STUDY PROTOCOL

PHYSIOLOGY OF SOLID AND LIQUID BOLUS MOVEMENT IN HEALTHY SWALLOWING

(Experiments 2, 4 and 6 of NIH Grant 5R01DC011020

***Physiological Flow of Liquids Used in Dysphagia Management*)**

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1. Introduction

This protocol covers three experiments (experiments 2, 4 and 6) that form part of a larger project entitled *Physiological Flow of Liquids Used in Dysphagia Management*. The project has been funded by the National Institutes of Health since 2015 (Grant number 5R01DC011020).

The overall goal of the project is to collect measurements of bolus movement (i.e. liquid flow) through the oropharynx (i.e., mouth and throat) during swallowing. The factors that are expected to influence bolus movement include the consistency of the food or liquid as defined by the International Dysphagia Diet Standardisation Initiative (www.iddsi.org) and the forces applied during swallowing (e.g., tongue pressures and swallowing muscle contraction). The objective is to determine how these factors interact to influence movement of a bolus through the oropharynx, both in healthy adults and in adults who have swallowing impairment.

Experiments 1 and 3 of the project involve basic science bench experiments, in which we will develop and test the liquid stimuli for use in the subsequent human subject experiments. Experiments 1 and 3 involve collaboration with co-investigators Dr. Ben Hanson (University Colllege London) and Dr. Lisa Duizer (University of Guelph) and consultant Dr. David James (University of Toronto, Mechanical Engineering).

Experiments 2, 4 and 6 (which comprise the focus of this protocol) explore swallowing in healthy adults, i.e., those with no known swallowing impairment.

Experiments 2 and 4 explore swallowing behaviour across a range of liquid stimuli (i.e., thin, slightly-thick, mildly-thick, moderately-thick, extremely thick) developed in experiments 1 and 3 and collect measures of liquid flow and swallowing behaviour in healthy adults. Experiment will take place at the Swallowing Rehabilitation Research lab of the Toronto Rehabilitation Institute. Videofluoroscopy x-rays for Experiment 2 will be conducted on a purchased service basis in the diagnostic imaging department at the Toronto General Hospital.

Experiment 6 is a new experiment that builds on the results of experiments 2 and 4 by exploring swallowing behaviours across different commercial barium products and with solid foods of different consistencies (minced and moist, soft & bite-sized, regular) in comparison to liquids. This experiment will be conducted in young healthy adults under 60 years of age. For experiment 6, data are collected in two parts: (a) a lab session (without x-ray), held at the Swallowing Rehabilitation Research Lab of the Toronto Rehabilitation Institute; and, (b) a videofluoroscopy x-ray session. The videofluoroscopy x-rays will be on a purchased service basis in diagnostic imaging department at the Toronto General Hospital.

Experiment 5 (for which a separate protocol will be submitted at a later date) will collect the same measures of liquid flow and swallowing behaviour in adults with swallowing impairment due to 5 different etiologies, and will be a multi-site study involving co-investigators Dr. Mark Bayley (Toronto Rehabilitation Institute – Brain and Spinal Cord Program), Drs. Anthony Burns and Cathy Craven (Toronto Rehabilitation Institute – Lyndhurst Centre – Brain and Spinal Cord Program), Drs. Douglas Chepeha and Andrew Hope (Princess Margaret Hospital Head and Neck Cancer Centre) and Dr. Emily Plowman (University of Florida, Gainesville).

2. Steering Committee

In addition to the PI, co-investigators and consultants named above, Dr. Julie Cichero and Mr. Peter Lam, who are co-chairs of the *International Dysphagia Diet Standardisation Initiative* (www.iddsi.org) will serve as consultants to the project. Together, this team of 12 key personnel will form the steering committee for the project. An annual face to face meeting and quarterly teleconference calls are planned for study oversight and progress review.

3. Purpose and Specific Aims

Dysphagia (swallowing impairment) is a serious condition, involving two primary functional concerns[1]:

1) the ability to swallow safely, without material entering the airway (penetration-aspiration);
2) the ability to swallow efficiently, without leaving residue behind in the pockets of the pharynx.

Impaired swallowing safety is linked to pneumonia[2] while impaired efficiency contributes to risk of malnutrition[3-8]. Dysphagia is estimated to affect 6.7% of hospital admissions in the USA with an annual attributable cost of $547 million[9, 10]. Dysphagia is common in the elderly[5, 11] and in individuals with stroke[12], brain injury[13], head and neck cancer[14-16], cervical spine injury or surgery[17], and developmental or neurodegenerative conditions[18-20]. When an individual presents with dysphagia, the most common intervention is to alter the consistency of the foods and fluids they consume[21, 22]. Thicker liquids flow more slowly (making them easier to control and making penetration-aspiration less likely). Pureed/ minced/soft foods are thought to be easier to transport than unaltered solid foods. **Despite the simplicity of these ideas, we lack evidence to guide the modification of food and liquid textures for clinical benefit.**

The National Dysphagia Diet, a guideline that was previously in use in the USA, described four levels of liquid consistency: *thin*, *nectar-*, *honey-* and *spoon-thick* liquids and four levels of food texture: pureed, mechanically altered, advanced and regular. Although viscosity ranges were proposed for these categories, these lacked empirical evidence. **Viscosity measurement is complex and not practical for caregivers, clinicians or institutional kitchens to perform.** A

systematic review published by the *International Dysphagia Diet Standardisation Initiative* (IDDSI) in 2015 concluded, "**there is a need to classify food and fluid behavior in the context of the physiological processes involved in oral transport and flow initiation"**[23]**.** In this project, we are addressing this challenge with a pivotal and comprehensive study **to determine physiological-rheological correlates (i.e. bolus flow and swallowing kinematics) across a continuum of consistencies in healthy and disordered swallowing.** To do this, we will prepare starch- and gum-thickened liquids in 5 consistencies (*Level 0 - thin*, *Level 1 - slightly-thick, Level 2 - mildly-thick, Level 3 - moderately-thick* and *Level 4 - extremely-thick*) according to the IDDSI framework. Additionally, we will study physiological correlates of bolus movement with three levels of food texture: *Level 5 – minced & moist, Level 6 – soft & bite-sized and Level 7 – regular*. Operational definitions for these consistencies have been developed by IDDSI based on validated low-technology tests that can be performed by caregivers to verify consistency during meal preparation and at the point of meal delivery (https://iddsi.org/framework/food-testing-methods/). Liquid flow is tested using the IDDSI Flow Test, which classifies consistency based on gravity-flow through a standard syringe (https://iddsi.org/framework/drink-testing-methods/). Previous phases of this grant have involved the development and characterization of liquid stimuli using the IDDSI Flow Test as well as validation of the testing method. IDDSI tests of solid food characteristics include measurements of particle size, hardness and stickiness/ cohesiveness. In experiments 2, 4, 5, and 6 of this project, we will collect videofluoroscopic and physiological measures of bolus flow and swallowing behavior across a range of liquid consistencies, across different commercial barium products and across foods of different consistency.

4. Methods

Participants:

Experiments 2 and 4 will involve the participation of a single sample of participants in the following sub-groups:

i) 40 healthy adults, aged under 60 years old, recruited from the Toronto population at large (already complete);

ii) 40 healthy adults, aged over 60 years old, recruited from the Toronto population at large (90% complete);

Experiment 6 will involve the participation of another sample of participants:

i) 20 healthy adults, aged under 60 years old, recruited from the Toronto population at large.

Participants will participate in only one of the two samples (Experiments 2&4 or Experiment 6) . Recruitment for Experiment 4 was terminated on July 24 2018 due to technical issues

encountered with the equipment that could not be repaired by the manufacturer. We will recruit an equal number of male and female participants within each age-group. Participants of all ethnic and racial groups will be accepted, however adequate comprehension of the English language consent documents will be required.

The target age ranges for the age sub-groups have been selected based on our previous research, which suggests that significant age-related differences in tongue pressures in swallowing are detectable over the age of 60[24-27]. Experiment 6 only includes healthy adults under 60 years of age at this time as this preliminary study exploring barium products/concentration and solids. The results will inform our decision to run a similar study in healthy older adults in the future.

Exclusion Criteria:

- The healthy adult participants for Experiments 2, 4, and 6 will be accepted into the study, provided that they have no prior history of swallowing, motor speech, gastro-esophageal or neurological difficulties, chronic sinusitis or taste disturbance.
- Individuals with a history of surgery to the speech or swallowing apparatus (other than routine tonsillectomy or adenoidectomy) will be excluded.
- Similarly, due to the requirement to swallow stimuli containing a significant carbohydrate load, individuals with Type 1 Diabetes will be excluded.
- For experiment 6, individuals who wear dentures will be excluded.
- Due to the fact that neurological impairments comprise an exclusion criterion, individuals with cognitive communication difficulties that may hinder comprehension of the study documents will be excluded from this study.
- For experiment 6, individuals with known allergies to medical adhesive will be excluded.
- Individuals with known allergies to ingredients of the food and liquid products used in the experiment will be excluded.
- As a further precaution due to the use of radiation in experiments 2 and 6, we will exclude women who report current pregnancy and individuals who report that they have had an x-ray to the neck in the past 6 months.
- Finally, individuals who report that they are occupationally exposed to radiation will be advised that they should not participate if they believe their occupational radiation exposure may exceed half the allowed Ontario annual limit of 20 mSv.
- These exclusion criteria will be confirmed using a self-report questionnaire form at the time of intake into the study (see Appendix A). Any questions will be clarified through discussion with the research assistant responsible for participant intake, and, where necessary with the principal investigator.

Children will not be involved in this protocol due to the use of radiation.

Recruitment:

We will conduct a broad public advertising campaign through local newspapers, magazines, websites, mailings and posters at community centres, seniors' residences, places of worship, and around the University of Toronto and the University Health Network. In particular, for experiment 2, we anticipate advertising in a seniors' magazine (*50Plus*) and its associated website, which has been useful in previous studies. All participants in experiments 2 and 6 will be required to attend an intake appointment to confirm their eligibility to participate, introduce them to the research protocol, complete the intake questionnaire, and obtain informed consent.

Stimuli:

We have previously developed an array of stimuli in the target consistencies, defined using the International Dysphagia Diet Standardisation Initiative (IDDSI) testing methods (www.iddsi.org). Barium stimuli will be prepared using commercially available barium products (either E-Z-Paque® powdered barium, Polibar Plus liquid barium suspension, or E-Z-HD® powdered barium), prepared in either 20% or 40% w/v barium concentration. All stimuli will be prepared in the Swallowing Rehabilitation Research Laboratory not longer than 6 hours prior to scheduled use, according to a strict standard operating procedure. Barium stimuli will be transported to the radiology suite at Toronto General Hospital, as per routine clinical procedures.

Data to be collected from each participant during intake (Experiments 2 and 6):

The following types of data will be collected from participants in both Experiments 2 and 6:

a) An intake questionnaire noting age, sex, ethnicity and race data and confirming eligibility based on the absence of reported exclusion criteria.

b) During the intake process, we will ask to review a list of conditions that could alter the results of the research study and identify whether any of these conditions apply. The disclosure of any medications that they are currently taking, allows us to control for the possible influence of medication on oral sensory and motor function. Medications do not qualify as the basis for exclusion. However, it is important for us to collect information regarding the use of benzodiazepines and neuroleptic medications that are known to have possible effects on swallowing, particularly with respect to causing xerostomia (dry mouth).

Data Collection Procedures:

<u>Experiment 2:</u> Prior to data collection, a nasal cannula will be placed around the participant's head with flexible prongs resting in their nostrils to measure airflow.

A single use disposable tongue bulb for the hand-held Iowa Oral Performance Instrument (IOPI) will be placed inside the participant's mouth. Tongue pressure signal will be collected at the anterior position during 3 anterior maximum presses and 3 saliva swallows.

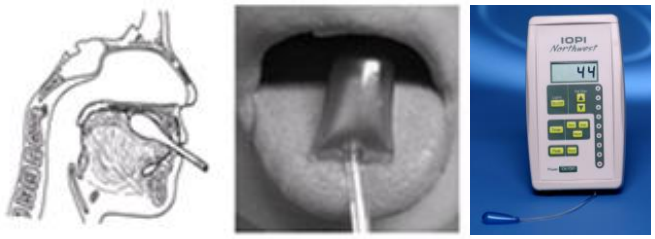

Image 1. Tongue pressure sensors.

Following sensor attachment, the participants will be seated on a chair inside the fluoroscopy unit. The videofluoroscopy recordings of swallowing involve a pulse rate of 30 pulses per second and video capture at 30 frames per second. The video output line from the fluoroscopy unit and the nasal cannula will then be connected to the KayPENTAX Digital Swallow Workstation Swallowing Signals Lab equipment, which is located on a properly insulated cart with an uninterrupted power supply and isolation transformer.

Participants will be asked to swallow 27 boluses (i.e., 3 boluses each of 9 different barium stimuli) in videofluoroscopy, with concurrent measurement of nasal airflow. All barium stimuli in Experiment 2 will be prepared using E-Z-Paque® powdered barium, in a 20% w/v concentration. Videofluoroscopy will be performed at maximum temporal resolution (30 pulses/second) and captured at 30 frames/second. The order of stimulus presentation will follow a randomized block design. Participants will be allowed to take natural sized sips of each stimulus from cups containing 40 ml. Cup weights before and after each sip will be taken on a digital balance so that sip volume and mass can be calculated.

Experiment 4: Experiment 4 was terminated on July 24 2018 due to technical issues encountered with the equipment that could not be repaired by the manufacturer.

Experiment 6: Experiment 6 will involve three sessions: 6-0 (protocol review and consent); 6-1 (a non-radiographic session held in the Swallowing Rehabilitation Research Lab at the Toronto Rehabilitation Institute); and 6-2 (a videofluoroscopy). Sessions 6-0 and 6-1 can be scheduled back to back on the same day, if convenient.

Session 6-0 (Consent)
In this session, we will review the study protocol with the participant and answer questions.

Session 6-1 (In-lab Session)

Session 6-1 will begin with the following non-swallowing tasks:

- Completion of a questionnaire regarding dental history.
- Oral inspection to document the number of teeth present and to note the location of any missing teeth.
- Measurement of participant height using a stadiometer.
- Measurement of neck circumference using a tape measure.
- A lateral view photograph capturing the participant's nose, jaw and neck (but not the eyes).
- A frontal view photograph of the participant's mouth, with the teeth clenched and the lips spread. This will provide a measure of dental occlusion between the upper and lower teeth.
- A measure of stimulated saliva (the Saxon Test), using a 2x2 inch of folded gauze that is chewed for 2 minutes, expectorated and then weighed prior to being discarded.
- Measurement of tongue strength using a single use disposable tongue bulb for the hand-held Iowa Oral Performance Instrument (IOPI). Tongue pressures will be collected at the anterior position during 3 anterior maximum presses and 3 saliva swallows.

Once these tasks have been completed, a nasal cannula will be placed around the participant's head with flexible prongs resting in their nostrils to measure airflow.

Surface electromyography (sEMG) electrode patches will be attached over the belly of the masseter muscle on each side of the participant's face, with a reference electrode attached to the forehead. Individuals with facial hair in the target sensor location (i.e. sideburns) will be asked to shave prior to sensor attachment.

Following sensor attachment, the participants will be seated on a chair and the nasal cannula and sEMG sensors will then be connected to the KayPENTAX Digital Swallow Workstation Swallowing Signals Lab equipment, which is located on a properly insulated cart with an uninterrupted power supply and isolation transformer.

Participants will then be asked to chew and swallow 9 different boluses, as follows:

- One IDDSI Level 5 minced & moist bolus (with barium)
- One IDDSI Level 6 soft & bite sized bolus (with barium)
- One bite of a Carr's table water cracker (with barium)
- A second bite of a Carr's table water cracker (without barium)
- A third bite of a Carr's table water cracker (without barium), which will be expectorated when ready to swallow
- One gummy candy
- A second gummy candy, which will be expectorated when ready to swallow
- One baby carrot , which will be expectorated when ready to swallow

- A strip of 2-coloured chewing gum, which will be expectorated after 20 chewing cycles

The minced & moist and soft & bite-sized stimuli will be prepared according to a standard recipe including a pureed bread mix (Darlington), cocoa and a vegetable-based oil (either olive oil or canola oil) and mixed with E-Z-Paque® barium powder. The Carr's Table Water Cracker will be smeared with E-Z-Paque barium prepared in a paste consistency with chocolate pudding (IDDSI level 4). The gummy candy will be a commercially available candy (Squish Red Roses, https://squishcandies.ca), comprising a round, fruit-flavoured gummy approximately 1.5 cm in diameter. The chewing gum will involve two colours of Hubba Bubba tape gum. For all tasks, participants will be allowed to take natural sized bites or spoons-full from pre-portioned cups. Cup weights will be taken on a digital balance before and after each bite so that bolus volume and mass can be calculated. Photographs will be taken of the expectorated boluses to allow for image-based measurement of particle size. Sips of water will be made available to participants between tasks, if desired.

<u>Session 6-2 (Videofluoroscopy)</u>

Prior to data collection, a nasal cannula will be placed around the participant's head with flexible prongs resting in their nostrils to measure airflow.

Surface electromyography (sEMG) electrode patches will be attached over the belly of the masseter muscle on each side of the participant's face, with a reference electrode attached to the forehead.

A coin or a metal washer of known size will also be attached to the participant's face with medical tape to act as a measurement scalar on the radiographic images.

Following sensor attachment, the participants will be seated on a chair inside the fluoroscopy unit. The videofluoroscopy recordings of swallowing involve a pulse rate of 30 pulses per second and video capture at 30 frames per second. The video output line from the fluoroscopy unit and the nasal cannula and sEMG sensors will then be connected to the KayPENTAX Digital Swallow Workstation Swallowing Signals Lab equipment, which is located on a properly insulated cart with an uninterrupted power supply and isolation transformer.

Participants will then be asked to swallow 22 different boluses, as follows: 1 thin bolus with a cued swallow, 12boluses of thin barium prepared in either 20% or 40% w/v concentrations using different commercially available barium products (E-Z-Paque® powdered barium, Polibar Plus liquid barium suspension, and E-Z-HD® powdered barium), 3 boluses of mildly-thick barium (prepared with E-Z-Paque® powdered barium), and 6 solid stimuli, two each from IDDSI levels 5,

6 and 7 (minced & moist, soft & bite-sized and regular). The minced & moist and soft & bite-sized stimuli will be mixed with E-Z-Paque® barium powder. The regular stimulus will be a Carr's Table Water Cracker smeared with E-Z-Paque barium prepared in a paste consistency (IDDSI level 4). In addition to the swallowing tasks, five 3-second static recordings of the participant will be taken with the head in neutral (X2), chin up and chin down positions and during a voicing task (saying "ah"). Participants will also be asked to hold 1cc and 5cc water boluses in their mouth while the fluoroscopy is turned on to understand pharyngeal space. Task order will follow a randomized block design. For the liquid swallowing tasks, participants will be allowed to take natural sized sips of each stimulus from cups containing 40 ml. Similarly, for the solid food tasks, participants will be allowed to take natural sized bites or spoons-full from pre-portioned cups. Cup weights will be taken on a digital balance before and after each sip/bite will be taken on a digital balance so that bolus volume and mass can be calculated. Sips of water will be made available to participants between tasks, if desired.

Data Processing:

Signals collected from the participants (which may include tongue-pressure, sEMG, and nasal airflow waveform data) will be segmented using an automatic segmentation algorithm developed previously in the PI's lab. Similarly, the videofluoroscopy recordings will be spliced into single bolus clips and the audio channel will be muted to remove cues that might bias rating. Blinded videofluoroscopy rating will then be performed in duplicate by trained raters in the Steele Lab following established standard operating procedures (https://pubs.asha.org/doi/10.1044/2019_JSLHR-S-18-0448). Discrepancies between raters will be flagged and resolved at consensus meetings, as required. These procedures will yield a large number of parameters, as listed below:

a) Maximum isometric tongue-pressure amplitude (in mm Hg);
b) Rise-time to peak tongue-pressure (in ms);
c) Decay-time for tongue-pressure (in ms);
d) Tongue-pressure area-under-the-curve;
e) Peak masseter sEMG amplitude (in μV);
f) Rise-time to peak sEMG amplitude (in ms);
g) Decay-time for sEMG (in ms);
h) sEMG area-under-the-curve;
i) Number of chewing cycles;
j) Duration of chewing cycles and overall chewing activity;
k) Duration of apnea (ms);
l) Breathing pattern pre- and post- swallow;
m) Bolus transit time from ramus of mandible to vallecular pit (in ms);

n) Bolus dwell time in pharynx from ramus of mandible to laryngeal vestibule closure (in ms);
o) Pharyngeal bolus transit time from ramus of mandible to upper esophageal sphincter opening (in ms);
p) Bolus transit time from ramus of mandible to tail exiting the upper esophageal sphincter (in ms);
q) Amount of residual left behind in the valleculae and pyriform sinuses after the initial swallow;
r) Pixel-based measures of hyolaryngeal excursion and of pharyngeal area at rest and during maximum constriction;
s) Number of swallows for the bolus.

Data Analysis:

We will model the impact of bolus consistency on measures of chewing and videofluoroscopic measures of pharyngeal bolus flow (i.e., the interval from the bolus passing the mandibular ramus until laryngeal vestibule closure; pharyngeal transit time) and pixel-based measures of post-swallow residue. The analysis will involve linear mixed model ANOVAs with repeated measures. A stepwise analysis approach will be used, first identifying relevant influences of tongue-pressure and nasal airflow patterns across stimuli. The influence of variations in bolus volume will also be explored using univariate tests, and, if confirmed to be significant, will be used as a covariate in the subsequent statistical models. Similarly, differences in the dependent variables as a function of sex or age (continuous or divided into groups) will be explored first in a univariate fashion, and, if significant, these between-participant factors will be included in the model.

For Experiment 2, **our main hypothesis is that liquids with similar gravity-flow properties will show similar pharyngeal bolus flow.** Our goal will be to detect differences in bolus flow measures ≥200 ms as a function of consistency, with a medium effect size (Cohen's $d \geq 0.5$)[96]. We hypothesize that the healthy participants in these experiments will use higher amplitudes of tongue pressure and/or submental muscle contraction (sEMG) during oral propulsion of starch-thickened stimuli, thereby achieving a similar outcome for both starch- and gum-thickened liquids in terms of pharyngeal bolus flow. Model fit for different covariance structures will be explored using restricted log likelihood estimation. Age-group (< vs. > 60 years) will be used as a between-groups factor while bolus consistency will be used as the within-participants factor. Sample size calculations have been performed using the data from the PI's previous grant, in which ultrasound measures of the duration of hyoid movement differed by 200-400 ms between age-groups and tongue-pressure amplitudes varied by 10-35 mm Hg depending on the liquid studied. A power calculation shows that 36 participants per group will be needed to

detect this difference with 80% power (α=0.05). Allowing a margin for attrition, we have therefore planned to enroll n=40 per participant group: total N=80 for Experiments 2 and 4. This sample size will also be adequately powered for Experiment 4 to detect differences ≥10 mm Hg in tongue-pressure amplitudes.

For Experiment 4, **our main hypothesis is that liquids with similar flow properties based on the IDDSI gravity-flow tests will elicit different tongue pressure and sEMG measures based on their actual viscosities.** This hypothesis is predicated on the idea that healthy adults modulate oral phase propulsive forces used for boluses of differing consistency with the goal of establishing uniform pharyngeal flow (as hypothesized for Experiment 2). Significant contrasts are expected between the two extremes of the liquid continuum: [*thin* and *slightly-thick*] vs. [*moderately-* and *extremely-thick*]. We expect that measures for the *mildly-thick* liquids will fall in between, but that differences may not be large enough to achieve statistical significance versus the extremes in pairwise comparisons. We predict that barium stimuli will elicit higher amplitudes of tongue-pressure than non-barium stimuli based on their increased density.

Experiment 6 is exploratory, with the goal of identifying differences in the following measures across stimuli:

- Oral processing time
- Number of chewing cycles
- Chewing duration
- Chewing force
- Bolus characteristics after chewing (photographs of the chewed bolus for measurement of particle size, and tests of bolus consistency using the IDDSI testing methods)
- Bolus flow measures (as described above for experiment 2)

The planned analyses will begin with univariate analyses of the effects of participant factors (sex, height, jaw length, neck length, neck circumference, number of occlusal pairs of teeth) on the physiological parameters of interest (chewing force, number of chewing cycles, chewing time, oral processing time). Any participant-level factors that are found to be significant will then be carried forward as covariates into linear mixed model ANOVAs with repeated measures, exploring relationships between the physiological parameters of interest and the dependent variables of interest (bolus particle size at the end of chewing and swallowing parameters as outlined for experiment 2). The results of these preliminary analyses for experiment 6 will inform the design of future experiments.

5. Risks and Benefits

Risks

The following risks will be disclosed to all participants in Experiments 2 and 4 prior to obtaining their consent to participate:

a) It is possible that participants may dislike the taste or texture of some of the stimuli in the study. Participants will be reminded that they are free to discontinue participation at any time.

b) It is possible that participants may experience some fatigue during the data collection sessions. Participants will be reminded that they should disclose any fatigue or discomfort to the research team, and that they are free to discontinue any particular session or to withdraw from the study at any time.

c) Participants will receive exposure to radiation during the videofluoroscopy. Based on a previous videofluoroscopic study that we have conducted in healthy adults, Experiment 2 is expected to involve 118+/-18 seconds of radiation exposure[28], with an associated dose estimate of < 0.35 milliSieverts. Experiment 6 is expected to involve a maximum of 190 seconds of radiation exposure, with an associated dose estimate of < 0.5 millisieverts. We will terminate the protocol at the earliest opportunity following 3.5 minutes of exposure.

A dose of 0.5 mSv corresponds to a risk of 1 in 2,280,000 of developing a radiation-induced stochastic effect from a videofluoroscopy[29], which is considered very rare. Background radiation exposure is known to occur in everyday activities such as flying a plane (0.005 mSv per hour) or smoking cigarettes (0.18 mSv per half pack) as well as during medical tests such as a chest x-ray (0.02 mSv) or a CT scan (10 mSv). According to Health Canada, the average Canadian experiences between 2 and 4 mSv background radiation exposure each year.

d) Aspiration (entry of material into the airway) is a possible risk during the videofluoroscopic swallowing study that will be performed. This risk is always present for videofluorscopic swallowing studies, which are intended to document the presence and severity of swallowing abnormalities, including (but not limited to aspiration). When aspiration is observed, standard procedures will be followed to encourage coughing and throat clearing to expel the aspirated material. The protocol will be terminated immediately. Any participant who experiences aspiration will be counseled regarding aspiration prevention strategies and aspiration-risk following the videofluoroscopy.

e) Choking is an extremely unlikely event. However, in the event of choking, routine emergency procedures will be followed. All study personnel carry current CPR certification.

f) In the unlikely event that an incidental finding is noted on the videofluoroscopy (such as a diverticulum or a mass) the attending SRRL licensed speech-language pathologist will consult the on-call radiologist and generate a clinical report documenting the observation. These findings will be communicated with the participant as per usual clinical practice.

Benefits
There are no benefits anticipated for participants in this study.

6. Privacy and Confidentiality

Routine practices for ensuring the confidentiality and privacy of all participants will be followed in this study. All research personnel at the Toronto Rehabilitation Institute are required to sign a confidentiality agreement at the time of hire. Participants will be assigned a non-identifying alphanumeric study code, and the master key for this code will be retained separately by the Principal Investigator in a password-protected file on a secure, password-protected, encrypted research server. Daily back-up of this research server is performed centrally at the Toronto Rehabilitation Institute to protect against data loss. Hard copies of the participant consent forms will be maintained in a binder, kept in a locked filing cabinet in the Swallowing Rehabilitation Research Lab.

All waveform and videofluoroscopic data will be stored electronically on the secure, password protected, encrypted research server. Photographs will be stored initially on the memory card of the lab digital camera, which is stored behind a locked door in the lab, and will be deleted from the memory card following transfer to the research server and labelling with a nonidentifying filename; transfer to the server will take place within 24 hours following collection. Any hard copy data will be transcribed into an electronic file (stored on the server), and the hard copy records will be stored in a locked filing cabinet in the Swallowing Rehabilitation Research Lab. Only the participant's alphanumeric study code number will appear on the data collection sheets and in the data collection files.

Access to participant information and experimental raw data will be restricted to the study personnel named in this application. All records will be destroyed after 10 years under the supervision of Professor Steele.

7. Compensation

Data collection for each participant will involve 2 separate appointments: a) intake; b) videofluoroscopy. The in-lab session for Experiment 6 will be convened immediately after intake, during the same session. Each appointment is expected to last a maximum of 90 minutes. An honorarium of $50 will be provided per participant following completion of the final data collection session to cover expenses associated with participation in the study.

8. Conflicts of interest

Professor Steele, the principal investigator, holds current and prior research contracts with Bracco Canada and Nestle Health Science, who are manufacturers of the barium products and thickening agents that will be used in this study. She has also served in an advisory capacity on expert panels for Nestle Health Science. These relationships will be disclosed to participants in the study information sheet. All products for use in the study will be purchased. Neither Bracco Canada nor Nestle Health Science will have any role as sponsors of this study. Professor Steele will not receive any financial payment, either personally or to the lab, related to the use of Nestle or Bracco products in this study.

9. Informed Consent Process

All participants who show an interest in participating will be provided with detailed information about this study via the Participant Information Sheet and Consent Form. Only after confirming they have understood all the information that is provided and after verifying they have no more questions, can they sign the consent form. A copy of the consent form will be provided to them.

The consent form includes a specific section requesting consent to use of study-related images for future educational and teaching purposes.

10. Scholarly Review

This study has undergone scientific review by the MFSR Study Section of the National Institutes of Health (USA) and has been funded.

11. Additional Ethics Reviews

Additional ethics approvals have been separately obtained for other experiments in the overall project as follows:

- Experiment 1 involved bench-top work to develop and test experimental stimuli with no human subjects or animal involvement, so did not require ethics approval.
- Experiment 3 was a sensory experiment, in which a panel of trained raters will be asked to describe the taste, texture and mouthfeel of the stimuli developed for the study. This experiment was be run independently by Professor Lisa Duizer at the University of Guelph. Separate ethics applications were submitted at the University of Guelph regarding this experiment (Protocols 15MY022 and 16SE020).
- Experiment 5 involves several different experiments to measure bolus flow in individuals with swallowing impairment due to different etiologies. At UHN, ethics protocols 16-5190, 16-6310 and 17-5421 cover these subprojects. An ethics protocol has also been

submitted at the University of Florida, which operates as a subgranted collaborating institution related to one arm of the project (Protocol IRB201701608).

12. Contracts

There are no contracts required for experiments 2, 4 and 6, which will be conducted exclusively at the Toronto Rehabilitation Institute. Subgrants have been requested, and contracts will be set up separately for the collaborations required for Experiments 1, 3 and 5 of the overall project.

Clinical Trials

Not applicable.

13. Budget

All costs for this study will be covered under the existing funding award from the National Institutes of Health. The budget and budget justification is included in Appendix C.

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Appendices

Appendix A. Exclusion Criteria Questionnaire

This is a list of conditions that could alter the results of this research study, or impact your eligibility to participate.

Please read the list and let us know if any of these apply to you, so that we can be certain that you meet the requirements to participate in the study.

a) Medical or Occupational Conditions:

- People with a prior medical history of stroke
- People with a prior medical history of acquired brain injury
- People with a diagnosis of Parkinson's Disease
- People with a diagnosis of Multiple Sclerosis (MS)
- People with a diagnosis of Amyotrophic Lateral Sclerosis (ALS)
- People with a diagnosis of Huntingdon's Disease
- People who have slurred speech or facial muscle problems
- People who have a swallowing disorder
- People who have Type I (insulin-dependent) Diabetes
- People who have had surgery in the head and neck area (other than tonsillectomy or adenoidectomy)
- People who have had radiation to the head and neck for cancer
- People who experience extreme mouth sensitivity (for example, when you go to the dentist)
- People who wear dentures
- Women who are pregnant
- People who have allergies to barium or any of the food products used in the study
- People who have had an x-ray of their neck in the past 6 months
- People who work in a setting where they are exposed to radiation

b) Medication, Drug and Alcohol Use

- People who are taking sleeping pills or medication that makes them drowsy
- People who are taking "anti-Parkinson's" medications like Levodopa
- People who are experiencing dry mouth as a side effect of medication
- People who use drugs (Cocaine, Methamphetamine, Heroin, Ecstacy, etc.)
- People who are taking medicine that affects their sense of taste or smell

Appendix B. Race and Ethnicity Form

This study is funded by the National Institutes of Health in the United States.

As a condition of that funding, we are required to track the cultural heritage of participants in our study, to ensure representation of minority groups.

If you are willing, please tell us which of the following racial groups you would identify yourself with most closely:

- ☐ Asian
- ☐ Black or African-American
- ☐ Hawaiian/Pacific Islander
- ☐ Native American Indian
- ☐ White
- ☐ Other: _____
- ☐ I prefer not to disclose my racial heritage

In addition, please tell us whether Spanish or Portuguese is your mother tongue:

- ☐ Yes
- ☐ No

Appendix C. Budget

The amounts below cover anticipated costs for Professor Steele and her lab associated with the NIH grant for the next year, including ALL costs associated with the proposed experiments. The approved direct costs in the notice of award for the 2019-2020 grant year are $427,559 US.

Salary Costs

Person	Project Role	FTE	Budget
Melanie Peladeau-Pigeon	Lab manager	0.6	$56,000
Emily Barrett	Clinical Research Coordinator	0.4	$35,000
Talia Wolkin	Clinical Research Coordinator	0.4	$35,000
Pooja Gandhi	Clinical Research Coordinator	0.4	$35,000
Renata Mancopes	Post-doctoral fellow	0.4	$35,000
		Total Salary Costs	$196,000

Salary costs will cover all required staff time for participant recruitment, data collection and data analysis

Experiment Costs

Item	Budget
Videofluoroscopies X 25 participants @ $200 plus one-time admin cost of $400	$ 4,400
Participant honoraria X 25 participants @ $75	$1,875
Supplies (barium, food, sensors)	$2,000