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TITLE: Home telemonitoring of bulbar function by acoustic measurement of swallowing and speech sounds in ALS

PRINCIPAL INVESTIGATOR: Andrew Geronimo, PhD

CONTRACTING ORGANIZATION: The Pennsylvania State University

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**6. AUTHOR(S)**

Andrew Geronimo, PhD

E-Mail: ageronimo@pennstatehealth.psu.edu

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

The Pennsylvania State University
500 University Ave., Rm. C1607
Hershey, PA 17033-0850

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**14. ABSTRACT**

We propose a longitudinal home study of ALS patients to assess bulbar progression via a smartphone-based, self-administered remote speech and swallow assessment (rSSA). This application will be used to take a weekly 'snapshot' of bulbar health by recording the audio of speech and swallowing sounds. The overall hypothesis is that this monitoring protocol can be used 1) in a way that is satisfactory to the patient, 2) to provide a set of digital biomarkers that are sensitive to dysarthria and dysphagia, and 3) with higher temporal resolution than standard measures to allow for the study of speech and swallow pathology co-evolution in ALS.

**15. SUBJECT TERMS**

Amyotrophic lateral sclerosis, speech, swallowing, remote monitoring

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## 1. INTRODUCTION

We propose a longitudinal home study of ALS patients to assess bulbar progression via a smartphone-based, self-administered remote speech and swallow assessment (rSSA). This application will be used to take a weekly 'snapshot' of bulbar health by recording the audio of speech and swallowing sounds. The overall hypothesis is that this monitoring protocol can be used 1) in a way that is satisfactory to the patient, 2) to provide a set of digital biomarkers that are sensitive to dysarthria and dysphagia, and 3) with higher temporal resolution than standard measures to allow for the study of speech and swallow pathology co-evolution in ALS. This proposal features the cross-discipline collaboration of content experts in ALS quality of life (Simmons), mobile health technologies (Geronimo), and the collection, analysis, and interpretation of speech/swallow sound data (Lee/Madhavan).

## 2. KEYWORDS

Amyotrophic lateral sclerosis, dysphagia, dysarthria, remote patient monitoring

## 3. ACCOMPLISHMENTS

**What were the major goals of the project?**

1) Design, administer and describe weekly remote speech and swallow assessments (rSSA).
2) Validate rSSA against standard assessments for speech and swallow. Compare rSSA outcomes to clinical measures employed as part of standard bulbar management by the speech-language pathologist.
3) Analyze the association between dysphagia and dysarthria measures over the 24 weeks of the study.

See the statement of work and the progress meeting milestones in the next section.

**What was accomplished under these goals?**

1) Design, administer and describe weekly remote speech and swallow assessments (rSSA).
   This has been fully completed and is deployed to active research subjects. A copy of the statement of work for Aim 1 is provided below, along with the date items were completed, if applicable.

*Table 1: Progress on SOW for Aim 1. Differentials are given between actual completion date and proposed completion date, with the grant period officially starting on 10/1/21. NC – not completed, NS – not started.*

| | Proposed Timeline (months) | Date Completed | Actual Timeline (months) | Differential (months) |
|---|---|---|---|---|
| Major Task 1: Regulatory Approval | | | | |
| • Refine inclusion criteria and screening protocol | -7 | 2/24/2021 | -7 | 0 |
| • Finalize consent form and human subjects protocol | -7 | 2/24/2021 | -7 | 0 |
| • Develop monitoring plan | -7 | 4/6/2022 | 6 | 13 |
| • Departmental Scientific Review | -6 | 3/4/2021 | -6 | 0 |
| • Penn State Hershey IRB Review | -6 | 7/13/2021 | -2 | 4 |
| • Annual continuing renewal of study protocol with IRB | 5,16 | 2/11/2022 | 4 | -1 |
| • Milestone Achieved: IRB Approval from PSHMC | -5 | 7/13/2021 | -2 | 3 |
| • Milestone Achieved: DoD HRPO regulatory approval | 0 | 9/20/2021 | 0 | 0 |
| Major Task 2: Prepare Research Materials for Study | | | | |

| | | | | |
|---|---|---|---|---|
| • Complete data use agreement with Aural Analytics | -1 | NS | | |
| • Application and Database development | -1 | 4/1/2022 | 6 | 7 |
| • Acquire hardware for study | -1 | 10/27/2021 | 0 | 1 |
| • Complete training course on MBSImP | -1 | 4/26/2022 | 6 | 7 |
| • Develop rSSA kit and instructions | -1 | 4/6/2021 | -5 | -4 |
| • Finalize data collection instruments in REDCap | -1 | 4/11/2022 | 6 | 7 |
| • Pilot testing of rSSA kits | 0 | 4/6/2021 | -5 | -5 |
| • Milestone: Research materials ready for start of study | 0 | 4/26/2022 | 6 | 6 |
| Major Task 3: Conduct Study | | | | |
| • Recruitment materials distributed | 0 | 4/25/2022 | 6 | 6 |
| • Study site training | 0 | 10/14/2021 | 0 | 0 |
| • In-person recruitment during ALS clinic visits | 0-15 | 11/10/2021, NC | 1 | 1 |
| • Schedule subject visits | 0-21 | 5/9/2022, NC | 7 | 7 |
| • Clinical Activities (ALSFRS-R, FVC, MIP, MASA completed at study visits 1-3) | 0-21 | 4/8/2022, NC | 6 | 6 |
| • Research Activities (SIT and MBS completed at study visits 1 & 3) | 0-21 | 5/9/2022, NC | 7 | 7 |
| • Home Activities (Surveys completed monthly and rSSA completed weekly) | 0-21 | 5/17/2022, NC | 7 | 7 |
| • Recruit listeners and conduct SIT intelligibility scoring | 0-21 | NS | | |
| • Conduct SSF analysis | 0-21 | 8/19/22, NC | 10 | 9 |
| • Submit amendments, adverse events, protocol deviations as needed | 0-21 | | | Ongoing |
| • Monitoring visits after 1st, 10th subject enrolled and study closeout | 1,6,24 | 6/8/2022, NC | 8 | 7 |
| • Milestone: First subject Consented and Enrolled | 1 | 4/11/2022 | 6 | 5 |
| • Milestone: 10 subjects enrolled | 6 | NC | | |
| • Milestone: Fully enrolled (20 subjects) | 12 | NC | | |
| Major Task 4: Describe the study cohort | | | | |
| • Create analysis plan to describe study cohort | 1 | 8/19/2022 | 10 | 9 |
| • Interim analysis of Aim 1 for grant reporting and presentation | 6-8 | 8/19/2022 | 10 | 4 |
| • Final analysis for dissemination, final grant report | 21-23 | NS | | |
| • Milestone: Present interim results of Aim 1 at ALS conference (NEALS 2022) | 11 | 11/1/2022 | 13 | 2 |
| • Milestone: Platform presentation of final results of Aim 1 at ALS conference (NEALS 2023) | 23 | NS | | |
| • Milestone: Manuscript submission to clinical journal | 24 | NS | | |
| • Milestone: Incorporate findings into grant proposals | 18--24 | NS | | |

2) Validate rSSA against standard assessments for speech and swallow. Compare rSSA outcomes to clinical measures employed as part of standard bulbar management by the speech-language pathologist

As of the time of this report, we have 5 subjects enrolled in the study who have each completed a clinical and radiographic examinations of swallowing, standard speech intelligibility recordings, and weekly home recordings of their speech and swallow.
The plan for performing these analyses were formulated as part of the grant writing and study startup process. Preliminary analysis has been performed for the analysis of standard and remote swallowing assessments. For the remote spontaneous swallowing frequency assessments, audio data is downloaded. WavePad software is used to listen to the audio

files via Bose QC35 headphones. Swallows are identified as swallows per minute and a total over 10 minutes is calculated.

In the next months, data collection from listeners will begin, who will perform ratings of speech intelligibility. Prior to this, the audio recordings need to be edited and cleaned for each target word and sentence. As each recording naturally contains extraneous noises (e.g., coughing sound, clearing throat, etc.), careful and consistent editing needs to done. To do so, Speech Production Laboratory lab members have had weekly meetings in Fall 2022 to discuss any extraneous noises detected in files and handle them consistently. Once this part is done, the edited audio files will be analyzed acoustically as planned, and data collection from listeners will begin.

*Table 2: Progress on SOW for Aim 2. Differentials are given between actual completion date and proposed completion date, with the grant period officially starting on 10/1/21. NS – not started.*

| | Proposed Timeline (months) | Date Completed | Actual Timeline (months) | Differential |
|---|---|---|---|---|
| Major Task 1: Analysis of rSSA compared to standard speech and swallow assessments | | | | |
| • Create analysis plan for extracting and comparing outcomes related to swallow (MBSImP, rSSA spontaneous swallow task) | -1 | 10/1/2021 | 0 | 1 |
| • Create analysis plan to for extracting and comparing outcomes related to speech (SIT, rSSA speech battery) | -1 | 10/1/2021 | 0 | 1 |
| • Interim analysis for grant reporting and presentation of results | 6-8 | 8/19/2022 | 10 | 3 |
| • Final analysis for grant reporting and presentation of results | 21-23 | | | |
| • Milestone: Complete analysis plan | -1 | 10/1/2021 | 0 | 1 |
| • Milestone: Platform presentation submission to International Symposium on ALS/MND 2022 | 21-23 | NS | | |
| • Milestone: Manuscript submission for motor-speech findings | 24 | NS | | |

3) Analyze the association between dysphagia and dysarthria measures over the 24 weeks of the study.
   Data collection to meet this goal is ongoing, although the sample size at this point is too small to warrant interim findings. We expect the first three subjects enrolled in the study to finish their participation in November 2022.

*Table 3: Progress on SOW for Aim 3.: Differentials are given between actual completion date and proposed completion date, with the grant period officially starting on 10/1/21. NS – not started.*

| | | | | |
|---|---|---|---|---|
| Major Task 1: Describe the longitudinal relationship between assessments of dysphagia and dysarthria | | | | |
| • Create analysis plan to compare speech and swallowing outcomes | -1 | 10/1/2021 | 0 | 1 |
| • Milestone: Complete analysis plan | -1 | 10/1/2021 | 0 | 1 |
| • Milestone: Conference submission on dysarthria/dysphagia interactions in ALS | 24 | NS | | |

**What opportunities for training and professional development has the project provided?**
See invited presentations and submitted poster abstract. The PI has been able to present this work in the context of larger remote monitoring efforts within the Hershey ALS clinic. Preliminary results from the swallowing analysis will be presented at the Northeast ALS Consortium Annual meeting in November 2022.

Carrie Reichwein was able to successfully complete the MBSImP training in April 2022, for which she earned 21 contact hours of continuing education credit. She applies this training to her work on the study and in her professional role as a speech-language pathologist.

**How were the results disseminated to communities of interest?**

Project conceptualization and preliminary results have been shared with the scientific community at international outlets for ALS and digital health research.

Additionally, we plan to share ongoing results of the study at an upcoming patient research group meeting hosted by the Hershey ALS clinic.

**What do you plan to do during the next reporting period to accomplish the goals?**
We are approximately 3-6 months behind in our recruitment goals. We plan to continue recruiting ALS subjects for the study at our site at Hershey, and initiating the listener phase of the study procedures at University Park. Our goal remains to enroll 5 subjects per month until we have met the enrollment goal of 20. A revised enrollment plan is given below. Continued meetings with the study team will be used to troubleshoot ongoing data collection issues and work on a plan for analysis and dissemination.

*Table 4: Enrollment table including the original schedule of enrollments, actual enrollment, and a revised plan for enrolling 20 subjects.*

| | 2021 | 2022 | | | | 2023 | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | |
| Planned | | 5 | 5 | 5 | 5 | 0 | 0 | 0 | 0 | 20 |
| Actual | | 0 | 4 | 1 | | | | | | 5 |
| **Revised Plan** | | **0** | **4** | **3** | **5** | **5** | **3** | **0** | **0** | **20** |

## 4. IMPACT

**What was the impact on the development of the principal discipline(s) of the project?**
A significant care gap exists in tracking bulbar pathology in the traditional and tele-ALS clinics. A tailored assessment that can be self-administered regularly to monitor bulbar changes is needed. Access to speech and swallowing data measured at such a fine timescale allows us to better respond to clinical changes. It also serves a research purpose to determine the co-evolution of dysphagia and dysarthria due to bulbar neurological involvement in ALS.

**What was the impact on other disciplines?**
Presentation of this work at the local, national, and international level has garnered much interest both in the field of ALS and other neuromuscular disease and dementia.

**What was the impact on technology transfer?**
N/A

**What was the impact on society beyond science and technology?**
N/A

## 5. CHANGES/PROBLEMS

**Changes in approach and reasons for change**
There have been three substantial changes to the protocol since initial approval:

1) Change in the platform used for performing smartphone-based recordings of speech. The original platform quoted in our proposal was through a company called Aural Analytics. When reaching out to them after receiving the grant, they were no longer interested in pursuing a partnership at the discussed price point. We had to look for other options. We took the route of an alternative smartphone speech collection tool using the open-source Beiwe software (https://www.beiwe.org/). This allows us to design our own survey schedule, manage patients, and download data from the data server, which has been set up in Amazon Web Services. This pivot has led to the majority of delays (approximately 6 months), since the PI was responsible for preparing this database for production. *This change has little to no expected effect on the outcomes, as the data collection via smartphone and external microphone, as well as the prompts used to gather speech data, remain unchanged.*
2) Modification to allow for partial completion of the MASA. This was implemented because the best clinical practices for doing a swallowing assessment do not involve the elicitation of a gag or choking response or the evaluation of pharyngeal phase.
3) Removed original inclusion criteria which required a minimal rate of change in speech or swallowing. Addition of Inclusion to clarify that patients with feeding tube may be enrolled as long as they maintain consistent daily oral intake. We believe removal of these changes will allow us to recruit a greater proportion of patients seen in ALS clinic.

There have also been changes to the study team, including an updated monitor, new research coordinator, and student investigators.

**Actual or anticipated problems or delays and actions or plans to resolve them**
The project experienced longer than expected startup time due to delays in software development and change of research coordinator. The project enrolled its first participants in May 2022.

Since collection of data from subjects went live in May 2022, we have experienced some inconsistencies with data upload from subject smartphone devices, particularly on those using the iOS operating system. While not ideal, this is affecting the minority of total speech recordings. Our study team is following up as necessary to ensure we have the most complete data possible. The PI is working with the Beiwe team to correct these issues and will push an update to the application to users when it is available.

**Changes that had a significant impact on expenditures**
None

**Significant changes in use or care of human subjects**
None, other than the modified inclusion criteria mentioned above.

**Significant changes in use or care of vertebrate animals**
N/A

**Significant changes in use of biohazards and/or select agents**
N/A

## 6. PRODUCTS

**Conference Abstracts**

Geronimo, A.M., Reichwein, C., Madhavan, A., Simmons Z, “Tracking dysphagia in ALS with audio recordings of spontaneous swallowing”, Accepted to the Northeast ALS Consortium Annual Meeting 2022, Clearwater, FL, November 1, 2022.

**Invited Presentations**

Geronimo, A.M. (May 19, 2022) "Inhale, exhale, upload: Digital Health in the ALS Clinic," “Experiences in Digital Health from the ALS Clinic” AFTD Holloway Summit 2022, Miami, FL,75 in attendance, Invited. International.

Geronimo, A. M. (March 15, 2022). "Inhale, exhale, upload: Digital Health in the ALS Clinic," MDA Clinical & Scientific Conference, Muscular Dystrophy Association, Nashville, TN, USA, 100 in attendance, Invited. International.

Geronimo, A. M. (October 7, 2021). "Pioneering decentralized multidisciplinary ALS care using digital health and targeted remote monitoring technologies," Northeast ALS Consortium Annual Meeting 2021, Virtual, peer-reviewed/refereed, Invited. International.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

**What individuals have worked on this project (*new study team members emphasized*)**

PI: Andrew Geronimo, Ph.D.
Co-I: Zachary Simmons, M.D.
SLP: Carrie Reichwein, M.S., CCC-SLP
Coordinator: ***Cristie Crawford, BS***
Statistician: Erik Lehman, M.S.
Data Monitor: ***Kelly Nye, B.S.***
Co-I: Ji Min Lee, Ph.D., CCC-SLP
Co-I: Aarthi Madhavan, Ph.D., CCC-SLP
***Graduate Student (Lee Lab): Elizabeth Krajewski***
***Graduate Student (Lee Lab): Nicole Perrotto***
***Undergraduate Student (Lee Lab): Erica Jackson***

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
No

**What other organizations were involved as partners?**
N/A

## 8. SPECIAL REPORTING REQUIREMENTS

Not Applicable

## 9. APPENDICES

**Abstract accepted to the Northeast ALS Consortium Annual Meeting 2022 (to be presented 11/1/22)**

## Tracking dysphagia in ALS with audio recordings of spontaneous swallowing

**Andrew Geronimo**, PhD, Assistant Professor, Department of Neurosurgery, Penn State College of Medicine, Hershey, PA

**Carrie Reichwein**, MS, CCC-SLP, Department of Otolaryngology – Head and Neck Surgery, Penn State College of Medicine, Hershey, PA

**Aarthi Madhavan**, PhD, CCC-SLP, Assistant Professor, Department of Communication Sciences and Disorders, The Pennsylvania State University, University Park, PA

**Zachary Simmons**, MD, Professor, Departments of Neurology and Humanities, Penn State College of Medicine, Hershey, PA

### Background

Dysphagia in ALS may lead to severe complications, such as malnutrition, dehydration, and aspiration pneumonia. Spontaneous swallowing frequency (SSF) has been found to be a biomarker for airway clearance health, and has been shown to be reduced in those with dysphagia.

### Goals/Hypothesis

To determine the feasibility of conducting measurements of SSF using a smartphone application, and to determine the potential of SSF to reflect established clinical assessments of swallowing in persons with ALS.

### Methods

Participants with a diagnosis of ALS and functional changes in speech or swallow were enrolled at the Penn State Hershey Medical Center. At the initial study visit, quantification of swallowing was completed by the SLP (CR) using the Mann Assessment of Swallowing Ability (MASA); we report a modified MASA summary score since the items for "gag", "cough reflex", and "pharyngeal phase" were not assessed (range 34-180, impairment decreasing with score). Subjects also completed a modified barium swallow study (MBSS) which was scored by the SLP using the MBS Impairment Profile (MBSImP, range 0-55, impairment increasing with score).

Subjects downloaded an application on their smartphone (Beiwe2), which prompted them to perform weekly 10-minute recordings of spontaneous swallowing using an external microphone adhered to the skin just below the lateral cricoid cartilage. Swallows were identified in recordings by AM.

### Results

Five participants (2 female, median age 70 years (range 66-80)) have been enrolled. MASA totals ranged from 129-180 and MBSImP scores ranged from 3-13. An inverse relationship between the modified MASA score and the MBSImP was found via linear regression ($r^2 = 0.79$, $p = 0.043$).

Over 2-101 days on the study, subjects completed 0.9 SSF recordings per week (range 0.49-0.91). The first SSF recording for each subject ranged from 0.1-0.9 swallows per minute and showed no significant relationship to the MASA or MBSImP scores.

### Discussion

This technique appears to be feasible for home measurement of spontaneous swallow in persons with ALS. Poor adherence may be attributed to inconsistent app performance. Preliminary results will be re-assessed in the complete cohort when data is available.