A. Specific Aims

Musculoskeletal disorders and disease that interfere with normal movement patterns and reduce quality of life reach almost every sector of public health. From Cerebral Palsy to stroke and arthritis, an effective and efficient movement retraining tool would enable patients to resume activities of daily living, improve quality of life, and reduce the burgeoning cost of health care. The long-term goal of this research is to develop novel, portable haptic movement retraining technology, capable of providing accurate and efficient feedback to patients with various musculoskeletal disorders.

Conventional movement retraining relies on a therapist's observational analysis and interpretation of patient movements. As a result, therapists provide verbal suggestions and/or manipulative therapy with the intent to alter a specific movement pattern. Movement retraining is particularly difficult for patients with neurological sensory deficits and in cases when critical attributes, such as muscle activations and joint loads are not easily discernible. Biofeedback, typically with a visual display, is a promising auxiliary approach but is often limited to providing only one parameter as feedback to the patient, such as an electromyographic signal from a muscle.

By combining recent advances in wearable haptic feedback devices with software capable of computing human kinematics and kinetics in real-time, we will create a new framework for movement retraining, capable of integrating multiple modes of biofeedback. The following specific aims will be addressed:

A.1 Develop a novel haptic biofeedback system for movement retraining

Our first aim is to *develop a novel movement retraining system*, *capable of sensing musculoskeletal kinematics, kinetics and muscle activations from EMG, while providing patients with real-time haptic, visual, and auditory feedback.* To achieve this aim we will:

- Integrate new and existing feedback hardware and sensing hardware into a unified communicating architecture
- Implement musculoskeletal analysis and decision software in real-time

The challenge in establishing such a system lies in creating software that will run in real-time and integrate with an array of feedback devices. The outcome from this aim will be a generic biofeedback framework that will provide a rich arrangement of measurements and feedback.

A.2 Identify patient capacity for multimodal biofeedback

Our second aim is to *identify patient capacity for multimodal biofeedback*. We will perform experiments to systematically address two fundamental questions:

- How many feedback modalities can an individual process and respond to in a useful way?
- What is the optimal sequence for introducing biofeedback modalities?

While answering these questions, we will also gain insight into how long it takes to adjust to a new movement pattern given each new feedback modality.

A.3 Application to knee joint osteoarthritis (OA)

Our final aim is to *use multimodal haptic biofeedback to reduce the knee adduction moment in patients clinically diagnosed with tibiofemoral OA*. The adduction moment applied to the knee joint during gait is a dynamic loading parameter that is related to the onset, severity, and progression of the disease. We will answer the following hypothesis:

> ***Hypothesis 1*:** Movement retraining using multimodal haptic biofeedback will reduce the knee adduction moment by 30% after only three training sessions.

This work will fundamentally change the way movement retraining is performed, providing a generic platform for researchers who wish to explore the use of multimodal haptic feedback for the treatment of movement disorders

B. Background and Significance

B.1 Movement retraining for musculoskeletal disease and neurological disorders

Movement retraining has been used as a treatment strategy for a broad range of musculoskeletal disease and neurological disorders in an effort to alter the mechanical loads placed on skeletal tissue and restore 'normal' function. Walking is integral to our existence and remains a central focus for movement retraining, often referred to as gait retraining. Walking is also amenable to using movement training due to its repetitive nature. For these reasons, we will focus on movement retraining modalities that are intended to influence gait and gait-related disorders.

Knee joint osteoarthritis (OA) is a significant public health problem that would benefit greatly from movement retraining. Altering ones walking gait can alter the loads placed on the knee, potentially reducing the risk of developing OA and halting disease progression. Specifically, the knee adduction moment during walking has been linked to the development, progression, and severity of tibiofemoral OA[69,2]. The knee adduction moment provides an estimate of the load placed on the medial compartment of the joint[69] and reducing the knee adduction moment promises to be an effective form of prevention and treatment for medial compartment tibiofemoral OA. Traditionally, exercise and physical therapy have been used to strengthen muscles surrounding affected joints[23,44] in an attempt to reduce loads. Orthopaedic surgery has also focused on reducing the loads on the medial part of the knee. An example of this is a high tibial osteotomy (HTO), which has been shown to reduce the knee adduction moment[75,65]. However, it should be noted that HTO is not effective in all cases and patients with large knee adduction moments prior to surgery maintain these high moments following surgery[65]. Attempts at gait retraining to reduce the adduction moment during walking have been made through the use of shoe wedges[40,41], variable stiffness shoes[22], and external valgus braces[20,63]. These modalities report 6-8% reductions in the knee adduction moment following intervention. We are aware of only one study that has attempted a total body movement adaptation, in which one subject was trained to adopt a new gait based on biomechanical post-hoc analysis[26]. This study showed that an adapted gait was comparable to a high tibial osteotomy in terms of reduced knee adduction moment. However, it should be noted that the subject was an expert in the field of biomechanics and the retraining session took nine months to complete.

Hip OA has been directly correlated with the loading patterns in the hip joint during ambulatory motion[27,66]. Many patients naturally alter gait to reduce hip pain from dysplasia[71] and OA[35,76]. It is feasible that a patient's ambulation could be retrained to change biomechanical loads in order to slow or stop the onset on hip OA. Hip arthroplasty resulting from musculoskeletal disease often leads to gait asymmetry, which can be corrected through movement retraining. The most effective forms of treating OA both in the hip and the knee are either through surgery or prolonged rehabilitation. Both of these methods are invasive, expensive and are not guaranteed to work. OA is a public health problem requiring a new method of movement retraining that is both more effective and less expensive than current treatment modalities.

Stroke is a neurological disorder that requires movement retraining for recovery. In some instances stroke patients lose the ability to produce enough muscle force (often unilateral weakness[52]), and thus strength training[18,73] and therapist-assisted ambulation[31,57] have been used to improve gait. In other situations the stroke patient simply needs to 'relearn' how to activate muscles in a coordinated fashion. Functional electrical stimulation[47,10], treadmill training[45,62], partial body weight support treadmill training[74,59], and robot-aided rehabilitation[38,32,16] have all been used to help facilitate this relearning process. In some cases, stroke patients suffer from sensory deficits and are unable to obtain normal afferent feedback, such as proprioception or tactile sensations from certain areas of the body. For these patients, it is important to compensate for these sensory deficits. One approach is to externally lock the joint where sensory feedback is impaired (e.g. an ankle-foot orthosis[53]). Another approach, which has shown great

potential over traditional therapy methods, is biofeedback training[72]. This training feeds back signals to the patient, which would otherwise be impaired. Visual electromyographic (EMG) feedback[12], force feedback[21], and position feedback[49] have all shown substantial benefits for gait retraining of stroke patients, but have only been used in isolation. Displaying multiple channels of biofeedback from varied sources has the potential to make movement retraining more intuitive for the patient, inducing quicker and more effective rehabilitation.

Many other neurological disorders would benefit from novel and effective movement retraining strategies. Children with Cerebral Palsy, for example, benefit from methods that are similar to stroke, including muscle strength training[19], lower limb orthoses[55], and functional electrical stimulation[42]. Other movement-impaired neurological disorders which would benefit from a more efficient and effective form of movement retraining include spinal cord injury [5,81,8], traumatic brain injury [39,30], and Parkinson's disease [56,28].

B.2 Real-time feedback for movement retraining

Feedback is vital to movement retraining. While intrinsic feedback such as vision and proprioception provide patients with a general sense of motion, in most cases extrinsic feedback from a trainer or external device is necessary for complete movement retraining[70]. Extrinsic feedback can provide knowledge of results (KR) of musculoskeletal attributes that are not easily attainable such as internal joint torques or muscle activation levels and can provide knowledge of performance (KP) giving the patient feedback of how well they are achieving their target goal.

Extrinsic feedback can be administered post hoc or in real-time. In traditional physical therapy, post hoc feedback is given to the patient by a trained therapist. The therapist observes the patient's movements, and afterwards provides verbal suggestions about potential movement changes. In some cases, the patient is video recorded and is able to watch themselves after training. The therapist can then point out specific changes in the video, which may help the patient learn, and provide the patient with positive reinforcement.

In contrast to post hoc feedback, real-time feedback provides the patient with immediate information on results and performance during the actual training session. Because of this, retraining can be more effective and retraining times shorter. Real-time feedback also provides motivation to continue improving through testing. Real-time feedback can be given in a variety of ways during movement retraining. Verbal suggestions from a therapist can be considered the simplest and most common form of real-time feedback. However, this feedback is only useful when the therapist is able to observe and clearly communicate the desired corrections. Automated sensing and display of biological parameters is a powerful alternative and is often referred to as biofeedback. Biofeedback can give detailed physiological information to the patient that would be difficult or impossible for a therapist to provide (e.g. internal forces/moments or muscle activation levels). Biofeedback often utilizes sensors with high precision for such measures as segment positions or joint angles. A variety of biological attributes can be measured in real-time including EMG[54,11], joint angle[43,15], position[3], pressure or ground reaction force[25,82], internal forces/moments, bone accelerations/shock[17], heart rate, and perspiration levels. The methods for displaying biofeedback vary and include visual[51,79,17,14,11], verbal[34,14], or sense of touch through grounded[67,46,37] and ungrounded[50,60,6,7] devices.

B.3 Multimodal haptic feedback

Most forms of biofeedback only provide a single piece of information to the user. An example of this is a system that measures an EMG signal in one muscle and then displays this to the user during ambulation[1]. Most movement retraining tasks require many different musculoskeletal changes, so providing multiple modes of sensing and multiple modes of feedback that can be intuitively provided to the patient has the potential to significantly enhance rehabilitation.

Although vison provides a rich source of feedback, it requires continual cognitive demand, thereby limiting its' use to clinic or laboratory-based feedback.

One method that offers much promise for providing *intuitive* feedback for motion retraining is haptic feedback. While visual feedback is sensed through sight and auditory feedback by hearing, *haptic feedback provides a sense of touch*. Through forces and vibrations applied to the skin, users can feel feedback on different places on the body, akin to providing an augmented sense of proprioception. Recent advances in wearable haptic devices[6,7] provide the possibility of displaying intuitive feedback directly at the location of movement correction. By using several haptic devices combined with visual and auditory feedback a rich source of feedback can be achieved. The important question here is 'how many modes of feedback can an individual process in a useful way?'

Another distinct advantage of haptic feedback over vision and auditory feedback is that users do not have to pay constant attention to a visual or audible display. This is an important point if our long-term goal is to create a system capable of being used during everyday activities. Haptic devices can provide feedback, without the cognitive demand of vision or auditory feedback.

B.4 Significance

The development of multi-modal haptic biofeedback technology promises to fundamentally change the way movement retraining is performed. More rapid, efficacious, and cost-effective movement retraining would have broad reaching clinical impact. The impact in reducing the onset and progression of osteoarthritis and improving the recovery from stroke alone would be immense:

- Osteoarthritis (facts provided in a report from the Centers for Disease Control and Prevention (CDC, 2007))
    - Arthritis is the leading cause of disability among U.S. adults
    - 46 million U.S. adults (1 in 5) reported doctor-diagnosed arthritis
    - Nearly 19 million U.S. adults report a limitation in activity each year due to arthritis
    - Arthritis results in 750,000 hospitalizations & 36 million outpatients visits per year
    - $81 billion in direct medical costs in 2003 due to arthritis
    - $128 billion in total costs in 2003 due to arthritis [>1% of U.S. 2003 GDP]
    - A 1% decrease in the incidence of arthritis would reduce the total cost of arthritis by $1.3 billion per year or a savings of more than $3.5 million per day
- Stroke
    - There are an estimated 4.0 and 4.5 million stroke survivors in the US (National Stroke Association [www.stroke.org] and American Stroke Association (ASA) [www.strokeassociation.org])
    - 700,000 - 750,000 first-ever or recurrent strokes per year[80,13]
    - More than half of stroke survivors have chronic residual disabilities and functional impairments[64,61].

C. Preliminary Studies

To illustrate the potential of biofeedback for movement retraining, we performed a preliminary study with 6 healthy volunteers using a single channel of visual and vibration feedback (3 subjects with each feedback mechanism). The study evaluated the ability of subjects to adjust their walking gait to reduce the knee adduction moment, which was conveyed in real-time using either a monitor or a small vibration sensor attached to the subjects forearm. To our knowledge, this was the first time haptic feedback has been used to alter gait mechanics and provides a foundation for multi-modal movement retraining.

C.1 Methods

Three-dimensional segmental motions and ground reaction forces were recorded from subjects walking at a self-selected speed using an 8-camera Vicon motion capture system (OMG plc, Oxford, UK) and instrumented force plate treadmill (Bertec Corp., Columbus, OH), respectively. Retro-reflective markers (n=36) were placed on the subject's torso and lower limb for the purpose of calculating three-dimensional joint kinematics and kinetics[9]. Marker trajectories were collected in real-time using Vicon Nexus software and sent via TCP/IP to a separate workstation running Matlab (Mathworks Inc., Natick, MA), where calculations of the knee adduction moment were performed and the feedback was created. Since the first peak of the knee adduction moment has been shown to be most closely associated with knee OA[75,36,58], feedback was provided based on this first peak. The cross-product between the ground reaction force vector and the knee joint center was used to calculate the knee adduction moment for real-time feedback. Visual feedback was displayed on a monitor in front of the treadmill and vibration feedback was provided using a C2 Tactor (EAI Inc.) strapped to the forearm (Figure 1). The vibration device was controlled using the Matlab xPC real-time operating system via a linear current amplifier.

Figure 1. Subject walking at self-selected speed on force plate treadmill with the ability to visually monitor their peak knee adduction moment in real-time.

After a brief period to allow subjects to become accustomed to walking on the treadmill, we recorded marker and force data for 15 steps to establish the baseline peak knee adduction moment. The feedback we provided during the experiment was related to this baseline value. During each step, subjects received either visual or vibration feedback of the peak knee adduction moment of their left leg. When visual feedback was provided, it was shown on a stair-step plot (Figure 2), which displayed peak knee adduction moment from the current step along with the previous 9 steps (left leg only). The baseline moment was displayed as a red dashed line for comparison. A short delay (~100 ms) meant that the left leg was still in late stance when the feedback was provided allowing adjustments to be made on the subsequent step.

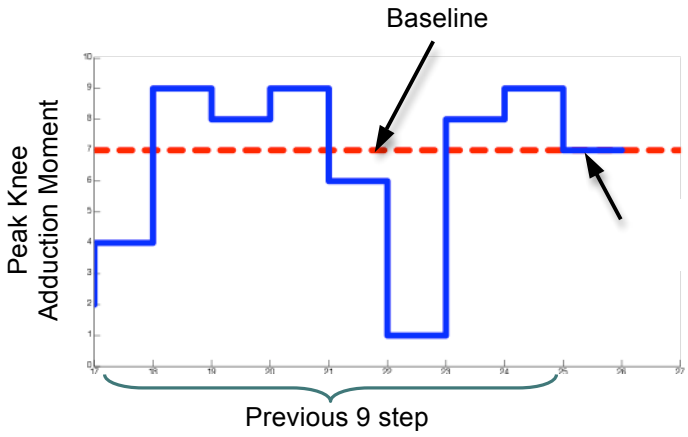

Figure 2. Stair-step plot provided visual feedback of current and previous peak knee adduction moment during walking, relative to a baseline measure.

When vibration feedback was provided, only the peak knee adduction moment from the current step was presented. To reduce ambiguity in stimulus levels due to lower perceptual resolution and memory effects, the vibration amplitude was limited to one of three levels. During late stance of the left leg, a 0.5 sec burst of vibration was provided. If the peak knee adduction moment on that step was 80% of the baseline knee adduction moment or greater, a large amplitude vibration was presented. If the peak knee adduction moment was 60-80% of the baseline, a low amplitude vibration was presented, and if it was less than 60% of the baseline, no vibration was presented. The goal was then to minimize the amplitude of the vibration.

Subjects were instructed to try various gait modifications and attempt to reduce the knee adduction moment, based on the feedback provided. They were instructed to attempt to converge on a gait that was comfortable, symmetric, and sustainable for a reasonable amount of time. We provided a few suggestions of modifications but made it clear that any approach could be attempted. Our suggestions included: walking with toes pointed inward or outward; increasing lateral trunk sway; loading the inside or outside of the foot; taking longer or shorter strides; and adjusting step width.

Once the patient decided that an acceptable gait modification was reached, they practiced it for 1-2 minutes and then we recorded a post-training set of 20 steps, 10 with the feedback on and then 10 with the feedback switched off. The peak knee adduction moment for this post-training set was compared to the baseline case to determine the effectiveness of the gait modification. Subjects were then asked to describe their chosen gait modifications and rate the awkwardness of the new gait compared to their normal gait (on a scale of 0-10, with 10 being extremely awkward).

C.2 Results

Both visual and vibration feedback were successful in reducing the knee adduction moment, with an average reduction of ~15% (Table 1). The awkwardness ratings were also similar between feedback mechanisms. However, the amount of time it took to converge on a modified gait pattern was longer with vibration that vision (Trial time, Table 1). This was likely due to the fact that at least a 20% reduction in knee adduction moment was required to signify a change in vibration feedback; therefore, more iterations were required to identify effective strategies.

Table 1. Summary results comparing vision and vibration feedback to reduce the knee adduction moment during walking at a self-selected speed. Both groups were able to reduce the knee adduction moment, however, subjects with vision feedback took less time to find an acceptable, modified gait pattern, indicated by the smaller trial time in the vision group.

Feedback	Baseline Adduction Moment (%ht*wt)	Post-Trial Adduction Moment (%ht*wt)	Percent Reduction	Trial Time (sec)	Awkwardness Rating
Vision	4.72	3.90	16.10%	353	6.0
Vibration	4.37	3.68	14.17%	882	5.3
All Subjects	4.55	3.79	15.14%	618	5.7

The reductions in knee adduction moment demonstrated with one channel of *haptic or visual feedback were 2-3 times greater than those achieved with shoe wedges*[40,41] or variable stiffness shoes[22]. These results were achieved in only one session of 15-20 minutes duration.

It is important to note here that gait alterations were self-selected by subjects in this experiment. Since only a single channel of feedback was given, the level of knee adduction moment

reduction depended on the type and severity of gait alteration chosen by each subject. A haptic feedback system capable of delivering multiple channels of feedback to explicitly inform gait adaptations might produce even greater results than those shown here.

D. Research Design and Methods

D.1. Develop a novel haptic biofeedback system for movement retraining

Recent advances in haptic displays and real-time musculoskeletal analysis software has laid the foundation for the development of a novel multi-modal haptic biofeedback system. We have designed a system capable of measuring one musculoskeletal parameter (the knee adduction moment) that feeds back to one device in real-time. Building from this preliminary work, *our first aim is to create a system capable of sensing full musculoskeletal kinematics and kinetics and up to four muscle activations from EMG, while providing patients with haptic, visual, and auditory multimodal feedback simultaneously*. To achieve this, we will first integrate sensor hardware and feedback hardware into a centralized system where feedback displays are informed by sensor measurements. The necessary hardware components include: haptic feedback devices, visual and auditory displays, motion capture system, force plates, and EMG sensors. Once unified hardware architecture has been established, software will be developed and integrated for musculoskeletal analysis and feedback decisions. Such software should be robust and efficient enough to compute feedback synergies in real-time. Final system software will be written using C++ and Matlab xPC real-time (www.mathworks.com) and will integrate with existing software packages from Vicon (www.vicon.com) and C-Motion (www.c-motion.com).

D.1.1 Integrate new and existing feedback and sensing hardware into unified communicating architecture

Recently, our group developed a new wearable device utilizing rotational skin stretch for haptic feedback[7]. This device attaches to the skin and provides patients with tactile feedback through two circumferentially rotating contact points (Figure 3).

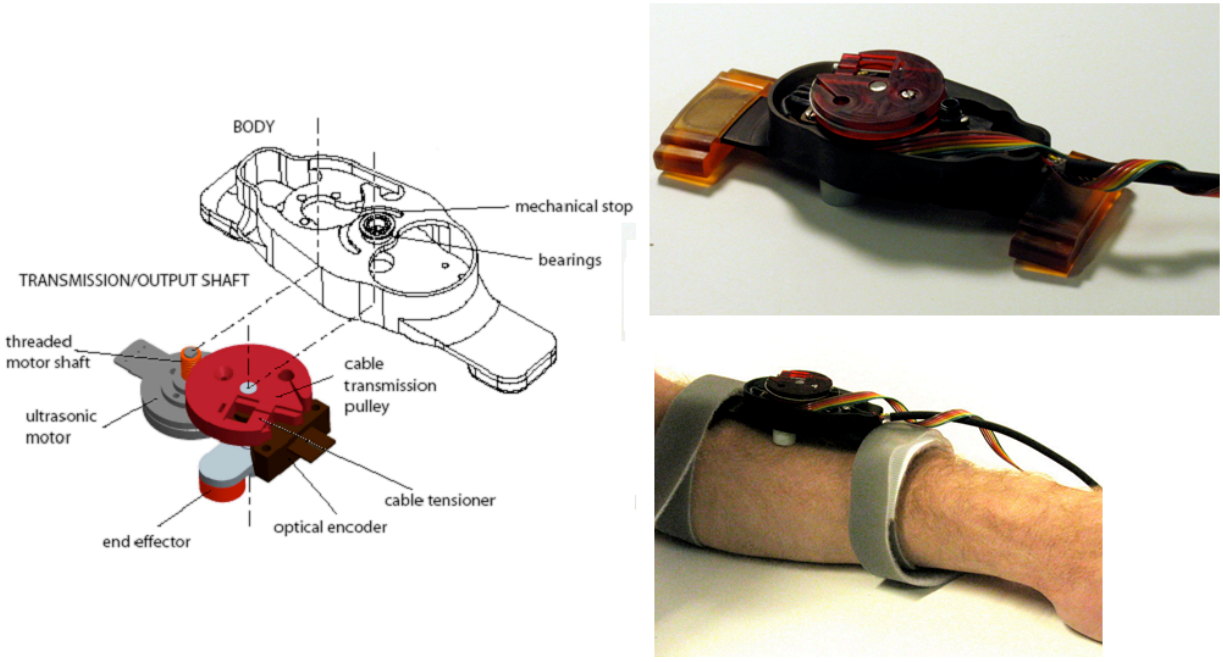

Figure 3. Wearable skin stretch device for haptic feedback. The rotating end-effector contacts the skin and can feed-back desired joint moments or angular positions by rotating. The device can be attached to many different places on the body. Further work is underway to miniaturize these devices.

The device can be programmed to rotate in either direction at variable speeds. As the device rotates farther from its natural position, the patient's skin is stretched giving the sense of a torque being applied. As the device rotates faster and slower, the user is given a sense of rotational velocity. Already, rotational skin stretch has been shown to be useful for displaying velocity and

position information for patients with impaired proprioception[6]. We intend to use this same mechanism as biofeedback for corrective movement retraining about musculoskeletal joints. Rotations of the skin stretch device might correspond to desired joint positions or moments, or relay the error between the desired and actual joint position or moment. Skin-stretch is particularly well-suited for rotating joints since feedback is administered in an intuitive, rotating fashion.

As yet, rotational skin stretch has only been designed to attach to the human forearm. Since in our application the device will be used to feedback joint information, it is likely that it will be most effective if it is attached to the skin near the rotating joint. Thus new versions of rotational skin stretch need to be designed and manufactured that can be attached in close proximity to the knee joint, hip joint, ankle, pelvis, shoulder, neck, etc. Since it is beyond the scope of this project to design devices for all of the human musculoskeletal joints, we will focus on making two devices: one to attach on the quadriceps near the knee joint and one to attach to the lower back to inform trunk angle.

While rotational skin stretch provides an intuitive way of haptically displaying desired positions and moments for a given joint, vibration is a natural fit for communicating Cartesian positions and forces at a point on the musculoskeletal frame. Our prior work suggests that skin-stretch can be complementary to vibration[7], giving us confidence that subjects can respond to simultaneous skin stretch and vibration feedback without being confused. A vibration motor, similar to that found in a cell phone, can provide the patient a sense of a force being applied at the attachment point. For example, attaching one vibration motor on the medial side of the knee joint and one on the lateral side could be a way of communicating desired knee movements. Activating the medial side motor would indicate the desire to move the knee more laterally and activating the lateral motor to move the knee medially.

In our preliminary study, a vibration motor was successfully used to feedback three levels the knee adduction moment, a value otherwise not obvious to the patient. This vibrotactile motor, a C2 Tactor, made by EAI Inc, was specifically designed for human haptic feedback. The C2 Tactor's resonant frequency is 250 Hz which is near the peak sensitivity for the Pacinian corpuscles, the fast-acting mechanoreceptor that responds to vibratory stimulus[29]. Thus activating the C2 Tactor at 250 Hz results in the highest amplitude vibration output and the highest range of human sensitivity. Subjects in the preliminary study were able to easily discern vibrations even while walking on the treadmill. For the current study, we will use the C2 Tactor but will need to obtain additional motors to further extend the capability of vibrotactile feedback. We plan to purchase another C2 Tactor and two smaller vibrotactile motors with 250 Hz resonant frequencies.

After obtaining the required sensing and feedback hardware, a unified structure will be implemented connecting all of the hardware together. Basic communications will be established between sensing hardware and feedback hardware in such a way that activity on any one sensor could produce a response on any of the feedback devices. This will be achieved using Matlab's xPC real-time kernel (Mathworks, Natick, MA). A computer running Matlab's real-time software for input/output devices and will be used to read in marker trajectories, ground reaction forces, and EMG signals and output vibration amplitude signals to the vibrotactile motors (powered by external amplifiers) and speed and direction signals to the rotational skin stretch devices (also powered by external amplifiers).

D.1.2 Implement musculoskeletal analysis and decision software in real-time

The function of the analysis and decision software is to turn motion capture, ground reaction force, and EMG sensor signals into haptic, visual, and auditory feedback for the patient. Feedback should be displayed in such a way as to encourage appropriate musculoskeletal

corrections for movement retraining. The possibilities for mapping sensor signals to feedback are virtually endless, but we will implement this mapping in the following fashion:

- Four points of Cartesian kinematic correction will correspond to each of four vibration motors
- Two musculoskeletal joint angles or torques will correspond to each of two rotational skin stretch devices
- Timing or cadence for repetitive tasks will correspond to auditory feedback
- Four muscle activation levels will correspond to visual bars displayed on a monitor.

The main analysis and decision software will be written using Matlab xPC real-time software and hardware. Vicon Nexus software (OMG plc., Oxford, UK) will be used to compute real-time kinematics, and receive ground reaction forces and center of pressure data from a Bertec instrumented treadmill (Bertec Corp, Columbus, OH). Inverse dynamic calculations will be performed in real-time using C-Motion's Visual3D software to estimate joint moments. Muscle activity will be measured using a 16-channel EMG system (Delsys, Boston, MA). All data will be sent in real-time to a computer running Matlab xPC.

Within Matlab, generalized analysis and decision structures will be designed to compare desired kinematics, inverse dynamics, and muscle activation levels with signals from the patient. Feedback decision laws for each signal will be established to automatically determine the type and amount of feedback to be administered while the patient is retraining. In summary, Matlab xPC will be used to perform the following:

- Receive kinematics from Vicon Nexus software
- Receive inverse dynamics from C-Motion's Visual3D software
- Receive ground reaction forces from Bertec force plates, integrated into Vicon Nexus software
- Receive EMG signals from Delsys EMG amplifier hardware
- Output haptic, visual, and auditory feedback signals directly from the Matlab xPC computer

D.2 Identify patient capacity for multimodal biofeedback

The second aim of this study is to *identify patient capacity for multimodal biofeedback*. It is unclear how patients will be able to process and respond to multiple feedback modalities simultaneously. Our intent is to perform experiments that include up to five different modalities of feedback and determine if subjects will be able to accurately correct movements in response to these feedback modalities. It is also important to determine the best method for applying multiple modes of feedback to optimize learning and minimize rehabilitation time. Therefore, we will determine if individuals will learn to correct complex movements more quickly when feedback modalities are applied and learned sequentially instead of in parallel.

D.2.1 Subject recruitment

To test the learning and retention capability of the haptic biofeedback system, we will perform experiments on 20 healthy participants. Since the long-term application of our biofeedback system is for patients with musculoskeletal or sensory-deficit neurological disorders and is not designed for those with neurological learning impairments, it is reasonable to test the limits of this system with healthy individuals instead of patients with disorders requiring movement retraining, since both groups should posses the same cognitive learning capabilities. We will recruit an equal number of male and female adults.

D.2.2 How many feedback modalities can an individual process and respond to in a useful way?

Using a subset of the haptic biofeedback system described in Section D.1, we will test subjects' ability to make corrections for five distinct movement modalities while walking on a treadmill. Each movement modality will receive correction information from a corresponding feedback modality. For this study, lower extremity limb corrections will be fed back only to the left leg. Subjects will be instructed to make movements corrections to both sides of the body equally to produce a symmetric gait. Table 2 shows the pairing between musculoskeletal and feedback modalities.

Table 2. Movement modalities that will be implemented and their corresponding feedback modalities.

Movement Modality	Feedback Modality
Toe in, toe out	2 vibrotactile motors on foot
Knee joint position lateral/medial	2 vibrotactile motors on knee
Trunk sway	Rotational skin stretch device on lower back
Step frequency (stride length)	Auditory metronome
Tibialis anterior muscle activation (EMG)	Visual bar plot

For the 'toe in, toe out' modality, one vibration motor will be placed on the lateral, outside aspect of the left shoe and one on the medial, inside aspect. The medial motor will be placed on the shoe near the first metatarsal and when activated will be a cue that the subject should make corrective movements by 'toeing out'. Conversely, the lateral vibration motor will be placed on the outside of the shoe near the fifth metatarsal and will indicate when the user should toe in. If the subject is in the acceptable range both vibration motors will be turned off. The toe in, toe out position will be measured while the foot is in contact with the ground.

The medial-lateral knee joint position will be informed in a similar fashion to the toe in, toe out modality. One vibration motor will be placed on the medial and one on the lateral side of the left knee joint. Medial vibration motor activation will be a signal to move the knee laterally, and lateral vibration motor activation to move medially. In this way, the vibration motors act as a pseudo-force pushing the joint away. Vibration feedback for the foot and knee will be updated during the second half of each stance phase of gait for the left leg. Each vibration cue will last for 500 milliseconds.

Rotational skin stretch will be used to inform trunk sway. The two attachment points of a rotational skin stretch device will be adhered to skin on the lower back, and the entire device will be bound with a strap extending around the subject's waist. The difference between the desired and actual trunk angle will produce a skin stretch rotation. If the user's trunk angle trajectory follows the desired trunk angle trajectory perfectly, then the skin stretch device will not move, staying in its natural un-stretched position. Otherwise, the device will rotate to an angle proportional to the trunk angle error. In this way the user will feel a twisting sensation in the direction of desired trunk sway. This feedback will update continuously throughout the trial.

Subjects' will be informed of the desired step frequency via a metronome displayed audibly through computer speakers. A beep will occur during each step while the left foot should be in contact with the ground. Each new beep will be calculated from the previous left foot contact. Based on the speed of the treadmill, this will effectively display to the user a desired stride length.

Finally, desired muscle activation will be displayed visually through a computer monitor. The display will be similar to that used for the preliminary study to show baseline and real-time knee adduction moments. A dashed red line across the screen will correspond to the desired tibialis anterior muscle activation. During the left leg swing phase the maximum filtered EMG signal will be displayed as a solid blue line representing muscle activation for the current step. The subject

will be able to see the previous 10 steps and will be instructed to attempt to make the solid blue line match up with the dashed red line.

Utilizing the feedback and movement pairings described in Table 2, subjects will be tested on three separate days spaced one week apart. Sessions will last ~60 mins and will consist of a baseline data collection period and a movement retraining period. During the baseline period, subjects will walk at a self-selected speed on the treadmill for five minutes. During this time, baseline values will be recorded for each of the five feedback modalities. After this, subjects will perform the movement retraining period, walking for 45 minutes. During this phase, the haptic multimodal biofeedback system will be used to attempt to correct each of the five movement modalities while the subject walks on the treadmill. Subjects will either have feedback modalities introduced sequentially or all together in parallel (see D.2.3).

Data will be collected throughout the retraining trials and we will determine:

- How many of the subjects were able to accurately correct all five movement modalities by the end of the last testing day?
- The total number of movement modalities achieved

We will also determine how long it takes subjects to learn each of the five modalities. This will provide some insight into the *duration of learning*. Additionally, for those who were able to learn all modalities during testing session 1 or 2, we will examine the length of time taken to achieve the same level of movement adjustments during session 2 or 3. This will elucidate the amount of *learning retention*.

D.2.3 What is the optimal sequence for introducing biofeedback modalities?

The same testing session as described above will be used to answer our second fundamental research question. Subjects will be split into two groups – a *sequential learning group* (n=10) and a *parallel learning group* (n=10). The sequential group will be given one new feedback modality at a time. Once the appropriate musculoskeletal correction is attained, the next feedback modality will be added. This will continue until all the feedback modalities are being applied simultaneously. Conversely, the parallel learning group will be given all feedback modalities simultaneously from the beginning.

Within each learning group, there will be two subgroups, each learning a different set of movement corrections (see Table 3). The first group will be trained to learn a strategy requiring more toeing in (15 deg), more medial knee position (5 cm), a 20% increase in trunk sway, a 15% increase in stride length, and a 15% increase in tibialis anterior activation. The second group will be trained to do the following: more toeing out (15 deg), more lateral knee position (5 cm), a 15 deg increase in trunk sway, a 15% decrease in stride length, and a 15% increase in tibialis anterior activation. We will use different configurations to infer different retraining strategies. Strategies may have more or less coupling between desired movement modalities.

The two different gait configurations are intended to be as different from each other as possible. Since decreasing trunk sway and decreasing tibialis anterior muscle activation may be difficult for many subjects, both configurations require an improvement. Percent increase or decrease for each modality will be based on an initial baseline period where subjects walk with their normal gait on the treadmill. Baseline values will be recorded during this initial period, and the desired changes based on these baseline values plus the percent increase or decrease.

Table 3. Experimental groups (n=5 in each group). Square brackets [ ] indicate the order in which different modalities are prescribed. Note that in the parallel learning groups (1B and 2B), all modalities will be provided simultaneously.

Group 1A Sequential Learning Gait 1	Group 1B Parallel Leaning Gait 1	Group 2A Sequential Learning Gait 2	Group 2B Parallel Learning Gait 2
[1]: Toe *in* (15 deg)	All Group 1A modalities **[5]**	**[1]**: Toe *out* (15 deg)	All Group 2A modalities **[5]**
[2]: Knee *in* (5 cm) & **[1]**	All Group 1A modalities **[5]**	**[2]**: Knee *out* (5 cm) & **[1]**	All Group 2A modalities **[5]**
[3]: *Increase* trunk sway (15 deg) & **[2]**	All Group 1A modalities **[5]**	**[3]**: *Increase* trunk sway (15 deg) & **[2]**	All Group 2A modalities **[5]**
[4]: *Increase* stride length (15%) & **[3]**	All Group 1A modalities **[5]**	**[4]**: *Decrease* stride length (15%) & **[3]**	All Group 2A modalities **[5]**
[5]: *Increase* Tib Anterior (15%) & **[4]**	All Group 1A modalities **[5]**	**[5]**: *Increase* Tib Anterior (15%) & **[4]**	All Group 2A modalities **[5]**

For the sequential learning subjects (Group 1A and Group 2A), one new feedback modality will be introduced at a time. After the subject makes successful musculoskeletal corrections on 10 consecutive left leg strides, the next new modality will be introduced. With each new feedback modality, the previous modalities will remain activated. The sequence of modalities to be introduced is given in Table 3: Toe in/out, Knee in/out, Increase trunk sway, Increase/Decrease stride length, Increase tibialis anterior activation. For those utilizing parallel learning (Groups 1B and 2B), all five feedback modalities will be activated from the beginning of the movement retraining period and remain on until the 45 minute period is over.

Data collected throughout the trials will be used to determine the following:

- Number of subjects in each group who were able to accurately correct all five movement modalities by the end of the last testing day
- Total number of movement modalities achieved for individuals in each group who didn't achieve all five modalities

Where possible, we will determine how long it takes each group to learn all five modalities giving us a comparison of the *duration of learning*. We will also examine *learning retention* of each group based on performance from one testing day to the next.

D.3 Application to knee joint osteoarthritis (OA)

Our final aim is to *use multimodal haptic biofeedback to reduce the knee adduction moment in patients clinically diagnosed with tibiofemoral OA.* Achieving this aim is necessary to demonstrate the potential for haptic biofeedback to influence a clinically-relevant population. A secondary outcome from achieving this aim will be providing a template for other researchers to use this novel technology for other clinical applications requiring movement retraining. Continuing from our preliminary study, we will attempt to retrain clinically diagnosed knee OA patients by using multiple modes of haptic, visual, and auditory feedback with the haptic biofeedback system developed in D.1. We will test the hypothesis that this novel retraining method will reduce the knee adduction moment by 30% after only three training sessions.

D.3.1 Patient recruitment and screening

Ten (10) subjects clinically diagnosed with mild or moderate medial compartment tibiofemoral osteoarthritis will be recruited for this study. Dr. Nicholas Giori, our clinical collaborator at the Veterans Affairs hospital in Palo Alto will perform screening and patient recruitment. We will attempt to recruit an equal number of males and females to this study. Patients will complete a Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire[68], to determine levels of function and disability in their affected knee. We anticipate the age range of our subjects, recruited from the VA Palo Alto medical hospital to be between 50 and 75 yrs.

The following is a list of *inclusion criteria*: Patients must be defined as having mild or moderate knee OA (defined from the KOOS questionnaire[68]), with pain originating from the medial side; patients must also be capable of walking continuously, unaided for at least 30 minutes; patients must also be able to walk at 150% of their self-selected walking speed; and patients must have a body mass index ≤ 30, to enable accurate marker location for motion capture.

Exclusion criteria include: hip or back pain that might limit subject's ability to respond to the movement retraining; rheumatoid arthritis; total knee replacements in either knee; peripheral neuropathy; previous history of traumatic knee injury.

Dr. Giori sees hundreds of patients each year, so we do not foresee any problems recruiting 14 suitable participants over a two-year grant period. Patients fitting our selection criteria will be referred to the study and asked to perform the movement retraining protocol at the Human Performance Laboratory.

D.3.2 Movement retraining through haptic biofeedback

We will use our multimodal haptic biofeedback system to perform movement retraining on the OA patients. We intend to implement feedback strategies well-suited to assist the patient in reducing the knee adduction moment. Performing high tibial osteotomy surgery typically reduces the knee adduction moment by 30% to 50% percent[75,65,78] and reducing the first peak correlates with the best long-term outcome[77,65]. Given these clinical findings:

> *Our first goal is to use haptic biofeedback to reduce the first peak in the knee adduction moment in patients by at least 30% after only three training sessions.*

Our movement retraining will focus on reducing the knee adduction moment of the knee with the most pain, as determined from a KOOS score for each knee. If cases of equal bilateral symptoms knees are equal, we will focus on reducing the knee adduction moment in the left knee. Our preliminary testing (Section C) indicated that subjects consistently reported that toeing in, increasing trunk sway, and increasing stride length were effective methods for decreasing the knee adduction moment. It was also noted that moving the knee medially reduced the knee adduction moment. To this end our experiment will focus on four corrective movements:

- Increased toe in during stance phase (15 deg)
- Increased trunk sway during entire gait (15 deg)
- Increased stride length (15%)
- Increased medial positioning of knee during stance phase (5 cm)

Similarly to the experiment outlined in Section D.2, two vibration motors will be placed on the foot to give the user feedback about toeing in, two motors on the knee to inform medial knee position, one skin stretch device placed on the lower back for trunk sway, and an audio metronome to set the step frequency (and hence, stride length). Based on whichever method produces the best results after analyzing data from Section D.2 testing, a sequential or parallel strategy will be used to apply the feedback modalities.

Each subject will receive biofeedback on three different days spaced one week apart. During the first session, patient will walk on the instrumented Bertec treadmill for five minutes without any feedback to measure baseline values for the four movement modalities as well as uncorrected knee adduction moment. After baseline testing, a 20-minute training session will ensue where the subject will attempt movement corrections based on biofeedback modalities. On the second and third days of training, the patient will only complete the 20-minute training session. Patients will be encouraged to continue the modified gait pattern between training sessions.

D.3.3 Testing the hypothesis: knee adduction moment will be reduced by 30% after three training sessions

Data will be collected during trials to calculate the reduction in knee adduction moment, time taken to learn new movement strategies, and level of retention between testing days. We will also use the following data to determine how well patients are able to respond to biofeedback corrections:

- Percent reduction in knee adduction moment for each patient
- Length of time each to learn new gait
- Retention rate of learning between sessions
- Pain, using a visual analog scale from 1-10

A repeated-measures ANOVA design will be used to compare the change in the above parameters within each training session (from beginning to end) and between training sessions (the end of one session compared to the beginning of the next session, as well as the end of each training session).

D.3.4 Power calculations

Ten subjects will be recruited as a conservative estimate based upon a power analysis for percent reduction in knee adduction moment from our preliminary data. Using vibration feedback, we showed a reduction in the knee adduction moment from 4.37 ± 0.9 to 3.68 ± 0.59 (%ht x wt). Based on these data, a group size of 8 will yield a power of greater than 80% for detecting a 15% difference between sessions, with an alpha of 0.05 (single-sided). We anticipate a greater than 15% reduction in the knee adduction moment following three weeks of training with multi-modal feedback, so we believe 10 to be a conservative estimate, accounting for subject attrition.

D.4 Limitations and alternatives

We recognize several limitations with the proposed study. First, we do not know how many feedback modalities subjects will be able to respond to. As such, this work is exploratory, although we hope to gain some insights to this question following the experiments performed in Section D.2. Based on these findings, the number of feedback modes will be adjusted accordingly for the knee OA test in Section D.3. Also, we are aware that some of the feedback modalities may be redundant. For example, as a consequence of 'toeing in', the knee might also move in the medial direction. If this is the case, we will determine the redundant feedback modality and eliminate this modality for future studies utilizing a similar system.

It is possible that the types of prescribed biofeedback gait modifications and specific values for each correction modality will work well for some OA patients and not very well for others. Though this result is not ideal it would still be a significant finding. Future work would incorporate more complex gait analysis during the baseline training period at the beginning to determine which types and values of movement corrections would likely produce the largest reduction in knee joint loads. It could also be possible for future biofeedback retraining systems to build in smart biofeedback, which would make it possible to incrementally change the values of each feedback until the desired reduction in knee adduction moment was achieved.

We also recognize that this unique biofeedback system is currently limited to a motion capture laboratory with an instrumented treadmill and sophisticated software. Hence, the clinical applicability of this system is currently limited. However, once we understand some of the fundamental questions regarding multi-modal haptic feedback, we can estimate simple, surrogate outcome measures that have the potential to be measured outside the lab at a cost that would be available to individuals. Inexpensive in-sole pressure measurement devices coupled with accelerometry and gyroscopes, for example, might provide an adequate surrogate measure of the knee adduction moment during walking. This study will collect full-body

kinematics and kinetics, and future work will investigate the potential to take this technology out of the lab and into the clinic and home.

Finally, mild or moderate OA patients may not be able to reduce knee adduction moments by at least 30%. Since this type of haptic biofeedback has not been tested on OA patients before, outcomes are unclear. However, even a reduction of 15% in this population would be much greater than what is currently offered by traditional interventions and might be enough to slow the progression and severity of the disease. Such a finding would still prove that haptic biofeedback is effective for movement retraining, opening the door for others to utilize this type of training for different musculoskeletal or neurological disorders.

D.5 Time table for proposed studies

		Preliminary Work	Year 1	Year 2
Aim 1	Integrate sensing & feedback hardware into unified system			
	Implement musculoskeletal analysis and decision software			
Aim 2	Recruit healthy volunteers			
	Perform multimodal capacity testing			
	Analyze number of learned modes			
	Analyze best learning method: sequential or parallel			
Aim 3	Recruit knee OA patients			
	Perform movement retraining to reduce knee adduction moment			
	Analyze amount of reduction, learning time, and retention			

D.6 Summary and innovation

The potential to influence quality of life through efficient and effective motion retraining is tremendous, and multi-modal haptic feedback has the potential to fundamentally change the way movement retraining is performed. This research epitomizes the principles of bioengineering research, combining multiple disciplines of engineering, computer science, and medicine to develop a novel approach to influence human health and quality of life. This work addresses the goal of the current program annoucement [PA-06-418], to “support novel scientific technologies that have the potential to significantly advance our knowledge or the status of health-related research”. This work also directly reflects the mission of the National Institute of Biomedical Imaging and Bioeingeering (NIBIB), *to improve health by leading the **development** and **accelerating the application** of biomedical technologies*. We address this mission with two prominent innovations:

1. The development of a novel haptic multimodal feedback system for motion retraining
2. The implementation of this novel haptic multimodal feedback as a treatment modality for patients with tibiofemoral osteoarthritis

Outcomes from this research will also provide the foundation for further work (via an NIH RO1 mechanism), to understand the effectiveness and long-term retention effects of movement retraining in patients clinically diagnosed with tibiofemoral osteoarthritis. Finally, this fundamental work will provide a feedback framework for others to investigate novel interventions to prevent and treat a range of movement disorders and disease, as well as develop portable solutions for a clinical or home setting.

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