

# **Albert Einstein Healthcare Network**

## **Annual Progress Report: 2008 Formula Grant**

### **Reporting Period**

July 1, 2009 – June 30 2010

### **Formula Grant Overview**

The Albert Einstein Healthcare Network received \$135,484 in formula funds for the grant award period January 1, 2009 through June 30, 2011. Accomplishments for the reporting period are described below.

### **Research Project 1: Project Title and Purpose**

*E-Coaching to Support the Modification of Risk Factors of Metabolic Syndrome using Mediterranean Diet* - The Mediterranean Diet has been found to improve risk factors associated with Metabolic Syndrome. The purpose of this study is to determine if it is feasible and effective to deliver support for the Mediterranean Diet using interactive email support and coaching (e-coaching), and educational materials and links found on the internet. In addition, results of this study will be compared to a similar study that examines the effectiveness of face-to-face support for the Mediterranean Diet. This methodology will allow an examination of the feasibility of both modes of delivering MED diet education and support, as well as an examination of the effect of each method on outcome variables.

### **Anticipated Duration of Project**

1/1/2009 - 6/30/2011

### **Project Overview**

The objective of this study is to test the feasibility and effectiveness of adopting the Mediterranean Diet (MED) among low-income, older African American women who have been diagnosed with the Metabolic Syndrome (MSY) using email delivered MED support. Education regarding the MED will be presented in a 3-hour workshop followed by 6-months of weekly email coaching and support (e-coaching) that will also include use of internet links. The e-coaching support is based on a protocol developed for face-to-face MED support, which is grounded in social cognitive theory.

### **Specific Aims:**

1. To determine interest in and successful adoption of the MED delivered in a 3-hour workshop and support delivered via weekly emails for 6-months.
2. To assess the impact of the 6-month intervention on factors associated with MSY by measuring psychosocial, physical, and process outcomes.

3. To compare the outcomes of MED intervention delivered via email to outcomes of a similar study examining the impact of MED face-to-face support.

Twenty women will be recruited from a diabetes education program and primary care practices at the Albert Einstein Medical Center in Philadelphia, and through newspaper articles in community papers. Participants will be assessed pre-intervention and during the intervention at 3-month and 6-month intervals. Assessment measures will include: body mass index (BMI), abdominal obesity (waist size), waist-to-hip ratio, blood pressure, and fasting blood collection (A1c levels, glucose, lipoproteins, C-reactive protein); quality of life, social support, and symptoms of depression, and food composition (percent carbohydrates, fat, and protein). Assessment at 3-months will include all of these measures with the exception of the fasting blood collection. Physical activity will be recorded weekly and used as a covariate in statistical analyses.

### **Principal Investigator**

Nadine Uplinger, MS, MHA, RD, BC-ADM, LDN  
Albert Einstein Healthcare Network  
5501 Old York Rd.  
Philadelphia, PA 19141

### **Other Participating Researchers**

Vincent Figueredo, MD, Mathew McLaughlin, BS - employed by Albert Einstein Healthcare Network

### **Expected Research Outcomes and Benefits**

It is expected that this intervention will positively impact risk factors associated with MSY and will also have a public health benefit. Randomized, controlled studies like the Diabetes Prevention Program (DPP) have produced evidence that lifestyle interventions (that include improvements in diet) can reduce risk factors of diabetes. However, there is still a need to develop cost-effective and sustainable interventions to reduce risk factors associated with diabetes, heart disease, and the precursor to these diseases, MSY. Research indicates that the MED has been successful in improving risk factors for diabetes, heart disease, and MSY. Very few studies have been conducted in the U.S., and none of these studies were conducted among low-income African Americans. This intervention will test the feasibility of using email delivery of the MED protocol implemented in a similar 6-month face-to-face MED support intervention developed by this research team. If successful, email delivery could make MED support available to a larger number of participants at less cost to the institution and less time effort for participants than face-to-face MED support. The results of the intervention can be used to improve clinical care and improve risk factors associated with MSY. Specifically, it is expected that overweight participants in the intervention will reduce body mass index, reduce abdominal obesity, reduce or maintain blood pressure, and improve glucose control, lipid profile, well-being, social support, and quality of life. Findings from this study will be used to improve patient care and will be used to develop a larger, randomized controlled study.

## **Summary of Research Completed**

During this reporting period the method of conducting the study was changed from telephone coaching to “e-coaching.” E-coaching refers to communicating with study participants via email and conducting learning and motivational sessions through email and links to internet sites. The study changes were approved to commence in December 2009 and recruitment began January 2010. The Principal Investigator (PI), Tina Harralson, left Einstein on February 12, 2010. Nadine Uplinger who was originally a co-PI on this study was named PI. Tina Harralson remains a consultant on this study.

Fifteen eligible women were enrolled in the study in February 2010. They came to Einstein to complete their blood work, physical measurements, and study assessments. From that point forward, communication with the participants has been through email. Participants receive at least weekly communications containing educational materials regarding the benefits of the Mediterranean Diet, and motivational and diet tips. Participants are encouraged to ask questions and seek advice regarding nutrition and dieting. Several healthcare providers have asked to receive the emails, which they share with their patients. In addition, many of the participants report that they are adapting the Mediterranean Diet, and that they are sharing the educational materials they receive with friends and family members. Topics covered from the period between February 2010 and June 30, 2010 are listed in Table 1. Recipes and diet tips were also sent with the educational modules.

Topics
Introduction To Mediterranean Diet (Med Diet) & Lifestyle
Food Portions
Diet and Exercise
Importance of Breakfast
Barriers to Changing Lifestyle
Emotion, Stress, and Eating
Farmers Markets and Seasonal Cooking
Grains, Legumes, and Fiber
Med Diet and Blood Pressure
Med Diet and Diabetes/ Metabolic Syndrome
Watching out for Sodium in Processed and Fast Foods
Abdominal Obesity
Slow Food vs. Fast Food
Med Diet : What the Research Shows
The Ideals of Med Diet/Lifestyle Around the World

**Research Project 2: Project Title and Purpose**

*The Use of High Flow Oxygen during ED PSA with Propofol: A Randomized Trial* - The drugs used during emergency department procedural sedation and analgesia (PSA) can depress breathing and can cause patients to have dangerously low levels of oxygen (hypoxia) in their bloodstream. In previous research that we have conducted, extra low flow oxygen (3 liters a minute via nasal cannula) during PSA does not improve the rate of hypoxia during PSA with one common drug combination (midazolam and fentanyl). With another drug, propofol, it only has a small benefit. Because of the way propofol works in the body, we believe that high flow oxygen (15 liters a minute via mask) may reduce the rate of hypoxia.. The purpose of this project is to evaluate whether high flow oxygen significantly lowers the rate of hypoxia during emergency department procedural sedation with propofol.

## **Anticipated Duration of Project**

1/1/2009 - 6/30/2011

## **Project Overview**

The primary objective of this project is to show that high flow oxygen can lower the rate of hypoxic events by 20% compared to room air during emergency department procedural sedation and analgesia with propofol. This is a randomized, controlled trial. Any patient able to consent, who meets eligibility criteria, and needs sedation and analgesia for a painful, anxiety provoking procedure will be included. All patients that are eligible for the study will receive either high flow oxygen or room air during their procedural sedation with propofol. Patients and the health care team will be blinded to the gas delivered. Patients, five minutes before their sedation, will have a 100% non-rebreather mask fitted over their face, and it will be attached to one of two blinded tanks, the flow rate will be elevated to 15 liters a minute. The mask will remain on until the procedure has concluded and the patient is awake and ready for discharge. During the sedation, patients will have electronic monitoring of pulse oximetry, heart rate, blood pressure, respiratory rate, and end tidal carbon dioxide (ETCO<sub>2</sub>).

The primary outcome is the rate of hypoxic events between the two groups. Data to be recorded includes hypoxia, which is defined as any pulse oximetry saturation below 93%. Respiratory depression is defined as hypoxia, or an ETCO<sub>2</sub> level greater than 50 mmHg, less than 30 mmHg, a change of 10 mmHg or greater from baseline, or a loss of waveform. Vital signs are recorded every five minutes. Pulse oximetry and ETCO<sub>2</sub> are recorded electronically every 5 seconds. Trained research associates will note the time and vital signs at any point a patient meets our criteria for respiratory depression or hypoxia. Other data to be collected include demographics, drug dosage, time of procedure, time to readiness for discharge, and adverse events. To complete this study, we need approximately 60 patients per group.

## **Principal Investigator**

Kenneth Deitch, DO  
Albert Einstein Healthcare Network  
Albert Einstein Medical Center  
Department of Emergency Medicine  
5501 Old York Road, Korman Building  
Philadelphia, PA 19141

## **Other Participating Researchers**

Carl Chudnofsky, MD, Patricia Giraldo, MD, Paul Dominici, MD - employed by Albert Einstein Healthcare Network

## **Expected Research Outcomes and Benefits**

Over the past decade, the need to provide safe and effective procedural sedation has prompted an increasing number of emergency department (ED) clinical trials and the introduction of new agents, techniques, and monitoring devices. Yet, despite the knowledge gained by scientific study and clinical experience, early detection of respiratory depression and prevention of hypoxia remains a challenge. To reduce the incidence of hypoxia, the American Society of Anesthesiology recommends the use of supplemental oxygen for patients undergoing deep sedation, and suggests it be considered during moderate sedation. While these recommendations seem intuitive, there is a paucity of information regarding the risks and benefits of supplemental oxygen during ED procedural sedation.

The goal of supplemental oxygen is to increase oxygen reserves, thereby delaying or preventing the onset of hypoxia. However, increasing oxygen reserves is not without risk. It has been shown that super oxygenated patients desaturate only after prolonged apnea. This negates the use of pulse oximetry as an early warning device for respiratory depression, which is very concerning in light of the fact that emergency physicians rarely recognize respiratory depression in sedated patients who do not become hypoxic. In previous research we have conducted, physicians only recognize patients having respiratory depression once they develop dangerous levels of hypoxia.

Patients who have hypoxia during procedural sedation are at risk of other adverse outcomes such as vomiting and aspiration of stomach contents into the lungs, seizures, intubation and assisted ventilation, seizures, brain damage, and death. This is why such care is given to proper dosage of medications, and close clinical and electronic monitoring of patients undergoing PSA in the ED. Low flow supplemental oxygen has not been shown to confer much of a benefit. If high flow oxygen can be shown to be safe and is effective in lowering the rate of hypoxia during ED PSA, its use should be part of the standard of care.

## **Summary of Research Completed**

From July 1, 2009 to June 30, 2010, we have screened 840 patients who have presented to the Emergency Department and needed to have a procedure done under sedation for any painful condition. Of the screened patients, we have enrolled 92 out of our target of 120 patients (60 per group). Enrollment has been slower than expected, but we believe that we are on target to complete 120 patients by this fall. Once patient enrollment is completed, the blind will be broken and data will be analyzed.

## **Research Project 3: Project Title and Purpose**

*Performance Evaluation of Spatial Normalization Protocols for Brains with Focal Lesions* - The purpose of the current project is two-fold. First, we will evaluate several different protocols that involve spatially transforming images of focally lesioned brains. The evaluation will be conducted in a quantitative manner. The second purpose of the project is to build a small database of images of brains with focal lesions where anatomical landmarks are planted. These

brain images with landmarks can be used for future studies that aim to evaluate more spatial transformation protocols.

## **Duration of Project**

1/1/2009 – 06/30/2011

## **Project Overview**

Despite the importance of performance evaluation of the currently available protocols for normalizing focally lesioned brains, quantitative evaluation studies are very scarce. The current project is an evaluation study of four representative methods of spatial normalization in handling brains with focal lesions. The following protocols will be evaluated: affine-only transformation, SPM5 Unified Segmentation approach with and without cost function masking, FNIRT (FMRIB's Non-linear Image Registration Tool, with and without cost function masking), and SyN (Symmetric Normalization, with and without lesion masking). The selection of these four protocols was based on the popularity of the method and good performance in previous evaluation studies.

The MRI scans in the current study are to be collected from previous research studies conducted at Moss Rehabilitation Research Institute. In those studies, a high resolution structural scan was obtained on a research-dedicated 3.0 Tesla Siemens Trio scanner using a 3D MPRAGE volumetric sequence with the following parameters: TR = 1620ms, TI = 950ms, TE = 3ms, flip angle = 15°, 160 contiguous slices of 1.0 mm thickness, FOV = 192x256mm<sup>2</sup>, matrix = 192x256, 1NEX, and 1mm<sup>3</sup> isotropic voxel size.

The first step of the protocol begins with a neurologist, with extensive experience in neuroanatomy and lesion detection, supervising the principal investigator in planting the landmarks in the correct locations. For each normalization algorithm (and with and without cost function masking except for the affine-only method), a root mean square displacement (RMSD) of the distances between the 24 anatomical landmark locations (16 cortical and 8 subcortical) on the normalized individual brain and the homologous landmarks on the custom template brain will be computed in each individual. Then the individual brains' RMSD values will be subjected to a 4X2x2 repeated measures ANOVA with normalization method (Affine vs. SPM5 vs. FNIRT vs. SyN) and cost function masking (with vs. without) as within-subject factors and group (stroke vs. TBI) as a between-subject factor. Examination of main effects and subsequent post-hoc t-tests will reveal which method combination provides the most robust normalization results in presence of focal lesions. Our working hypotheses are that 1) cost function masking (or constrained cost function masking for SyN) will improve the results of normalization and 2) a large deformation method (SyN) with constrained cost function masking will outperform other protocols, yielding the least RMSD.

## **Principal Investigator**

Junghoon Kim, PhD  
Institute Scientist

Moss Rehabilitation Research Institute  
60 E. Township Line Rd.  
Elkins Park, PA 19027

### **Other Participating Researchers**

Brian Avants, PhD, H. Branch Coslett, MD - employed by University of Pennsylvania  
Myrna Schwartz, PhD, John Whyte, MD, PhD - employed by Moss Rehabilitation Research Institute

### **Expected Research Outcomes and Benefits**

This project does not directly contribute to improving the quality of health in patients with stroke or traumatic brain injury (TBI). However, it will greatly improve the quality of the research that is needed for improving the status of their health. Specifically, this project aims to find out what type of spatial transformation/normalization protocol is better suited to provide robust results for brains with focal lesions. In fact, focal brain pathology has been one of the major challenges in neuroimaging studies of stroke and traumatic brain injury. Without a valid protocol of spatial normalization, interpretations on any group-level whole brain map may be questioned. Thus, the project information regarding which protocol yields the most robust results for brains with focal lesions will be useful for future neuroimaging studies in these populations.

### **Summary of Research Completed**

*Completion of a left hemisphere stroke database:* In total, we had images of twenty brains with stroke and nine brains with TBI that were completed in landmarking. However, a subgroup analysis was not deemed feasible due to the small number of TBI brains. Thus, it was decided that only the brains with stroke would be analyzed in the subsequent analysis. Using the brains with stroke could yield a very interesting comparison between left and right hemisphere landmarks because it may allow us to compare differential effects of normalization on each hemisphere caused by the presence of lesion.

*Lesion frequency map:* To visualize the topography of left hemisphere lesions, a lesion frequency map was made out of 20 brains with stroke (Figure 1).

*Normalization of the brains:* In the interest of being able to compare our results to previous studies, only the non-linear registration aspect of each normalization algorithm was tested. To achieve this, the 12 parameter affine registration of each subject was computed in SPM5 and applied to their corresponding T1 anatomical image, landmarks, and lesion mask. Then, each subject was mapped to the standard MNI Colin27 template using SPM5 unified segmentation, FNIRT (FSL non-linear registration tool), and ANTS. Normalizations were computed both with and without cost function masking for all three methods. The parameters for each method, such as amount of regularization and number of non-linear iterations, were kept at the default for each method (the affine component of each was removed completely, as this was already computed). The defaults were the values packaged with each software, which are presumably optimized for healthy subjects.

*Reliability assessment:* To examine the intra-rater reliability, our three raters re-planted landmarks on 10 randomly selected brains. This was done approximately 6 months after the initial landmarking. Figure 2 shows the average distance between the two landmarks planted by the same rater for each subject. Anatomical landmarks with more than 3 mm distance between the two measurements were excluded from further analysis.

*Calculation of performance parameters:* Root mean square error (RMSE) around the template landmark (i.e., landmark manually planted on the template) is plotted in Figure 3. Statistical analysis (ANOVA's) revealed that 1) cost function masking does not improve normalization results significantly and 2) ANTS and SPM5 outperform affine normalization, while FSL did not.

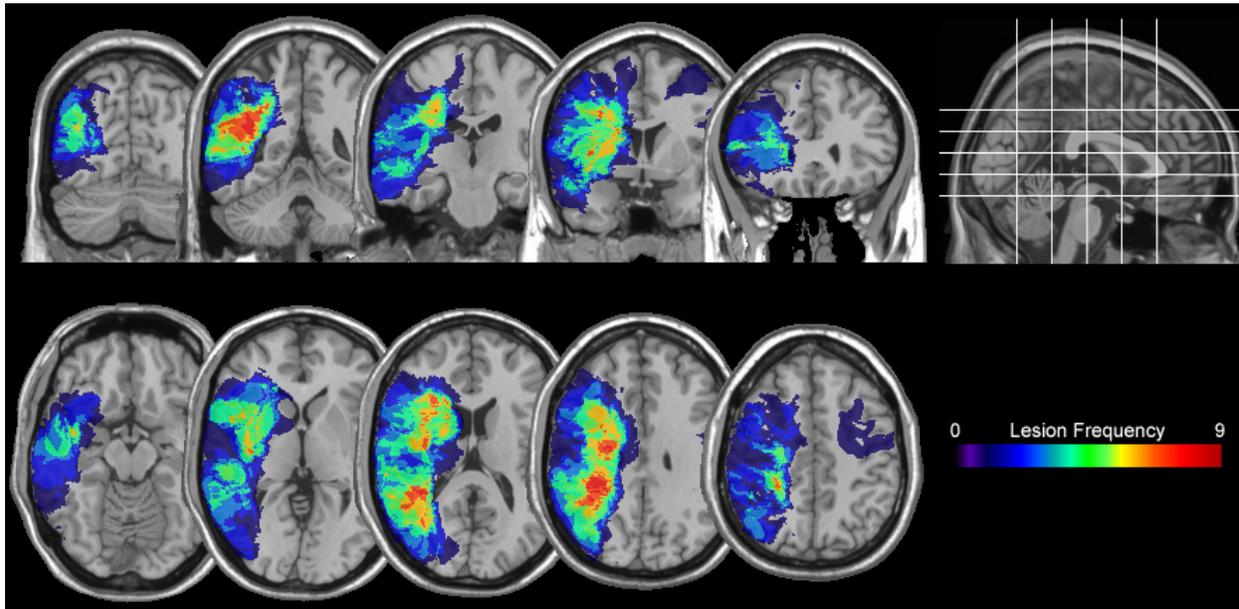


Figure 1. Lesion frequency map

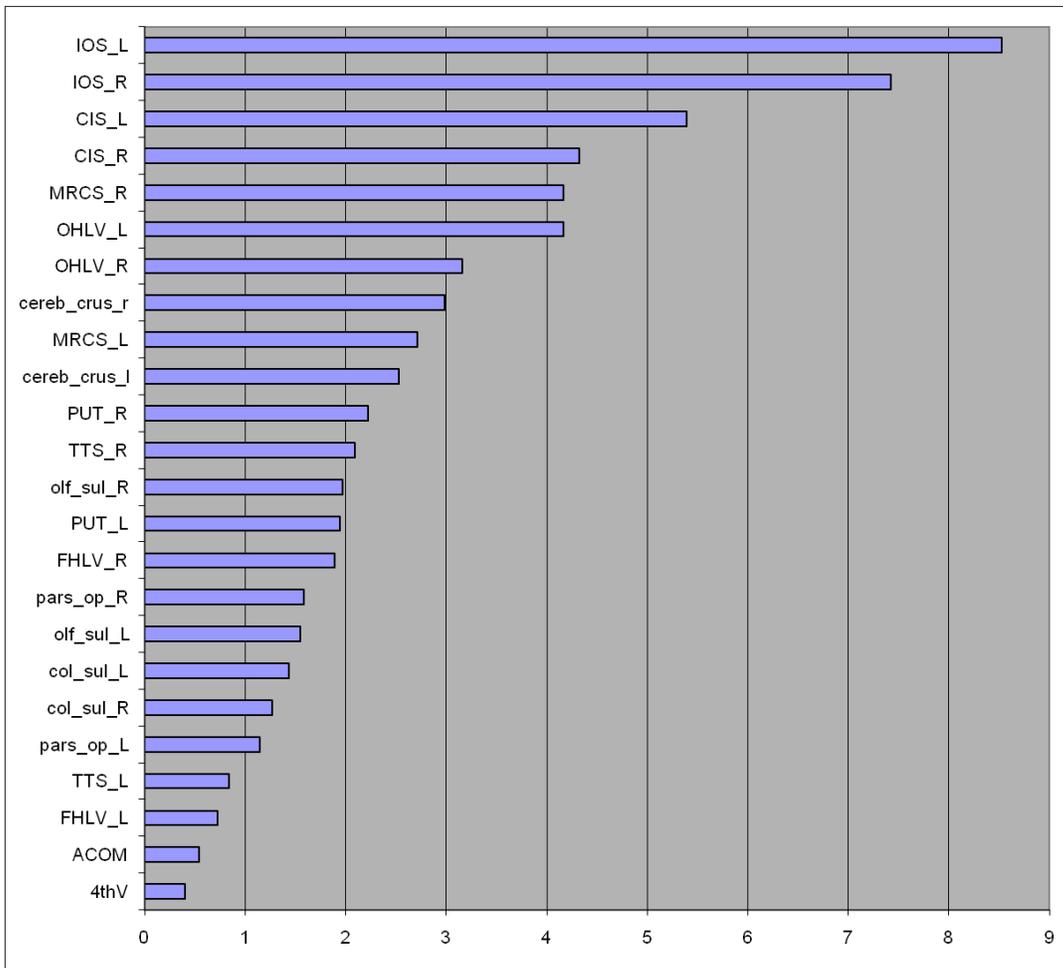


Figure 2. Reliability measured by the distance between the two measurements

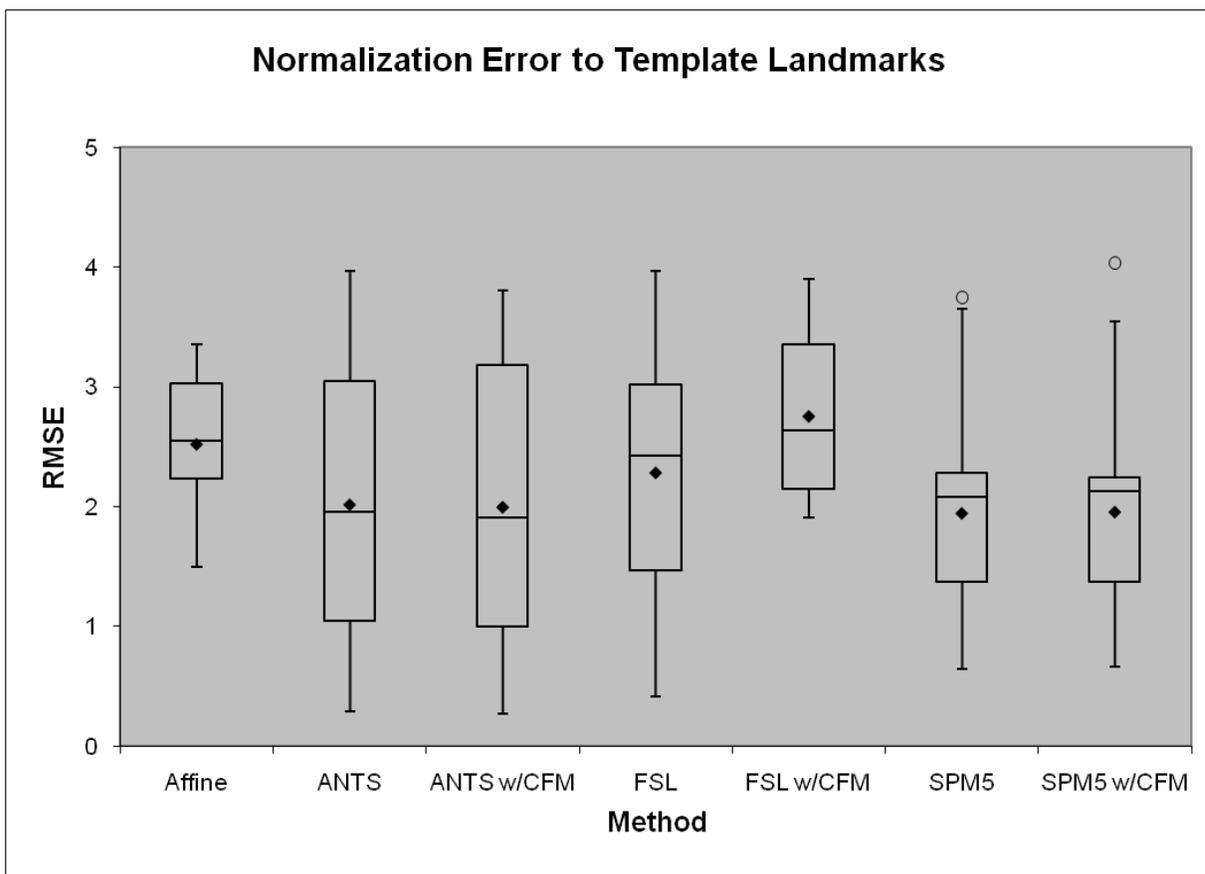


Figure 3. RMSE for different normalization protocols

#### **Research Project 4: Project Title and Purpose**

*Development of a Haptic Virtual Environment for Upper Limb Rehabilitation* - The overall goal of the project is to develop a low cost virtual reality (VR) system for upper limb rehabilitation that provides both visual and haptic feedback to participants. This goal will be accomplished with three specific development aims. The first aim will be to test several system components before final acquisition. The second aim will be to construct and test the system to ensure proper functioning. The third aim will be to prepare for future use of the system by planning experiments with stroke patients and developing proposals for additional funding.

#### **Duration of Project**

1/1/2009 - 6/30/2011

#### **Project Overview**

Upper limb movement disorders are common and debilitating consequences of stroke. Treatments for these disorders often fail to restore adequate use of the patient's limbs, significantly affecting everyday functioning. Beyond the impact on individuals, stroke patients

place a significant burden on the health care system, with stroke-related medical and disability costs totaling \$62.7 billion each year in America alone. The past decade has witnessed rapidly growing interest in the use of virtual reality (VR) technology for treatment of stroke patients. VR applications have a number of desirable features from a rehabilitation perspective. First, VR presents an opportunity to create rehabilitation scenarios that are highly relevant to real-world functioning with a reduced workload for the clinician. Second, VR permits greater control and repeatability of tasks than is possible with many traditional behavioral therapies. Third, VR applications permit delivery of enhanced feedback and guided practice, which has been shown to result in learning which is in some cases superior to learning in real-life settings. Finally, the virtual environment (VE) allows the training procedure to be temporarily “paused” for the purpose of evaluation and discussion with the patient or rehabilitation staff. Although previous studies indicate VR rehabilitation is beneficial to stroke patients, many of these systems have had limited forms of patient feedback and have been prohibitively expensive. The overall objective of the proposed research is to develop a low cost VR system for upper limb rehabilitation that provides both visual and haptic feedback to participants. This goal will be accomplished with three specific development aims. The first aim will be to test several system components before final acquisition. The second aim will be to construct and test the system to ensure proper functioning. The third aim will be to prepare for future use of the system by planning experiments with stroke patients and developing proposals for additional funding.

### **Principal Investigator**

Steven A. Jax, PhD  
Institute Scientist  
Moss Rehabilitation Research Institute  
1200 W. Tabor Rd.  
Sley 427  
Philadelphia, PA 19141

### **Other Participating Researchers**

Laurel Buxbaum, PsyD - employed by Moss Rehabilitation Research Institute  
Katherine Kuchenbecker, PhD, Pulkit Kapur, BS - employed by University of Pennsylvania

### **Expected Research Outcomes and Benefits**

Stroke patients often exhibit problems moving their arms and hands. These movement deficits significantly affect the stroke patient’s ability to function in the everyday world. Alongside traditional treatments, novel therapeutic methods utilizing virtual reality (VR) technology have recently begun to be tested. Although significant progress has been made in applying VR to rehabilitation of stroke patients, existing VR systems have at least two significant limitations. One limitation is that most systems rely primarily or solely on visual information to deliver feedback to the patient. Although visual feedback is important for upper-extremity control, feedback from other sensory modalities, especially tactile (touch) feedback, can be critical for control of the upper limbs. A second limitation of existing VR systems is that they are often prohibitively expensive, limiting the likelihood that rehabilitation centers will be able to utilize

the technology. The proposed research seeks to develop a visual plus haptic VR system for upper limb rehabilitation that addresses both of these limitations. Once the system is designed, we will present our work on the design of the system at a national conference and in a scientific journal so that other researchers and clinicians would be able to design and build a similar system. Once the effectiveness of this new system is verified in future studies, the system has the potential to affect the everyday lives of a large number of patients suffering from this common neurological disorder.

### **Summary of Research Completed**

In the final six months of the project, we again met all milestones proposed in the initial application. During the initial six month period, we acquired all of the components for the system, constructed the arm sleeve with tactors (see Figure 1a), and integrated all of the virtual reality (VR) system hardware. In the second and final six month period, we developed the software to record movements of the sleeve and display them on the computer screen (see Figure 1b). Extensive testing and modification of both the sleeve and the software were required to ensure maximal accuracy of the link between the movement of the participant's arm and the arm on the screen. These cycles of testing and modification took up the majority of the six month time period.

While beta testing of the system hardware and software was underway, the senior investigators on the project (Drs. Jax, Buxbaum, and Kuchenbecker) developed a plan for an initial experiment to confirm that the system works as intended. Rather than beginning testing with stroke patients, the target population for the VR system, we chose to first test neurologically intact participants because doing so would allow us to determine the system's functionality without concerns that failure could be due to deficits caused by the stroke and not the system itself. After several meetings, the senior investigators developed the experiment to determine whether vibrotactile feedback improves the ability of neurologically-intact young controls to match the visually presented target movements. The details of this experiment are described in the next paragraph.

After being consented, participants will be fitted with the arm sleeve on their left arms and complete any necessary calibration. Next, participants will complete the two-part familiarization phase. During the first part, participants will practice matching the visual target (without vibrotactile feedback) with 8 repetitions of a single movement (hammering; an action which will not be used later). During the first 5 repetitions, feedback (visual either with or without tactile, depending on block) will be present. In the remaining 3 repetitions, no feedback will be present to test participant's ability to maintain the learned movements without reliance on either type of feedback. In the second part of the familiarization phase, the vibrotactile feedback will be turned on and the participants will again complete 8 repetitions of the "hammering" movement (5 repetitions with feedback, 3 without). Following the familiarization phase, the test phase will begin. During the test phase, each participant will complete 4 blocks of trials, with 2 of the blocks including only visual feedback and the remaining 2 blocks including both visual and tactile feedback. Blocks will be counterbalanced using an ABBA ordering. Within each block, participants will perform eight repetitions of three movements (wiping table, raising hand to

mouth, figure 8 motion). The primary dependent variable will be the sum of squared deviations between the joint angles (shoulder and elbow) of the participant's arm and the target movement.

We have applied to the IRB for approval to complete this study, and we hope to begin the pilot testing once we receive approval. Should the results of the pilot study prove successful, we plan on testing stroke patients using a similarly designed study and then apply for additional external funding for a larger trial.

Finally, in addition to a conference presentation in the previous six month period (Kapur et al., 2009), we published a paper on this VR system in the proceedings of the IEEE Haptics Symposium Conference (Kapur et al., in press).

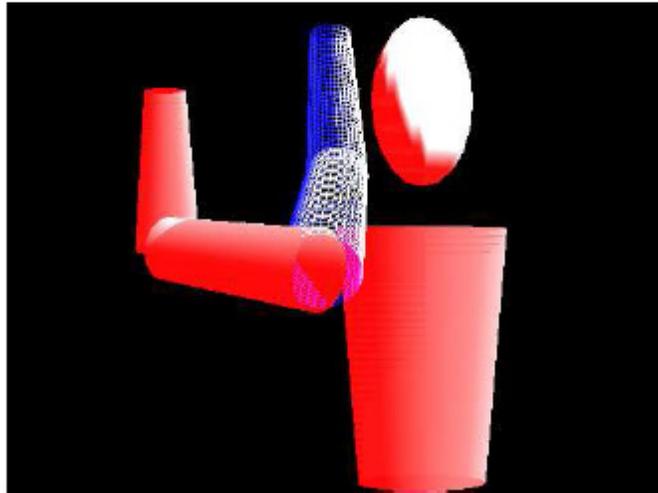
### References

Kapur, P., Premakumar, S., Jax, S. A., Buxbaum, L. J., Dawson, A. M., & Kuchenbecker, K. J. (2009, March). Vibrotactile feedback system for intuitive upper-limb rehabilitation. Demonstration presented at the 3rd World Haptics conference, Salt Lake City, Utah.

Kapur, P., Jensen, M., Buxbaum, L. J., Jax, S. A., & Kuchenbecker, K. J. (in press). Spatially distributed tactile feedback for kinesthetic motion guidance. Proceedings of the 2010 IEEE Haptics Symposium Conference.



(a) User wearing the tactile interface sleeve



(b) Graphical rendering of the user's arm pose

Figure 1.