Complete Project: Accelerating Upper Limb Rehabilitation in Stroke Patients by Engaging Synchronous Tongue and Wrist Motion

Co-PIs: Maysam Ghovanloo¹, PhD and Andrew Butler²,³, PhD

¹Georgia Institute of Technology, ²Georgia State University, ³VA Medical Center

Abstract

In the United States over 900,000 people have a stroke every year and more than half survive. Ninety percent of stroke survivors require therapy due to motor impairments, of which 80% involve upper limbs. There is a critical period, between 1 and 12 months following stroke, when the method of rehabilitation makes a significant difference in the level of functional ability a stroke survivor regains.

We propose to develop a new rehabilitation paradigm for the upper extremity (UE) by engaging the tongue and its major representation in the motor cortex. We propose to enhance the functionality and efficacy of an existing rehabilitation robotic exoskeleton, the Hand Mentor (HM) (Kinetic Muscles Inc., Tempe, AZ) by enabling stroke patients with little to no movement to control their paralyzed UE with their tongue motion, using a wireless, wearable headset, the external Tongue Drive System (eTDS), while enjoying an interactive and game-like graphical user interface (GUI). We hypothesize that stroke patients will be able to perform the rehabilitation tasks easily and repeatedly after a brief training and may additionally receive long-lasting functional benefits over a 12-week period of rehabilitation therapy due to resulting neuroplasticity. We hypothesize that the areas in the brain responsible for motor control of the tongue and the UE will remap intracortical pathways after an ischemic injury, establishing a new sensorimotor pathway for the paralyzed UE. In preparation for this study, we have succeeded in developing a prototype interface between the eTDS and HM (TDS-HM). Currently, both systems are connected to a laptop PC, which can be replaced by a smartphone in the future. With the TDS-HM prototype in place, we have divided the proposed research into 3 specific aims:

Aim 1. Development of the TDS-HM sensor signal processing (SSP) algorithm and GUI software: A new SSP algorithm with proportional control capability will be implemented to provide stroke patients with more natural movements of their wrist as they touch their palate with the tip of the tongue, like moving a finger on a touchpad. The position, speed, and direction of the tongue motions will be synchronized with the wrist motions. The GUI will be developed with feedback from Aim-2 to: first, provide subjects with interactive, goal-oriented, and motivating audiovisual biofeedback in an engaging game-like environment. Second, provide the research team with quantitative and intuitive data on the subjects’ performance, rate of improvement, and overall progress towards the designated objectives over the course of the trial.

Aim 2. Clinical trials: We will collect data on the functionality of the TDS-HM in a pilot clinical trial with at least six stroke patients. We will follow the same protocols established in the literature for improving UE function using the HM. We will then compare the results of TDS-HM use with HM use alone.

Hypothesis 2a: In a group of stroke survivors with severe hemiparesis, the TDS-HM therapy intervention will produce significantly greater improvement in wrist motor function from baseline to end of treatment (EOT: 60 hours of therapy) versus therapist-supervised dose-equivalent usual and customary care (DEUCC). Proving Hypothesis 2a: We will utilize clinical outcome measures to note improvement, including: active range of motion (AROM), grip strength, the Wolf Motor Function Test (WMFT), and the upper limb portion of the Fugl-Meyer Motor Assessment Scale (FMA). Meaningful improvements in these measures signify increased functional use of the hand in order to carry out daily tasks and participate in usual activities.

Hypothesis 2b: The TDS-HM therapy intervention will produce significantly greater improvement in hand functional health related quality of life (HRQOL) from baseline to EOT versus therapist-supervised DEUCC. Proving Hypothesis 2b: We will use the 5-item hand function and 9-item mobility subscales of the Stroke Impact Scale (SIS) as HRQOL outcome measures.

Aim 3. Submitting grants for external funding: The pilot data will support a grant application to the NIH-NINDS. This study is one of the first attempts to use a robotic device in severely impaired stroke patients as a physical intervention for recovery of motor function and, to our knowledge, the first effort to specifically use the combined TDS-HM. Should the TDS-HM prove more efficacious than DEUCC, we will propose a randomized clinical trial to determine the clinical effectiveness of TDS-HM training to improve UE motor function and HRQOL for patients with stroke. Results could be used to reduce costs for UE rehabilitation among select stroke patients and reassess how clinical facilities prescribe and deliver therapy targeting the UE.
Complete Project: Accelerating Upper Limb Rehabilitation in Stroke Patients by Engaging Synchronous Tongue and Wrist Motion

1. Introduction

In the United States over 900,000 people have a stroke every year and more than half of them survive [1]. Ninety percent of the survivors require therapy for motor impairments due to stroke, whereas the upper limbs are involved for approximately 80% of stroke survivors [2], [3]. The relative incidence of a stroke doubles every ten years for people older than 55. With the percentage of people over 65 years in the U.S. estimated to double by 2050, the number of stroke patients is going to increase by 5,000,000 [4]. Long-term motor rehabilitation is necessary in order to help stroke survivors move their paralyzed extremities again [2]. There is a critical period, between one and twelve months following the stroke, when the rehabilitation method and efficacy can make a significant difference in the level of functional ability a stroke survivor can regain [3]. Intense rehabilitation therapy given multiple times per day over many weeks has been shown to produce positive clinical outcomes. This mode of intense rehabilitation is usually performed in specialized rehabilitation clinics and is often associated with high costs due to the use of expensive therapy equipment and highly trained personnel. One solution to reduce these costs is to use rehabilitation robots [4]-[6]. The robots that are currently used, however, require the patient to have a minimum ability to move the upper limbs to operate the robot [7], which is not possible for patients with complete limb paralysis. There are few therapeutic solutions for those clients that have little or no movement capability following stroke, and there is a need to not only address those patients but also accelerate the rate of improvement in patients who undergo robotic rehabilitation.

The tongue has many inherent capabilities that can be exploited to overcome the above limitations (e.g. the need for voluntary upper limb movement) in the existing rehabilitation robots and even offer secondary benefits to stroke patients. For instance, the cortical area of the motor cortex occupied by the tongue and mouth rivals that of the fingers and the hand, providing the tongue with sophisticated motor control and manipulation capability with many degrees of freedom, evident from its role in speech and ingestion [8]. Furthermore, the tongue can move rapidly and accurately in almost every direction within the oral space. Its motion is intuitive and does not require thinking or concentration. Although speech is often affected by stroke, patients generally maintain their voluntary tongue control. Additionally, the tongue muscle fibers are quite fatigue resistant and can operate over extended exercise periods as long as the tongue can move freely. The position of the tongue is reflexively adjusted with changes in body position, allowing tongue-operated devices to be easily accessed while sitting or lying in bed. Lastly, noninvasive access to tongue motion is readily available [9].

We propose to develop a new rehabilitation paradigm by engaging the tongue and its major representation in the motor cortex. We propose to enhance the functionality and efficacy of an existing rehabilitation robotic exoskeleton, called the Hand Mentor (HM) by Kinetic Muscles Inc. (KMI, Tempe, AZ) [7], by enabling stroke patients with little to no movement to control their paralyzed upper limbs with their tongue motion, using a wireless and wearable headset, called the external Tongue Drive System (eTDS) [10], while enjoying an interactive game-like graphical user interface (GUI). In preparation for this study, we have succeeded in developing a prototype interface between the eTDS and HM, creating the TDS-HM prototype shown in Fig. 1. Currently both systems are connected to a laptop PC, which can be replaced by a smartphone in the future.

Our primary hypothesis for the proposed pilot study is that stroke patients who cannot benefit from robotic rehabilitation due to having little or no movement capability will be able to perform the rehabilitation tasks involving a combination of tongue and wrist movements easily and repeatedly after a brief training (30 min). It is our secondary hypothesis that the areas in the brain responsible for motor control of the tongue and the upper limbs will reorganize and remap intra-cortical pathways after an ischemic injury [11], establishing a new sensorimotor pathway for the paralyzed upper limb. Therefore, stroke patients may receive additional long-lasting functional benefits, over the 12-week period of rehabilitation therapy as a result of neuroplasticity.

Fig. 1. Playing a game on a PC using TDS-HM prototype.
Neuroplasticity refers to the ability of the nervous system to change its structure, function, and connections in response to experience or the environment [12], [13], when they routinely synchronize the activities in two key areas of the motor cortex, here, the tongue and hand. By using the HM robot as the rehabilitation device for paralyzed upper limbs in conjunction with the tongue motion, representations in the primary motor cortex may reorganize to some extent due to the neuroplasticity of the brain [14]. If this rehabilitation paradigm proves to be successful, patients will be able to facilitate similar motor activities without the assistance of either the robot or eTDS by simply engaging their voluntary tongue motions in sync with their desired upper limb movements.

This project will be a collaboration between Co-PI Ghovanloo, PhD, from Georgia Tech (GT) and Co-PI Butler, PhD, MBA, PT, FAHA, from Georgia State University (GSU) and Atlanta VA Medical Center (VAMC). Although not being tested in the current pilot study, the combined TDS-HM device has the potential of being used remotely in telerehabilitation settings. It is not only a novel method to deliver healthcare, but it can lower the healthcare costs and reduce the financial and emotional burden of stroke survivors and their families. Patients with completely paralyzed limbs will be able to use the low cost and portable HM in the comfort of their homes along with the wireless and wearable eTDS headset, based on their prescribed rehabilitation schedule, making the presence of in-person physical therapists unnecessary. Moreover, TDS-HM can accurately record the specific activities conducted during each exercise session and provide the patient, family members, clinicians, and healthcare providers with an objective summary of the patient’s progress over the course of the therapy.

2. Background

The HM is a motor rehabilitation device for upper limbs [6]. It has a handgrip and a computer-controlled pneumatic actuator with soft bladders (Fig. 1), which can sense the wrist position during flexion and extension via a rotary encoder. Clinical trials have shown a statistically significant improvement in the activities of daily living (ADL) for stroke patients using HM due to enhancement of their hand functionality [15]. Co-PI Butler was a clinical advisor to the developing team and has intimate knowledge of its range of applications, benefits, limitations, and impact on stroke patients’ rehabilitation [16].

The TDS was invented by Co-PI Ghovanloo in 2005 as an assistive technology (AT) for individuals with tetraplegia [10]. The TDS has since been continuously enhanced by Ghovanloo’s team [17]-[24]. The external version of the TDS (eTDS) consists of a wireless headset with bilateral extensions that position an array of four 3-axis magnetic sensors near the user’s cheeks, as shown in Fig. 1 [18]. These sensors are used to trace a small magnetic tracer, the size of a lentil (23 mm x 1.1 mm), which is glued temporarily near the tip of the user’s tongue. The 12-D magnetic field data measured at the sensors is sent wirelessly to a PC or iPhone where it is translated into commands by a sensor signal processing (SSP) algorithm enabling users to access a PC, smartphone, wheelchair, or other devices in their environment. The usability of the eTDS for high SCI patients has already been demonstrated in two clinical studies at the Shepherd Center in Atlanta [22], [23].

We intend to give stroke patients the ability to independently exercise movements of their paralyzed upper limbs at home, offering them a robotic device for motor rehabilitation that is controllable by their tongue motion. If successful, the proposed device will help stroke patients with unilateral upper limb impairment move their wrist voluntarily. Using the current TDS, as is, stroke patients will be able to flex or extend their wrist with the help of HM at a constant speed and stop the motion when the wrist angle reaches a desired position. While this switch-based control is quite useful, a smoother and more natural exercise would be controlling the wrist angle in a proportional fashion, for example, by sliding the tongue back and forth over the palate along the sagittal plane, while having the robot control the flexion and extension of the wrist in a synchronous fashion at the same proportional angle as the position of the tongue tip over a certain predefined anterior-posterior segment of the palate. We intend to add proportional control capability to the TDS as part of the proposed research and synchronize the HM position with that of the magnetic tracer along a 1-D trajectory.

Fig. 2 shows the block diagram of the proposed TDS-HM system. Depending on their hand movement ability, patients can generate commands either by moving their hands or their tongues. In one possible scenario, when patients reach the extent of their active range of motion, the tongue control engages allowing patients to reach a desired wrist angle by sliding the magnetic tracer over their palate. The changes in the magnetic field are measured by the quad eTDS 3-axis magnetic sensors (LF, LB, RF, and RB) and wirelessly delivered to the PC to be translated into a 1-D proportional command in real time by the SSP algorithm. Similarly, the actual wrist angle is measured by the HM and reported to the PC via the TDS-HM interface. The GUI software, running on the PC, then represents both the tongue position and wrist angle on the PC screen either directly or
embedded within an interactive game-like biofeedback to create a goal-oriented, motivating environment for patients to increase their active wrist range of motion over multiple repetitions, aided by their synchronous tongue movements. The TDS-HM software also controls the HM pneumatic actuators by activating its pump and valves to help patients reach their desired wrist angle, as instructed by the GUI.

3. **Specific Aims**

**Aim-1. Development of the TDS-HM SSP algorithm and GUI software:** A new SSP algorithm with proportional control capability will be implemented to provide stroke patients with more natural movements of their wrist as they touch their palate with the tip of the tongue, like moving a finger on a touchpad. The position, speed, and direction of the tongue motions will be synchronized with the wrist motions. Detaching the tongue from the palate will disengage the tongue and stop the robotic arm, similar to lifting the finger from a touchpad. The GUI will be developed, while being informed by feedback from Aim-2, with two key objectives: First, providing subjects with interactive, goal-oriented, and motivating audiovisual biofeedback in an engaging game-like environment. Second, providing the experimenter and research team with quantitative and intuitive data on the subjects’ performance, rate of improvement, and overall progress towards the designated objectives over the course of the trial.

**Aim-2. Clinical trial:** We will collect data on the functionality of the proposed system in a pilot clinical trial with at least six stroke patients. During this pilot study, we will follow the same protocols that have already been established for improving upper limb function using the HM, as documented in the literature [15], [16]. We will then compare the rehabilitation success of TDS-HM users with those who have only used the HM.

**Hypothesis 2a:** In a group of stroke survivors with severe hemiparesis, the TDS-HM therapy intervention will produce significantly greater improvement in wrist motor function from baseline to end of treatment (EOT; 60 hours of therapy) when compared with those who received therapist-supervised dose-equivalent usual and customary care (DEUCC). **Proving Hypothesis 2a:** We will utilize clinical outcome measures to note improvement, including: active range of motion, grip strength, the Wolf Motor Function Test (WMFT), and the upper limb portion of the Fugl-Meyer Motor Assessment Scale (FMMAS). Meaningful improvements in these measures will allow an individual post-stroke to regain functional use of the hand in order to carry out daily tasks and participate in usual activities.

**Hypothesis 2b:** In a group of stroke survivors with severe hemiparesis, the TDS-HM therapy intervention will produce significantly greater improvement in hand functional health related quality of life (HRQOL) from baseline to end of treatment (EOT; 60 hours of therapy) when compared with those who received therapist-supervised DEUCC. **Proving Hypothesis 2b:** We will use the five-item hand function subscale and nine-item mobility function subscale of the Stroke Impact Scale (SIS) as HRQOL outcome variable. The HRQOL will benefit from the improvements made in active range of motion, grip strength, and functional tasks by allowing patients to experience a greater level of participation in their usual activities.

**Aim 3. Submitting grants for external funding:** Our goal is to use the pilot data to support a grant application to the NIH-NINDS. This study represents one of the first attempts to use a robotic device in severely impaired stroke patients as a physical intervention designed to improve recovery of motor function and, to our knowledge, the first effort to use a combined TDS-HM in patients with severe impairment. Should the use of TDS-HM prove more efficacious than DEUCC, a randomized clinical trial would be proposed to systematically determine the clinical effectiveness in TDS-HM training to improve upper extremity motor function and quality of life for patients with stroke. The implications for such a possibility include reduced costs for upper extremity rehabilitation among select patients who have sustained strokes and a reassessment for how clinical facilities prescribe and deliver therapy targeting the upper extremity.

4. **Research Methodology**

Implementation of the TDS-HM proportional control algorithm and GUI software to merge the functionalities of the robotic hand and TDS in Aim-1 will be conducted at GT by Ghovanloo’s team and input from Co-PI Butler’s...
team, who will conduct the clinical study on the TDS-HM at GSU towards Aim-2. Both Co-PIs will be involved in the analysis and interpretation of the acquired data and writing of the subsequent grant(s) and publications.

A1. Development of the TDS-HM SSP algorithm and GUI software: The extension of the SSP algorithm from discrete to 1-D proportional control is the main technical component of this proposal, which we have already started working on and achieved promising results. A flow-chart of this SSP with actual measured data for implementation of the 1-D proportional controller is shown in Fig. 3. The left panel shows the magnetic field strengths in the x, y and z axes of 4 magnetic sensors (LF, LB, RF, and RB) of the eTDS headset (see Fig. 2) when the magnetic tracer is moved along a straight posterior-anterior trajectory. Sensor outputs form a 12-D vector, which is the input to the SSP algorithm. The SSP will first attenuate the earth’s magnetic field (EMF) and then determine whether the tracer is touching the palate (engaged) or not using a support vector machine (SVM) classifier, which will be trained based on the oral anatomy of each patient. If the tongue is engaged, the trajectory of the magnetic tracer on the palate is monitored and converted to a trajectory of the cursor on the screen and HM wrist angle. This conversion is a transformation from the highly nonlinear 12-D magnetic field space onto a linear 1-D space, for which there is no closed-form equation. Therefore, numerical methods are often required to solve the inverse magnetic localization problem [25]. These methods also require the exact sensor locations and calibration of the sensors which are cumbersome.

We are now using a much less computationally expensive method without exact localization of the magnet. In preliminary offline trials we used linear regression method with subsequent temporal averaging to map the tracer location onto a 1-D linear function. The regression curve after averaging is shown in blue on the right panel of Fig. 3, which is very close to a linear function in red, validating this approach. These results are quite promising and we plan to refine this approach and migrate it from MATLAB to C for real-time online testing.

We will develop a training GUI in LabVIEW environment for the 1-D proportional control of the wrist movement. This GUI will be merged with the existing GUI for discrete TDS [19]. Then with input from Aim-2 studies, an interactive GUI will be developed for hand exercise with TDS-HM. The GUI will include multiple steps for objective measurement of the active range of wrist motion interleaved with goal-oriented Flash games to be played with a combination of wrist and tongue movements. It will include various adjustable parameters to allow the experimenter to progressively increase the difficulty of the rehabilitation tasks over the course of TDS-HM therapy, while recording measures such as current wrist angle, maximally reached angles, range of tongue motion, game scores, and timing/accuracy of the issued discrete/proportional control commands.

A2. Study design and methods: At least six adult subjects with a unilateral ischemic or hemorrhagic stroke (within 3 to 12 months post-stroke) exhibiting persistent hemiparesis, as indicated by a score of 1-3 on the motor arm item of the NIH Stroke Scale, will be recruited from the post-stroke population. They must present with less than 10° extension of wrist and fingers and have significant impairment limiting their activities of daily living (ADL). They must be able to read and follow simple directions. They must have no receptive aphasia, as indicated by a score of 0 on the Best Language item of the NIH Stroke Scale. Sixty hours of therapist-supervised DEUCC will be compared with sixty hours of TDS-HM therapy. Clinical outcomes will include: active range of motion, grip strength, the Wolf Motor Function Test, the upper limb portion of the Fugl-Meyer Motor Assessment Scale, and the SIS. Those will be measured at baseline, immediately post-intervention, and two months post-intervention. Change in outcome score will be assessed in a mixed model analysis.

5. Anticipated Results, Timeline, and Possibility of Subsequent Sponsorship

Stroke is one of the most common neurological diseases. Rehabilitative therapy to minimize functional disability and optimize functional motor recovery for individuals with significant loss of voluntary wrist movement after stroke is quite limited. If impairment is severe enough, therapists may focus more on training...
compensatory functional movements without the use of the involved upper extremity so the patient can perform
daily tasks and transition to the home [26]. Therapists may also utilize passive treatment modalities, such as
stretching and passive range of motion to limit loss of mobility. However these treatments do not engage the
neural pathways necessary for neuro-remodeling and repair [27]. Rehabilitation robotics and telemedicine are
two hot topics that are heavily credited as potential solutions for rising healthcare costs. We are building upon
our prior multidisciplinary experience by merging two novel technologies, the HM and TDS, both of which are
low cost, portable, and usable in the home environment, to answer an important question: Does synchronous
tongue motion improve the upper limb function in stroke patients? The strong representation of the tongue in
the motor cortex, its agility, dexterity, and resistance to fatigue, along with the existing evidence in neural
reconfiguration in different brain areas by establishment of new sensorimotor pathways between them point to
a high probability of a positive outcome. We anticipate collecting sufficient pilot data for a subsequent grant to
support the idea that synchronization between the rich areas responsible for motor control of the tongue and
the upper limbs over long-term repetitive and interactive training can result in reorganization of the primary
motor cortex by establishment of intra-cortical pathways between them, leading to improvements in the upper
limb function in stroke patients with severe residual impairments. The TDS-HM system will minimize functional
disability and optimize functional motor recovery for these individuals. This system can be developed for use in
rehabilitation settings, such as inpatient hospital-based rehabilitation or skilled nursing facilities. With continued
development, we intend to deploy TDS-HM to patients' homes without losing the ability to observe their
progress, thereby extending and enhancing the home-based outpatient therapy they receive post-stroke.

We realize that our hypotheses may not be supported by the outcomes of this study. Should our results show
that participants using the TDS-HM do not make improvements greater than those seen with participants
receiving DEUCC, we will consider the possibility that the dose of treatment was insufficient, either in
frequency, intensity or duration. We will also have to consider that the TDS-HM does not allow for the neuro-
remodeling necessary for improvements to be made, either due to the games selected for the rehabilitation
protocol or a misjudgment of the potential of the tongue motor cortex to remodel for active control of the hand.
Follow-up studies can explore the use of different games with the TDS-HM, increasing the frequency and/or
intensity of the intervention, or extending the length of the treatment episode. We can also investigate how
other motor areas might remodel to regain voluntary control of the hand.

6. Budget and Justification

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<td>GRA at Georgia Tech at 25% (TBD)</td>
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<td>Physical therapist at GSU at 10% (TBD)</td>
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<td><strong>Other costs:</strong></td>
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<td>GRA Tuition (50%)</td>
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<td>Compensation for trial participants</td>
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<td><strong>Total</strong></td>
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Graduate Research Assistant (GRA), TBD (25% FTE for 24 months): The GRA will be supervised by Dr. Ghovanloo and
Dr. Butler will serve on his/her committee. GRA will design and develop the SSP algorithms, interfacing hardware, and
GUI. The GRA will be stationed at GT-Bionics lab. Salary $2,150/m, Tuition: $1,170/month, health insurance rate: 1.8%.
Physical therapist at GSU, TBD (10% FTE for 12 months) will recruit, consent, and run the experimental trials on stroke
patients. Salary $70,000. Funds will be allocated to human subject compensation at GSU at $25/session.

- Co-PI's will apply for matching funds through internal grants at GT and GSU (University Research Grants)
- Kinetic Muscles Inc. has donated two HM rehab robots to Co-PI Butler's lab to be used in this research.
- Both Co-PI's labs are equipped with all the necessary equipment to carry out the proposed research.

Appendix-1: Project Management and Timeline

This table shows the project timeline on a quarterly basis. The Co-PIs will meet regularly on a biweekly basis during this research and on a weekly basis during clinical trial periods. The GRA (and the physical therapist during the clinical trial periods) will attend all the meetings and have additional meetings with both Co-PI as needed. Development cycle of the proportional SSP algorithm and GUI software will continue over the course of the proposed research, as data from Aim-2 is used for further improvements. The first human subject trial will be conducted during the 2nd half of the first year. The main pilot clinical trial will be conducted during the 2nd half of the 2nd year using the latest TDS-HM technology at the VAMC and GSU simultaneously. During the last quarter of each year, Co-PIs will prepare proposals for subsequent funding and include the results after data analysis. We also anticipate disseminating the results in at least two conferences and two journal papers.

Ghovanloo and Butler

5
References:


BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
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<tr>
<td>Maysam Ghovanloo</td>
<td>Associate Professor</td>
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</table>

<table>
<thead>
<tr>
<th>eRA COMMONS USER NAME</th>
<th>ghovanloo22</th>
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EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

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<tr>
<td>University of Tehran, Tehran, Iran</td>
<td>B.S.</td>
<td>1994</td>
<td>Electrical Engineering</td>
</tr>
<tr>
<td>Amirkabir University of Technology, Tehran, Iran</td>
<td>M.S.</td>
<td>1997</td>
<td>Biomedical Engineering</td>
</tr>
<tr>
<td>University of Michigan, Ann Arbor, MI</td>
<td>M.S.</td>
<td>2003</td>
<td>Electrical Engineering</td>
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<tr>
<td>University of Michigan, Ann Arbor, MI</td>
<td>Ph.D.</td>
<td>2004</td>
<td>Electrical Engineering</td>
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A. Personal Statement

In this project, we intend to develop a new rehabilitation paradigm by engaging the tongue and its major representation in the motor cortex with an existing rehabilitation robotic exoskeleton, called the Hand Mentor by Kinetic Muscles Inc. to enable stroke patients with little to no upper limb movement to control their paralyzed limbs with their tongue motion. We will use a wireless and wearable headset, called the Tongue Drive System (TDS), which I have developed over the past few years. The hypothesis is that the stroke patients will be able to perform the rehabilitation tasks easily and repeatedly, and may receive additional long-lasting functional benefits due to the resulting neuroplasticity. I will oversee all the technical aspects of the proposed research and collaborate with Prof. Butler, who will be responsible for the clinical aspects. I have a long track record in design and development of novel medical instruments both in industry and academia. Among a wide variety of medical devices, my specific areas of interest are implantable microelectronic devices, miniaturized devices that are ultra low power, and assistive technologies. Over the past 7 years, I have led a research effort that transformed the TDS from a mere concept to a fully functional assistive technology that has been through two rounds of clinical trials. Over the past 8 years as a faculty, my research activities have been funded by various federal and non-federal agencies (e.g. NIH, NSF, Army Research Office, and Christopher and Dana Reeve Foundation), giving me valuable experience in project administration, student supervision, multidisciplinary collaboration, and dissemination of the results through publications and presentations. In conclusion, I have demonstrated the expertise, leadership, and motivation necessary to conduct productive research projects over the years, and I am truly enthusiastic to perform the proposed preliminary research to generate pilot data for subsequent funding.

B. POSITIONS AND HONORS

PROFESSIONAL EXPERIENCE

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<td>1997-2000</td>
<td>Senior R&amp;D Staff Engineer, IDEA Inc., Tehran Iran</td>
<td>Tehran Iran</td>
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<td>1999-2000</td>
<td>Founder and CEO, Sabz Negar Rayaneh Co. Ltd., Tehran, Iran</td>
<td>Tehran, Iran</td>
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<tr>
<td>2000-2004</td>
<td>Research Assistant, University of Michigan, Ann Arbor, MI</td>
<td>Ann Arbor, MI</td>
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<tr>
<td>2004-2007</td>
<td>Assistant Professor of Electrical and Computer Engineering, NC State University, Raleigh, NC</td>
<td>Raleigh, NC</td>
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<tr>
<td>2004-2007</td>
<td>Affiliated Faculty of Biomedical Engineering, University of North Carolina in Chapel Hill - NC State University joint department</td>
<td>Raleigh, NC</td>
</tr>
<tr>
<td>2007-2011</td>
<td>Assistant Professor of Electrical and Computer Engineering, Georgia Institute of Technology</td>
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2011-present  Associate Professor of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA
2011-present  Clinical Research Scientist, Shepherd Center, Atlanta, GA
2012-present  Adjunct Faculty, Wallace H. Coulter School of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA

HONORS AND OTHER SCIENTIFIC ACTIVITIES
1990  Candidate for the Iranian team in the 21st International Physics Olympiad
2003  Neural Interfaces Workshop Student Travel Assistance Program Recipient
2004  41st DAC/ISSCC student design contest 3rd place award in operational category
2004  Rackham Graduate School Distinguished Dissertation Award Nominee from EECS, Michigan
2009  Georgia Tech’s Faculty Communicator of the Year
2010  NSF CAREER Award

PROFESSIONAL AFFILIATIONS
2009- American Association for the Advancement of Science (AAAS)
2000- IEEE Solid-State Circuits Society
2002- IEEE Engineering in Medicine and Biology Society
2004- IEEE Circuits and Systems Society
2003- Member Tau Beta Pi, the Engineering Honor Society
2004- Member Sigma Xi, the Scientific Research Society

PROFESSIONAL ACTIVITIES
2012  Guest Editor, IEEE Journal of Solid-State Circuits, Special issue on ISSCC’11
2011-present  Associate Editor, IEEE Trans. on Biomedical Engineering
2010-present  Associate Editor, IEEE Trans. on Biomedical Circuits and Systems
2007-present  Associate Editor, IEEE Trans. on Circuits and Systems II, Express Briefs
2005  National Science Foundation, Review Panelist, Integrative, Hybrid, and Complex Systems

C. SELECTED PEER-REVIEWED PUBLICATIONS (Selected from 100 peer-reviewed publications)

MOST RELEVANT TO THE CURRENT APPLICATION

ADDITIONAL RECENT PUBLICATIONS OF IMPORTANCE TO THE FIELD (IN CHRONOLOGICAL ORDER)


RECENT BOOK CHAPTERS AND INVITED REVIEWS


D. RESEARCH SUPPORT

ONGOING RESEARCH SUPPORT

NSF 0953107

Ghovanloo (PI)

9/1/10 – 8/31/14

Brain-Tongue-Computer Interfacing

The goal of this project is to explore the human factors associated with the use of tongue motion as a mean for manipulation and control. It will explore the optimal use of brain-tongue interconnect and develop novel technologies that tap into rich inherent capabilities of the human tongue, particularly for those with disabilities.
Role: PI

R01 NS062031-02          Oweiss (PI)  8/1/08 – 7/31/13
A Wireless, Multiscale, Distributed Interface to the Cortex, National Institutes of Health
My role in this project involves development of a multi-carrier wireless link and its driving circuitry for a comprehensive scalable wireless neural recording system.
Role: Co-Investigator

R21 EB009437-01A1          Ghovanloo (PI)  9/1/09 – 8/31/13
EnerCage: A Scalable Array of Intelligent Wireless Sensor Modules to Energize and Track miniature Inductively-Powered Devices in Small Freely Moving Animals
The goal of this project is to develop a smart array of planar inductors that tile the bottom of a cage and wirelessly energize a batteryless headstage that allows wireless neural recording from a freely behaving animal for an unlimited period of time.
Role: PI

NSF 0824199               Ghovanloo (PI)  9/1/08 – 8/31/13
A Multichannel Wireless Implantable Neural Recording and Stimulating Systems for Hippocampal Electrophysiology Research on Memory
The goal of this project is to develop a 32 channel wireless implantable neural recording and stimulating systems for a variety of neuroscience research on behaving animal subjects, performing memory tasks.
Role: PI

NSF 0828882               Ghovanloo (PI)  1/1/09 – 12/30/12
Wireless Tracking of Tongue Movements for Wheelchair Control and Computer Access
The goal of this project is to explore the usability and assess the efficacy of the human tongue motion in accessing computers and controlling powered wheelchairs by able-bodied subjects.
Role: PI

COMPLETED RESEARCH SUPPORT

Ghovanloo (PI), ARRA: Development and Translational Assessment of A Tongue-Based Assistive Technology (RC1 EB010915-01), 9/30/09 - 8/31/11. This project involved further development of the Tongue Drive System and clinical evaluation of its usability and acceptability among potential end users (high-level SCI patients) in two major rehabilitation hospitals: Shepherd Center in Atlanta and Rehabilitation Institute of Chicago.

Ghovanloo (PI), Use of Tongue Movements as a Substitute for Arm/Hand Functions in Quadriplegics, Christopher and Dana Reeve Foundation, 9/1/07 – 8/31/9. This project involved development of the Tongue Drive system and performing human trials using the TDS prototype, and evaluating its efficacy in substituting arm and hand functions in accessing computers by emulating the mouse functions.

Ghovanloo (PI), Floating Gate Building Blocks for High Performance Operational Amplifier Circuits, GTronix, 7/1/08 – 12/31/08. This project involved using floating gate transistors with a tunable feature on Op-Amps to improve their performance by eliminating offset, increasing the input range, and improve linearity.

Ghovanloo, Tongue Drive: A Tongue Operated Magnetic Sensor Based Assistive Technology for People with Severe Disabilities, National Science Foundation, 8/1/07 – 7/31/08. This project involved design and development of a switched-based tongue-operated wireless assistive technology, called Tongue Drive, including its hardware, signal processing algorithms, and user interface software.

E. CURRENT TRAINEES

Uei-Ming Jow, Seung Bae Lee, Mehdi Kiani, Hyung Min Lee, Jeonghee Kim, Hangue Park, Abner Ayala-Acevedo, Jacob Block, Temiloluwa Olubanjo (Ph.D. Student, Georgia Tech, Atlanta, GA)
BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME
Butler, Andrew J.

POSITION TITLE
Professor of Physical Therapy

eRA COMMONS USER NAME
Abutler01

EDUCATION/TRAINING  (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>MM/YY</th>
<th>FIELD OF STUDY</th>
</tr>
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<tbody>
<tr>
<td>Loras College, Dubuque, Iowa</td>
<td>B.S.</td>
<td>05/87</td>
<td>Biology, Chemistry</td>
</tr>
<tr>
<td>University of Iowa, Iowa City, Iowa</td>
<td>Ph.D.</td>
<td>12/95</td>
<td>Motor Control</td>
</tr>
<tr>
<td>University of Iowa, Iowa City, Iowa</td>
<td>Post-Doc</td>
<td>09/96</td>
<td>Stroke and Aging</td>
</tr>
<tr>
<td>Texas Woman’s University, Houston, Texas</td>
<td>M.S.</td>
<td>12/98</td>
<td>Physical Therapy</td>
</tr>
<tr>
<td>Heinrich-Heine University, Duesseldorf, Germany</td>
<td>Post-Doc</td>
<td>07/01</td>
<td>Neuroimaging</td>
</tr>
<tr>
<td>Emory University, Atlanta, Georgia</td>
<td>M.B.A.</td>
<td>05/09</td>
<td>Bus. Administration</td>
</tr>
</tbody>
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A. Personal Statement

Andrew J. Butler, Ph.D.PT will be a Co-PI on this project with Dr. Ghovanloo at Georgia Tech. Dr. Butler is a neuroscientist and physical therapist with a special interest in motor control, neuro-rehabilitation, functional neuroimaging, and transcranial magnetic stimulation. He currently serves as the Director of the Neural Control of Movement laboratory at the Atlanta VA Medical Center (VAMC) and Director of the Clinical Neuroplasticity laboratory at Georgia State University. As such, Dr. Butler has developed an expertise in the modalities required to successfully accomplish the goals of the proposed study and will provide excellent feedback to Dr. Ghovanloo on clinical aspects of the project. As PI or co-investigator on several previous VA, university and NIH funded grants, Dr. Butler has laid the groundwork for the proposed research involving robotic devices for upper limb rehabilitation in stroke survivors. Dr. Butler and Dr. Ghovanloo have been in contact about rehabilitation projects since 2009 as Dr. Butler serves on the DSMB of Dr. Ghovanloo’s NIH clinic trial in which people with spinal cord injury used the TDS to control wheelchairs. Since that point, Dr. Butler and Dr. Ghovanloo have worked together on the development of a TDS controlled-robotic device for stroke rehabilitation. Dr. Butler has demonstrated a record of successful and productive line of research in an area of high relevance to the VA as reflected by his recent VA Industry Innovation Competition funding and NIH R21 awards.

B. Positions and Honors

Positions and Employment

2012- Professor Department of Physical Therapy, Georgia State University, Atlanta, GA
2002- Senior Research Investigator, Veterans Administration Medical Center (VAMC)
2007-2012 Associate Professor Department of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA.
2001-2007 Assistant Professor Department of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA.

Other Experience and Professional Memberships

2000- American Heart Association
1996- American Physical Therapy Association: Neurology and Research Section member
1989-1990 International Brain Research Organization
1988-1989 Sigma Xi, The Scientific Research Honor Society
1999- Organization for Human Brain Mapping
1989- Society for Neuroscience

Honors

2007 Appointed as Fellow to the Council of the American Heart and Stroke Association
C. Selected peer-reviewed publications.

Most relevant to the current application (Selected from 30 peer-reviewed publications)


Additional recent publications of importance to the field (in chronological order)


**D. Research Support**

**Ongoing Research Support**

1 I01RX- U.S. Department of Veterans Affairs, Butler (PI) 2/01/13-1/30/15
The aim of this research is to test the hypothesis there will be significant association between the fNIRS effective connectivity maps and the fMRI effective connectivity maps in people who suffered stroke greater than 12 months and in able-bodied controls
Role: PI

1 VA Innovation Initiatives (VAi2) Industry Innovation Butler (PI) 10/01/11-9/30/13
The aim of this field test is to quantify the cost, quality and access of using robotic telemedicine to improve function in people who suffered stroke greater than 12 months.
Role: PI

1 I01RX000421-01 Butler (PI) 11/01/10-10/31/12
Effects of sympathetic nerve activity on cortical excitability during a hand motor task
The aim of the project is to determine predictors and examine the effects of physiologically heightened sympathetic nerve activity on motor cortex intracortical inhibition and facilitation when a hand muscle is relaxed and performing a precision task.
Role: PI

1 U01NS056256. Weinstein (PI) 9/1/08-8/31/13
Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (I-CARE) for Stroke Initiative
The aim of this study is to compare the efficacy of a full-defined, evidence-based and theoretically defensible therapy program (ASAP) and an equivalent dose of usual and customary occupational therapy initiated within the earliest post-acute outpatient interval (1-3 months) for significant gains in the primary outcome of paretic upper extremity function 1 year after treatment.
Role: Co-Investigator

1 T32HD055180-01A1. Gregor (PI) 5/1/08-4/30/13
Training Movement Scientists: Focus on Prosthetics and Orthotics
This is a training grant to support Ph.D. students in Prosthetics and Orthotics at the Georgia Institute of Technology.
Role: Co-Investigator

**Completed Research Support**

The Georgia Tech/Emory Center (GTEC) for the Engineering of Living Tissues and the Atlanta Clinical and Translational Science Institute (ACTSI). Traynelis (PI) 10/1/09-9/30/10
The Role of NMDA Receptors in Motor Learning in Humans Recovering from Stroke and Brain
This study explores the mechanisms of motor learning in stroke survivors using TMS and behavioral testing.
Role: Co-Investigator
The aim of this study is to assess the neural effects of mindfulness meditation in cancer survivors. This study explores the neural mechanisms of mindfulness mediation on cognition using fMRI.

Role: Co-Investigator