngeal transit time* could be decreased as cricopharyngeal closing marks the end of the *pharyngeal transit time*.

A clear downward trend was also seen in the *total number of swallows,* with pudding*,* which decreased significantly post-stimulation. Three of the four participants (S1, S3, and S5), exhibited a change that was greater than the swallow-to-swallow variability observed in the

oropharyngeal comparison data. Whereas S4 did not show a change in *total number of swallows* it should be noted that he appeared to clear the pudding bolus effectively in 2 swallows pre-stimulation; therefore, it is not surprising that no change was seen post-stimulation. A decrease in *total number of swallows* could be of benefit clinically. However, it was of concern to observe fewer rather than more swallows in cases where pharyngeal residue was still a threat. This was the case with S1, S3 and S5; in each of the post-stimulation videos, pharyngeal residue was seen after all swallows were completed on one bolus. It is possible that this was due to inhibited pharyngeal sensation, post-stimulation. Fraser et al. (2002) found that the effect of pharyngeal stimulation was very sensitive to stimulus frequency. In healthy participants they found that stimulation was facilitative at 5Hz, but inhibitory at 10, 20, and 40Hz. Due to the peripheral tissue damage in the participants in the present study, it is reasonable to propose that 5Hz may have an inhibitory effect and that a different frequency may be more facilitative. This could be explored through further research.

Another downward trend was found in *cricopharyngeal opening duration.* Three of the four participants (S3, S4 and S5) had shorter opening durations post-stimulation. While group statistics were not significant, it was interesting to note that the decrease in S3 and S5 was greater than the swallow-to-swallow variability observed in the comparison data. Furthermore, effect size calculations suggested a large effect of

stimulation on *cricopharyngeal opening duration* (*d* = 1.452). As stated previously, it is possible that the stimulation inhibited the suprahyoid muscles resulting in decreased hyolaryngeal elevation; this, in turn could decrease *cricopharyngeal opening duration.* Additionally, it is possible that sensation was inhibited post-stimulation, accounting for this change; if the central nervous system is not receiving sensory information about the volume of material to be swallowed, it may not send the correct degree of cricopharyngeal relaxation impulses to the upper esophageal sphincter. Reliable information regarding *pharyngeal residue* would be essential in order to evaluate the functional significance of a shorter c*ricopharyngeal opening duration.* No increases were seen in pudding *pharyngeal residue* during the present study, suggesting an increase in overall efficiency of bolus transport. However, future studies using a more sensitive measure of pharyngeal clearance would be beneficial in supporting these interpretations.

Pharyngeal residue remained unchanged in most liquid swallows as well; S4, however showed decreased *pharyngeal residue* post-stimulation, suggesting an improvement in bolus clearance of liquids. There were a number of other variables that did not show change post-stimulation. For example, no change was seen in *epiglottic inversion* and *BOT-PPW contact.* It is possible that these outcomes indicate that the level of safety was maintained post-stimulation in individuals who displayed these characteristics before stimulation. This would be clinically

meaningful as it indicates that post-stimulation swallows may be faster without compromising safety. Alternatively, in those individuals where *epiglottic inversion* and *BOT-PPW contact* were not apparent in the pre-experimental swallow study, pharyngeal stimulation did not appear to enhance these physiological events. Thus, there was no benefit in improving the safety of the swallow from a biomechanical point of view.

Penetration/aspiration score did not show any clear trends with liquid or pudding swallows. Small participant numbers and ceiling/floor effects may have contributed to the inconclusive results seen with this variable.

The catheter was positioned with the electrodes sitting just above the cricopharyngeus. During stimulation, muscle contractions were often visible at higher intensities. It is likely that the tongue base was one area affected by the stimulation. This is supported by the fact that the most promising results of this study were seen in those participants with 50% or less of the base-of-tongue resected. The significant increase in *duration of BOT-PPW contact* provides support for the notion that sensorimotor control of the tongue base and/or the pharyngeal constrictors were facilitated by stimulation. Theoretically, increased base-of-tongue retraction can compensate for decrease posterior pharyngeal wall bulging, and vice-versa (Pauloski & Logemann, 1999).

It also can be speculated that, due to the moist mucosa of the oropharyngeal structures, the electrical stimulation reached beyond those

areas immediately surrounding the electrodes. In particular, stimulation reaching the suprahyoid muscles could have had an inhibitory effect. Inhibition of the suprahyoid muscles is associated with hyolaryngeal depression (Ludlow et al., 2006). Because the anterior aspect of hyolaryngeal elevation is necessary in order to pull open the cricopharyngeus, hyolaryngeal depression could be associated with decreased cricopharyngeal opening. Therefore, the trend for a decrease in *cricopharyngeal opening duration* supports the hypothesis of inhibitory stimulation of the suprahyoid muscles. Theoretically, hyolaryngeal depression is a concerning clinical indicator; however, a study by Ludlow et al. (2006) found that, surprisingly, the lowering of laryngeal structures did not seem to be associated with a functional disturbance in swallowing. Moreover, the patients in their study who showed the most dramatic laryngeal depression demonstrated the greatest improvements on the *National Institute of Health – Swallowing Safety Scale* (Ludlow et al., 2006).

There are several neural mechanisms that could be responsible for the post-stimulation changes observed in some of the swallowing variables. A proposed central mechanism suggests that sensory axons were stimulated and, in turn, recruited spinal motoneurons through a reflex pathway (Collins, 2007; Dean et al., 2008). This mechanism would result in a greater number of muscles fibres contracting during the swallow and would account for changes seen thirty minutes after stimulation. Other

research has demonstrated plasticity in the motor cortex following peripheral nerve stimulation and TMS (Stefan et al., 2000; Ridding, Brouwer, Miles, Pitcher, and Thompson, 2000). These researchers employed F-wave studies and suggested that plasticity was occurring at a cortical level, rather than in spinal motoneurons. A reverse protocol involving CNS stimulation would be required to confirm a centrally driven neural mechanism responsible for the changes seen in the present data. Research from Fraser et al. (2002) using a similar reverse protocol demonstrated that changes in sensory input can produce changes in the cortical representation of swallowing. Neuroplastic mechanisms such as long-term potentiation (LTP) and long-term depression (LTD) are congruent with the time course of the effect seen in these studies; however, animal studies would be needed to determine a specific mechanism (Fraser et al., 2002).

Limitations

The present study was exploratory in nature and showed encouraging results. Although the protocol for this study was successful in laying the foundational work for future studies into a therapeutic treatment option for dysphagic head and neck cancer patients, some limitations should be considered.

There were several limitations with the radiological footage that could be addressed in future studies. Firstly, videofluoroscopic footage was often cut off during swallows. While this is common practice during

clinical swallowing exams, it can be problematic for research purposes when considering variables such as *total number of swallows.* It is also problematic when interpreting durations and swallows required to clear pharyngeal residue. When possible, this should be explained to the radiologists prior to examination. It also may be beneficial to have audio to accompany the visual footage.

Another limitation of the present study is that the videofluoroscopic footage only was taken laterally, therefore limiting observations to one plane. When analyzing tongue base behaviour, biplanar footage would allow for assessment of both lateral and posterior pharyngeal wall movement/contact. Considering the significant role that the pharyngeal wall may play when the base of tongue has been resected, it could be interesting to include analysis of the lateral pharyngeal walls in future research. In addition, an AP view would allow for a different perspective when rating oral and pharyngeal residue.

Due to the exploratory nature of the present study, participant numbers were small. A control group, therefore, was not included and a placebo effect cannot be ruled out. The stimulation protocol used by Fraser et al. (2002) included a “sham” protocol resulting in different outcomes than those exhibited by the experimental group. Nevertheless, a similar sham protocol would be useful in ruling out a placebo effect with post-surgical head and neck cancer participants.

The results of the present study did not show any changes in *epiglottic inversion, BOT-PPW contact,* or *pharyngeal residue ratings*. As previously stated, it is possible that this reflects a true “no change” situation, but it should also be considered that the outcome measures may not have been sensitive enough to capture more subtle changes in these variables. Modified scales with a greater number of intervals allowing for more subtle distinctions could capture any possible changes missed in the current study.

Clinical Implications and Future Research

This study was the first to apply peripheral pharyngeal wall stimulation to a group of patients following surgical treatment for head and neck cancer. The goal of the study was to see if changes in swallowing parameters would be detected following post-electrical stimulation. If so, peripheral stimulation may ultimately serve as a priming technique for use prior to behavioural treatment, a protocol for use during behavioural treatment, or an intervention coupled to daily eating activities. While the results of this study are preliminary, they show encouraging trends. The findings suggested that stimulation of native pharyngeal tissue could result in improvements in the efficiency of bolus transport. There is no evidence at this point, however, to suggest that stimulation improves the safety of swallows. It is possible that airway protection may remain as an area to be targeted through therapeutic interventions such as behavioural modifications.

For many patients with moderate-severe dysphagia, enteral feeding is a necessary part of management. Patients receiving the majority of their diet via enteral feeds are at risk for atrophy of the swallowing musculature. Electrical stimulation of inactive musculature has been shown to be of benefit in animal studies. For example, encouraging results have been demonstrated using electrical stimulation during periods of inactivity to prevent atrophy of hindlimb muscles in rats (Boonyarom, Kozuka, Matsuyama, & Murakami, 2009). Electrical stimulation of the pharynx could create an avenue for keeping healthy, native muscle tissue active in patients with minimal or no oral intake without the risk of aspiration. Confirmation of this notion would require a stringent experimental protocol with a sham condition in two groups of patients who have homogeneous lesion sites.

All of the participants in the present study had moderate-severe dysphagia following surgical treatment for oropharyngeal cancer as well as adjunctive radiation or chemoradiation. Surgery involved the structures of the oropharynx, including the base of tongue, soft palate, and lateral and posterior pharyngeal walls. The most encouraging change seen in the present study was in *duration of BOT-PPW contact;* not surprisingly, the only participants who did not have contact between the base of tongue and posterior pharyngeal wall were those with resection of 75% or more of the tongue base. Future research looking at the effect of area and extent of resection could reveal useful information about candidacy for

stimulation. Other participant variables that could impact candidacy include time post-surgery and severity of dysphagia diagnosis.

The protocol used in the present study was guided by the work of Fraser et al. (2002) with non-dysphagic participants and participants experiencing dysphagia secondary to stroke. While this was a logical starting point, future studies exploring different frequencies and durations of stimulation, as well as time lapse post-stimulation could reveal different ideal stimulation parameters than those determined by Fraser et al. (2002). Given that the area of defect in the present study is different from that in Fraser et al.'s population, it is reasonable to suspect that the parameters for optimal stimulation might differ as well.

There is some debate regarding the suitability of using measurements from videofluoroscopy alone to assess the function of a three-dimensional system (Martin-Harris et al., 2005). If future studies included the use of two-dimensional manometry as well as videofluoroscopy, this would allow the researchers to look at the relationships between structural movements and propulsive pressures (Pauloski & Logemann, 1999). Manometric pressure information would assist in the interpretation of results and add to the strength of conclusions drawn about relations between variables. For example, how increased BOT-PPW contact relates to pharyngeal transport variables like *pharyngeal transit time.*

The present study served to illustrate functional outcomes associated with electrical stimulation of swallowing muscles. Studies examining central changes associated with the stimulation would be useful to determine what changes in the central nervous system, if any, accompany the functional changes seen peripherally; such studies are currently underway in our laboratory.

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APPENDIX A: RECRUITMENT LETTER

Date

Patient Name
Patient Address

Dear *Patient Name*,

We are currently conducting a research project in conjunction with the University of Alberta Hospital. We are interested in testing a new technique of swallowing therapy. Based on your medical treatment at iRSM (formerly known as COMPRU), we feel that you might be a good candidate for this therapy if you are interested. The study is aimed at seeing if we can improve the muscle response in your throat for swallowing. We also want to see how the stimulation of you throat muscles relates to the way that your brain interprets your swallowing behavior.

The purpose of this study is to examine the effect of a series of electrical impulses delivered to the back of the throat with a small electrical catheter. The catheter is placed through the nose into the back of the throat. There may be some gagging as the catheter is inserted, but you should be otherwise comfortable during the rest of the study. The catheter contains a small electrode which can deliver an electrical impulse. You may feel a small buzzing sensation.

We will be measuring swallowing function with barium X-rays before and after the procedure. You will be asked to swallow several mouthfuls of barium. X-rays are then used to measure swallowing function.

We will also be studying the part of the brain that controls swallowing. To do this, we will use a transcranial magnetic stimulator. The stimulator is positioned over a particular spot on your scalp. A brief magnetic pulse causes a small number of neurons in the brain to be excited. Pathways from these brain cells then excite nerve cells which control the swallowing muscles. By recording responses in the swallowing muscles we can determine if these brain pathways are getting stronger. We hope to demonstrate that a program of pharyngeal electrical stimulation enhances swallowing muscle strength and function.

If you decide to participate, we would require approximately 2 hours of your time. The study will take place at the University of Alberta Hospital in Dr. Daniel Sadowski's laboratory. You will be compensated for your transportation up to a cost of $10.00.

By participating in this study, you will add to our knowledge about how to best treat future patients with head and neck cancer. There are some small risks associated with the tasks in this study. For example, y**ou cannot participate in the transcranial magnetic stimulation experiment if you have a history of epileptic seizures** because, in a small population of people, the stimulation can induce an epileptic seizure. **You also cannot participate if you have any implanted biomedical devices (e.g., pacemakers, cochlear implants, etc.).** There is also a possibility that you may experience a mild headache for a few hours after the experiment. Finally, some patients may experience mild discomfort and gagging related to the catheter that is passed through your nose.

If you choose to participate, you may withdraw at any point in the study. The information that we collect from you will be completely confidential.

We will be contacting you in approximately two weeks to see if you are interested in participating in the study. At this time you can say "no" to participating in this study with no consequences to your treatment. Thank you for your time and consideration.

Sincerely,

Jana Rieger, PhD

Program Director, Functional Outcomes

iRSM

APPENDIX B: INFORMATION LETTER AND CONSENT FORM

INFORMATION LETTER TO STUDY PARTICIPANTS

Project Title: Neurostimulation to promote the recovery of swallowing following surgery for oropharyngeal cancer.

Principle Investigators:
Daniel Sadowski MD FRCP
Division of Gastroenterology
Dept. of Medicine
University of Alberta
(780) 735-6837

Purpose and Background:

The information contained in this letter pertains to both healthy volunteers and to patients being treated at iRSM.

Cancer of the head and neck is occurs in 400 Albertans every year. The treatment for this cancer can include surgery, radiation or chemotherapy. Following treatment, some patients can experience difficulty with swallowing. This can lead to weight loss and poor nutrition. Some of this swallowing difficulty results from impaired sensation of the tongue, mouth and pharynx (back of throat). This can result in muscular weakness. Recent studies have shown that stimulation of the back of the throat with electrical impulses can improve muscular strength and swallowing function.

The purpose of this study is to examine the effect of a series of electrical impulses delivered to the back of the throat with a small electrical catheter. The catheter is placed through the nose into the back of the throat. There may be some gagging as the catheter is inserted, but you should be otherwise comfortable during the rest of the study. The catheter contains a small electrode which can deliver an electrical impulse. You may feel a small buzzing sensation.

We will be measuring swallowing function with barium X-rays. You will be asked to swallow several mouthfuls of barium. X-rays are then used to measure swallowing function.

We will also be studying the part of the brain that controls swallowing. To do this, we will use a transcranial magnetic stimulator. The stimulator is positioned over a particular spot on your scalp. A brief magnetic pulse causes a small number of neurons in the brain to be excited. Pathways from these brain cells then excite nerve cells which control the swallowing muscles. By recording responses in the swallowing muscles we can determine if these brain pathways are getting stronger. We hope to demonstrate that a program of pharyngeal electrical stimulation enhances swallowing muscle strength and function.

Procedures:

a) Before the experiment begins you will be asked by a researcher several screening questions. This will be done to ensure that you are not put at risk in

the experiment.

b) A barium X-ray study will be done prior insertion of the study catheter
c) While you are comfortably seated, the catheter will be inserted in your nose and passed to the back of your throat.
d) We will then locate the spot on your scalp that produces a swallowing muscle response from the transcranial magnetic stimulator.
e) We will then stimulate the swallowing centre in your brain using the magnetic stimulator. You may experience a tingling sensation but no pain. If you experience discomfort, the stimulator intensity can be turned down.
f) We will then stimulate the back of your throat with electrical impulses for 10 minutes. You may experience a buzzing sensation but no pain. If you do experience discomfort, the electrical intensity can be turned down.
g) Magnetic stimulation will then be repeated after 30 and 60 minutes to see if there has been any change
h) The catheter in your nose will be removed
i) The X-ray swallowing study will then be repeated.

Risks:

In a small population of people, a transcranial magnetic stimulation will induce an epileptic seizure. **You cannot participate in the transcranial magnetic stimulation experiment if you have a history of epileptic seizures**. **You also cannot participate if you have any implanted biomedical devices (e.g., pacemakers, cochlear implants, etc.).** There is also a possibility that you may experience a mild headache for a few hours after the experiment. Please inform us if the headaches become severe and you want to withdraw from these experiments. In addition, some patients may experience mild discomfort and gagging related to the catheter that is passed through your nose.

Confidentiality:

All information will be held confidential (or private) except when professional codes of ethics or legislation (or the law) requires reporting. Your identity will be kept confidential. The information you provide will be kept for at least five years after the study is done. The information will be kept in a secure area (i.e. locked filing cabinet). Your name or any other identifying information will not be attached to the information you gave. Your name will also never be used in any presentations or publications of the study results. Only the investigators and the lab technician will have access to this code and any data arising from the study. After 5 years, this data will be destroyed.

Summary:

Your participation in the study is entirely voluntary. However, we will reimburse you for expenses incurred as part of your participation in the study (e.g. parking, taxi, meals, child care etc.). You are free to ask questions at any time, and you may withdraw from the study at any time without any consequence to you. While you may experience some direct benefit by participating, this is not clear given our current state of knowledge. Information gained from the study will help us

understand how swallowing can be improved in patients who have had surgery for head and neck cancer. The results of this study, once completed, can be provided to you at your request.

If you have any questions about this study, you may contact Dr. Daniel Sadowski (735-6837). You may also contact the Patient Relations Office of the Capital Health Authority (407-1040) if you have any other questions or concerns.

Part 1: Researcher Information

Name of Principle Investigator:

Dr. Daniel Sadowski MD FRCP
Division of Gastroenterology
Dept. of Medicine
University of Alberta
780-735-6837

Part 2: Consent of Subject

	Yes	No
Do you understand that you have been asked to be in a research study?		
Have you read and received a copy of the attached information sheet?		
Do you understand the benefits and risks involved in taking part in this research study?		
Have you had an opportunity to ask questions and discuss the study?		
Do you understand that you are free to refuse to participate or withdraw from the study at any time? You do not have to give a reason and it will not affect your care.		
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records/information?		
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, please provide your doctor's name: _____		

Part 3: Signatures

This study was explained to me by:

_____

Date:

_____

__

I agree to take part in this study. Signature of Research Participant: _____ Printed Name: _____
Witness (if available): _____ Printed Name: _____
I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate. Researcher: _____ Printed Name: _____
* A copy of this consent form must be given to the subject.

APPENDIX C: TRANSCANIAL MAGENETIC STIMULATION

SAFETY SCREENING QUESTIONNAIRE

Transcranial Magnetic Stimulation (TMS)
Safety Screening Questionnaire

(Based on recommendations developed during a workshop on the use of TMS. June 1996, Bethesda, MD, USA)

Please answer each of the questions in the appropriate check box, and provide a brief explanation in the space below those questions to which you responded 'Yes'.

		Yes / No
1.	Have you ever had a seizure?	☐ ☐
2.	Have you had an EEG (measure of 'brainwave' activity)?	☐ ☐
3.	Have you had a stroke?	☐ ☐
4.	Have you had a head injury, or surgery to the skull or brain?	☐ ☐
5.	Do you have any metal in your mouth (dental implants) or in other parts of your face or head (such as surgical clips, metal fragments from welding, shrapnel, etc.)?	☐ ☐
6.	Do you have any implanted biomedical device, such as a cardiac pacemaker, insulin pump, cochlear stimulator, or heart line?	☐ ☐
7.	Do you suffer from frequent headaches?	☐ ☐
8.	Have you ever had any other brain-related condition?	☐ ☐
9.	Have you ever had any illness that caused brain injury?	☐ ☐

10.	Are you taking any medications at this time?	☐	☐
11.	If you are a woman of childbearing age, are you sexually active, and if so, are you not using a reliable method of birth control?	☐	☐
12.	Does anyone in your family have epilepsy?	☐	☐
13.	Do you need further explanation of TMS and its associated risks?	☐	☐
14.	Have you had an adverse ('bad') reaction to TMS in the past?	☐	☐

A 'Yes' to any question requires further investigation, but does not necessarily mean that you should not participate in TMS experiments.

_____ _____

Name of subject Signature

_____

Date

APPENDIX D: EXPERIMENTAL PROTOCOL

Pharyngeal Stimulation Protocol

Lab Set-up and Preparations

Catheter Preparation:

_____ Soak catheter in .9% saline solution for 3-5 hours before using

_____ Mark catheter with distance from pressure sensor in cm (18 cm is the largest mark on catheter)

Instrumentation Preparation:

_____ Turn on computer and start *SPIKE 2* Program

_____ Open *HOT SPOT* and ensure that scale and other parameters are set on protocols

_____ Place pharyngeal electrode cable into amplifier inputs:

See attached instrumentation figure

_____ 0 to 0

_____ 1 to 1

_____ 2 to 2

_____ Connect output from Channel 1 on Amplifier to *ADC 0* on Micro1401.

_____ Connect TMS to *Event Input 0* for trigger

_____ ***Stimulator setup***

_____ Set stimulator width to 200 on stimulator

_____ Set current at **0.1** m amps (**X10** on the orange toggle)

_____ Set output switch on stimulator to down position (up position when running the stimulation program)

_____ Set Vmax (voltage regulator) to 280

_____ Connect stimulator to DAC output 1 on Micro 1401 (BnC connector) and input to back of stimulator

_____ Plug ground (green pin) into Amplifier

_____ Stop watch

_____ ***TMS setup***

_____ Plug TMS (relay box – blue) out + to Event Input Channel 0, on Micro 1401

Participant Preparations

_____Consent participant

NOTE: TIME of PRE STIMULATION SWALLOW EVALUATION: _____

_____Mark cranial vertex (CZ) on skull of each participant using a measuring tape and marker (1/2

distance from bridge of nose (nasion) to occipital notch (inion) and ½ distance between
the right and left tragus) (reference 10-20 EEG System)

_____Mark approximate area of pharyngeal cortex on scalp over both right and left hemispheres
Left Hemisphere: 4 cm + 2cm anterior to the vertex and 7.5 + 2cm lateral to the vertex
Right Hemisphere: 5 cm + 2cm anterior to the vertex and 7.5 + 2cm lateral to the vertex

_____Place mono-electrode on the thenar muscle **of dominant hand** attach red clip
_____Place mono-electroded on the back of the hand attach black clip
_____Place ground electrode for both catheter and thenar muscle on the clavicle (same lead)

_____Freeze the nasal passages and insert catheter transnasally

_____ Be sure participant is comfortable, is facing the window and has plenty of water with a straw nearby

***Note, it might be better to wait for 5 to 10 minutes before starting so that patient can habituate to the catheter.

Start Time **Procedures**
_____ Location of MEPs

1. Ensure that ***swallow2*** protocol is loaded on data collection
2. Connect catheter to preamplifier (be sure it is in channel 1)
3. Position catheter so that distance from nostril to pressure sensor is **18 cm**
4. Ensure that electrodes are in contact with pharyngeal wall by observing real-time EMG responses to wet swallows (an obvious deflection in amplitude of the EMG signal will occur)
5. Adjust catheter depth if necessary and then tape into place
6. LOAD ***hotspot*** program
7. Start with hemisphere contralateral to side of pharynx with most damage
8. With **side A up** on TMS, discharge TMS coil (held on parasagittal plane as cortex) at **30%** stimulator output (2.2 Tesla) starting at vertex and moving in an anterior and lateral direction toward cortical sites that evoke successively larger EMG responses.
9. Try four sites in near site that evokes largest EMG response to ensure largest response
10. Mark the scalp site that evokes the largest MEP
11. Obtain stimulus response curve for the hemisphere (see next section)
12. Repeat steps 6-9 on other hemisphere
13.

Start Time Obtain Stimulus-Response Curve

_____

1. Ensure that data collection protocol ***Hot spot*** is loaded
2. Ensure that electrodes are in contact with pharyngeal wall by observing real-time EMG responses to wet swallows.
3. Deliver 5 TMS pulses with irregular inter-stimulus intervals at 30% stimulator output at site evoking largest MEP (MEPs will be automatically recorded by data collection software) NOTE: MEP should be around **10 ms** post TMS pulse.
4. Go up to the level of stimulator output that evokes the larges MEP for that hemisphere.
5. Decrease stimulator output in 5% increments and repeat step 3.
6. Continue decreasing stimulator output by 5% increments and repeating step 3 until reach a threshold of an **MEP less than 20 µV** on two out of five trials.
7. Save MEP recordings and note hemisphere and final stimulator intensity (be sure you are saving the **top screen** xxx.smr format

Right hemisphere	Stimulator Value	Left hemisphere	Stimulator Value
Notes	Max =	Notes =	Max
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%

Start Time *****Repeat entire sequence for MEP and Stimulus-response Curve for Thenar Muscle (one hemisphere only (NOTE: MEP should be around 20-30 ms post TMS pulse)**

Right or Left Hemisphere – Circle	Stimulator Value
	Max
	-5%
	-5%
	-5%
	-5%
	-5%
	-5%

_____

Start Time Pharyngeal Stimulation: Load the program **Peripheral Stim**

1. Connect catheter to stimulator **(BE SURE TO CONNECT ELECTRODE 0 to simulator, AMP out = 0)**
2. Set electrical stimulation parameters (5Hz, pulse duration 0.2 ms using ***pulse.exe (go to Load Configuration once Spike 2 is loaded)***
3. Ensure that electrodes are in contact with pharyngeal wall by observing real-time EMG responses to wet swallows.

4. Starting at an intensity of 1.0 m amps and increase the current in **0.1** m amp intervals until the participant signals that the stimulation can be felt
    a. Note current setting _____ (Stmin)
5. Continue increasing current until participant reports maximum tolerance
    a. Note current setting _____ (STmax)
6. Decrease current back to 1.0 m amps and begin increasing until the stimulation can be felt
7. Repeat steps 4 and 5 for a total of 5 trials.

Trial 1	Stmin	Stmax
Trial 2	Stmin	Stmax
Trial 3	Stmin	Stmax
Trial 4	Stmin	Stmax
Trial 5	Stmin	Stmax
Discard highest and lowest values for STmin and highest and lowest values for STmax	Average 3 values = _____	Average 3 values = _____

8. Set the treatment stimulation intensity for:
    Tx Stim = STminAve + 0.75 (STmaxAve – STminAve)

    _____ +0.75 (_____-_____)
    = _____
    a. Note whether people report a sensation of tingling and pulsing at this level _____

_____ **NOTE: if the person cannot tolerate this level, go to .50 and start again.**

Tx Stim = STminAve + 0.50 (STmaxAve – STminAve)

_____ +0.50 (_____-_____)
= _____

Record new level and new time
Tx Level = _____
Start time = _____

9. Stimulate the pharynx for 10 minutes

******Stop Time**

_____

Load **Hot Spot** program and repeat stimulus-response curves for **Thenar and then Pharyngeal** areas.
BE SURE THENAR is input to CHANNEL 0

Start Time

Right or Left Hemisphere – Circle	Stimulator Value
	Max
	-5%
	-5%
	-5%
	-5%
	-5%
	-5%

SAVE DATA for Thenar
_____ Repeat entire sequence for MEP and Stimulus-response Curve for Pharyngeal area

Right hemisphere	Stimulator Value	Left hemisphere	Stimulator Value
Notes	Max	Notes	Max
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%
	-5%		-5%

Stop Time

_____
SAVE ALL DATA!!! RECORD TIME of POST STIMULATION SWALLOW EVAL _____

APPENDIX E: COMPARISON DATA

Pilot work was completed on archived videofluoroscopic footage collected from a convenience sample of 16 patients (15 males, 1 female). The average age of the patients at the time of their exam was 54 years. Only pudding swallows were analyzed for the pilot data. These data were analyzed in two ways: firstly, to determine the normal variance between two swallows in the same patient and secondly, to assess the variability between patients. It should be noted that unlike the participant data, the order of the two swallows in the comparison data are arbitrary; therefore, absolute values were used when calculating the difference between swallows. Because absolute values were taken, mean difference was not considered an accurate meaningful indicator of central tendency; hence, the difference found in the majority (70%) of the patients was used as a comparison point for interpreting the participant data. Calculations were completed for the durational variables, and discrete variables. For the dichotomous variables, the percent agreement between swallows was considered when interpreting the participant data.

Bolus Transport Efficiency Variables

Mean differences and standard deviations were calculated for each of the bolus transport efficiency variables in order to determine the normal variance between two swallows in the same patient (Table E1). As absolute values of the difference were taken, the mean difference was not an accurate indicator or central tendency. The difference found in the

majority (70%) of the patients was therefore calculated in order to make meaningful comparisons between this data and the participant data.

Table E1

Bolus Transport Efficiency Variables: Mean Differences, Standard Deviations and Differences in Majority between Swallows across All Patients

Variable	Mean Difference (SD)	Difference in Majority (70%)
Oral Transit Time	0.430 (0.535)*	0.334
Swallowing Response Time	0.260 (0.202)	0.383
Pharyngeal Transit Time	0.511 (0.560)	0.601
Cricopharyngeal Opening Duration	0.101 (0.081)	0.100

In order to assess the variability between patients, means and standard deviations were calculated for each bolus transport efficiency variable (Table E2).

Table E2

Bolus Transport Efficiency Variables: Means and Standard Deviations between Patients

Variable	Mean for Swallow 1 (SD)	Mean for Swallow 2 (SD)
Oral Transit Time	0.829 (0.833)	0.950 (1.320)
Swallowing Response Time	0.314 (0.744)	0.411 (0.819)
Pharyngeal Transit Time	1.501 (1.010)	1.741 (1.242)
Cricopharyngeal Opening Duration	0.424 (0.104)	0.434 (0.113)

Bolus Clearance Efficiency Variables

Mean differences, standard deviations, and differences in majority were calculated for each of the bolus clearance efficiency variables in

order to determine the normal variance between two swallows in the same patient (Table E3).

Table E3.

Bolus Clearance Efficiency Variables: Mean Differences, Standard Deviations and Differences in Majority between Swallows across All Patients

Variable	Mean Difference (SD)	Difference in Majority (70%)
Pharyngeal Residue	0.063 (0.250)	0
Total Number of Swallows	1.067 (1.033)	1

In order to assess the variability between patients means and standard deviations were calculated for each bolus clearance efficiency variable (Table E4).

Table E4.

Bolus Clearance Efficiency Variables: Means and Standard Deviations between Patients

Variable	Mean for Swallow 1 (SD)	Mean for Swallow 2 (SD)
Pharyngeal Residue	2.313 (0.873)	2.375 (0.806)
Total Number of Swallows	4.688 (2.387)	5.063 (2.768)

Safety and Effectiveness of Bolus Clearance Variables

Mean differences, standard deviations, and differences in majority calculated for each of the safety and effectiveness variables in order to determine the normal variance between two swallows in the same patient (Table E5). Agreement within patients was 94% and 100% for *epiglottic inversion* and *base of tongue to posterior pharyngeal wall contact*,

respectively. This suggests very little variability of these factors between swallows.

Table E5

Safety and Effectiveness of Bolus Clearance Variables: Mean Differences, Standard Deviations and Differences in Majority between Swallows across All Patients

Variable	Mean Difference (SD)	Difference in Majority (70%)
Penetration/aspiration score	0.563 (1.750)	0
Duration of BOT-PPW contact	0.143 (0.110)	0.167

In order to assess the variability between patients means and standard deviations were calculated for each safety and effectiveness variable (Table E6).

Table E6

Safety and Effectiveness of Bolus Clearance Variables: Means and Standard Deviations between Patients

Variable	Mean for Swallow 1 (SD)	Mean for Swallow 2 (SD)
Penetration/aspiration score	1.625 (1.746)	1.313 (0.602)
Duration of BOT-PPW contact	0.531 (0.255)	0.402 (0.187)