Horizons in Prosthesis Development for the Restoration of Limb Function

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J Am Acad Orthop Surg 2006;14: S198-S204

Abstract

The focus of our research program is the restoration of limb function through a biohybrid approach. We consider the limb conceptually as a biohybrid organ consisting of biological tissue, endoprostheses (including neural devices and joint replacements), and exoprostheses. The biohybrid limb maximizes biological function and functional articulations with optimized human-prosthesis interfaces. Our long-term goals are to create biomimetic prostheses, optimized control systems for prostheses, and optimized human-prosthesis interfaces using both limb lengthening and osseointegration techniques.

Because of the nature of both munitions and force-protection methods used in Iraq, the medical legacy of the Iraq conflict may well be the restoration of function after traumatic limb loss. Many service members have returned from Iraq with traumatic amputations—occasionally with the loss of multiple limbs—often at proximal levels at which restoration of function is difficult. Several barriers exist to successful prosthesis use and integration. Prosthetic sockets and other attachment devices are uncomfortable, hot, heavy, and irritating to the skin. Local scarring and poor socket fitting can lead to skin ulceration. Also, inadequate length of a residual limb, particularly in posttraumatic limb loss, can impair prosthesis fitting and cause loss of muscular strength and balance. In addition, loss of neuromuscular function, including sensory loss—particularly proprioceptive deficits—and loss of muscle strength, result in fatigue and impaired balance, thereby limiting ambulation in lower extremity prosthesis users. Long-term goals at the Center for Restorative and Regenerative Medicine are to develop biomimetic prostheses and to optimize the human-prosthesis interface with neural control devices, osseointegration, and the lengthening of residual limbs.

Contemporary Approaches to Prosthetic Lower Extremity Joints

Current commercially available lower extremity prosthetic devices are either passive-spring mechanisms or actively controlled variable-damping devices. Although extensive research has been conducted to advance prosthetic materials and construction techniques, little effort has focused on the advancement of lower extremity prosthetic joints in which both joint impedance and motive force are actively controlled. These capabilities are of critical importance if leg prostheses are to truly mimic biologic function.

The long-term goal of our prosthetics program is to develop lower extremity prosthetic systems that employ muscle-like actuation, biomimetic control, and peripheral neural sensory information to directly measure user intent. Using these systems, leg amputees will experience improved gait stability, metabolic economy, and prosthesis responsiveness to the user's actions and wishes. An example of this approach, currently under development in our center, is a new ankle-foot prosthesis.

Ankle-Foot Prostheses With Muscle-Like Actuation and Biomimetic Control

Commercially available ankle-foot prostheses are completely passive; consequently, their mechanical properties remain fixed, thus limiting walking speed and ability to negotiate varying terrain.[1] By contrast, normal human ankle stiffness varies both within each gait cycle and with walking speed.[2,3] Furthermore, some studies have indicated that one of the main functions of the human ankle is to provide adequate energy for forward progression of the body.[2-5] Below-knee amputees who use passive ankle-foot prostheses exhibit nonsymmetric gait patterns, balance difficulties, low gait speed, and higher metabolic rates while walking.[1] Thus, to mimic the behavior of the human ankle and to increase gait symmetry and walking economy, a prosthetic ankle-foot device should be able to actively control joint impedance, motive force, and joint position.

We have developed a powered ankle-foot platform for the experimental evaluation of a broad range of prosthetic ankle behaviors and control systems. We think that examining a broad range of characteristics is essential, not only to aid the development of an active ankle-foot prosthesis but also to better understand the role of human ankle biomechanics on balance, metabolic rate, gait pattern, and speed.

Biomimetic Ankle-Foot Prosthesis Design Specifications

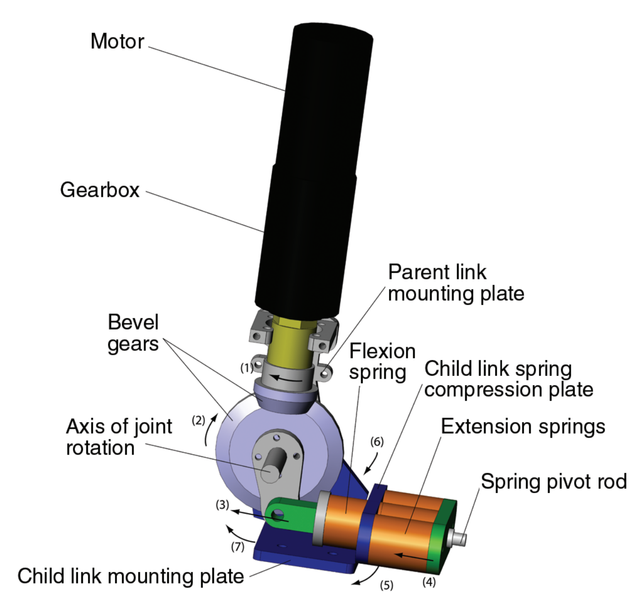
Understanding normal walking biomechanics provides the basis for the design and development of the biomimetic ankle-foot prosthesis. A level-ground walking gait cycle is typically defined as beginning with the heel strike of one foot and ending at the next heel strike of the same foot.[6] The main subdivisions of the gait cycle are the stance phase (~60%) and the swing phase (~40%). The swing phase is the portion of the gait cycle when the foot is off the ground. The stance phase begins at heel-strike, when the heel touches the floor, and ends at toe-off, when the same foot rises from the ground surface. We can further divide the stance phase into three subphases: controlled plantar flexion, controlled dorsiflexion, and powered plantar flexion.[2,3]

Controlled plantar flexion begins at heel-strike and ends at foot-flat. Controlled plantar flexion describes the process by which the heel and forefoot initially make contact with the ground. Researchers have shown that ankle joint behavior during controlled plantar flexion is consistent with a linear spring response, in which joint torque is proportional to joint position.[2,3] Controlled dorsiflexion begins at foot-flat and continues until the ankle reaches maximum dorsiflexion. During the controlled dorsiflexion period, ankle torque versus position often can be described as a nonlinear spring, in which stiffness increases with increasing ankle dorsiflexion. The main function of the human ankle during controlled dorsiflexion is to store the elastic energy necessary to propel the body upward and forward during the powered plantar flexion phase.[2,3] The powered plantar flexion phase begins after controlled dorsiflexion and ends at the instant of toe-off. Because the work generated during powered plantar flexion is more than the negative work absorbed during the controlled plantar flexion and controlled dorsiflexion phases for moderate to fast walking speeds,[2,3,5] additional energy is supplied along with the spring energy stored during the controlled dorsiflexion phase to achieve the high plantar flexion power during late stance. Thus, during powered plantar flexion, the ankle can be modeled as a torque source in series with the controlled dorsiflexion spring.

Based on these biomechanical descriptions of the human ankle, design specifications for the biomimetic ankle-foot prosthesis are as follows. The system must provide a large, instantaneous output power and torque (300 W and 127 Nm, respectively, for a 75-kg person[2]). The system must be capable of changing its stiffness within each phase of gait. The system also must be capable of controlling joint position during the swing phase.

All of the authors or the departments with which they are affiliated have received research or institutional support from the Veterans Administration. Dr. Hochberg has received research or institutional support from Cyberkinetics Neurotechnology Systems, Inc. Dr. Donoghue has received research or institutional support from Cyberkinetics Neurotechnology Systems, Inc. Dr. Donoghue has stock or stock options held in Cyberkinetics Neurotechnology Systems, Inc. Dr. Donoghue serves as a consultant to or is an employee of Cyberkinetics Neurotechnology Systems, Inc. Dr. Ehrlich has received research or institutional support from Biomimetics, Inc. Dr. Ehrlich has stock or stock options held in Biomimetics, Inc. Dr. Ehrlich serves on the Biomimetics Advisory Board.

Figure 1



Mechanical design of the rotary series elastic actuator. Torque is transmitted from the motor through the gearbox to the bevel pinion (arrow 1). This gear transfers torque to the large bevel gear (arrow 2). The rotational motion of the large bevel gear is converted into linear motion via the joint (arrow 3). This linear force is transmitted via the spring pivot rod into a compression force on the extension springs (arrow 4). The other end of the extension spring pushes on the structure that is rigidly attached to the child link (arrows 5, 6, and 7). For flexion, the direction of rotation of the motor is reversed, and the torque to the child link is transmitted via the flexion spring.

Mechanical Design of the Prosthesis

Four main mechanical elements constitute the system we have developed: (1) a high-power output motor (Maxon RE-max 40, Maxon Precision Motors, Fall River, MA); (2) transmission (gear head and bevel gears); (3) series springs; and (4) a carbon-composite leaf spring prosthetic foot. We combine the first three components into a rotary series elastic actuator (SEA) to mimic the behavior of the human ankle joint; the elastic leaf spring mimics the function of a human foot (Figure 1).

An SEA, previously developed for legged robots,[7,8] consists of a DC motor in series with a spring or spring structure via a mechanical transmission. The SEA provides precise force control by controlling the extent to which the series spring is compressed. Using a linear potentiometer, we can obtain the actual force applied to the load by measuring the deflection of the series spring. Because SEAs are force-controllable actuators, they are safer to use with human subjects than direct drive systems, which are position-controlled. With SEAs, a limiting maximum force can be specified that will not cause harm to the human user. All of these advantages make SEAs a good choice for human rehabilitation and augmentation applications.

A carbon-composite leaf spring structure is used to provide shock absorption during foot strike, energy storage during the early stance period, and energy return in the late stance period. A pilot study supports the hypothesis that a powered ankle-foot prosthesis allows for a more nearly natural gait than does a conventional passive prosthesis (unpublished data). In the design of biomimetic leg prostheses, we think that stiffness, damping, and motive torque control are important design goals.

Optimizing the Human-Prosthesis Interface

Three programs under way at our center have as their long-term goal the optimization of the human-prosthesis interface. These programs are improvement of the soft-tissue seal around an osseointegration device, development of neural control interfaces, and improvement of leg lengthening techniques.

Improvement of the Soft-Tissue Seal Around an Osseointegration Device

Osseointegration is a promising method of fixing a prosthesis directly to bone.[9] A titanium rod is screwed into the bone of the residual limb and protrudes from the skin; the exoprothesis is attached to the protruding rod. In true osseointegration, the living bone becomes fused with the oxide layer of the titanium, and this anchorage persists under normal conditions of loading—a true biohybrid approach. Among the benefits claimed for this technique is osseoperception, a term that denotes the ability of patients with osseointegrated devices to identify tactile thresholds through their prostheses, thus improving amputee perception of his or her environment.

Several fully internal osseointegrated devices have been described for orthopaedic applications. Indeed, titanium joint arthroplasties in use worldwide incorporate osseointegration principles. The application of these principles to amputees, however, has raised concerns because the titanium device is transcutaneous. The concerns are not about the integration of the device with bone but about the development of pathways around the implant through soft tissues, where environmental contamination could cause titanium corrosion and bone infection. Corrosion and infection could lead to further loss of bone length, resulting in a shorter residual limb and decreased function. Infection, bone loss, and loosening are common in transcutaneous orthopaedic implants.

Concerns about infection and loosening, and consequent loss of bone in residual limbs, led us to focus our attention on the interface of soft tissue—particularly skin—with osseointegrated prostheses. One way to develop an environmental seal, eliminating contact between the bone and the environment and restricting contamination of the prosthesis and bone, would be to promote dermal and epithelial growth into prosthetic surfaces. We are studying this topic with both tissue engineering and biomaterials approaches. To improve the soft-tissue interface with osseointegrated prostheses, we are pursuing two lines of investigation. First, we are determining the optimal surface chemistry and morphology of titanium for the attachment of epidermal keratinocytes and dermal fibroblasts. Second, we are developing a finite element analysis model to understand the mechanics of the skin-prosthesis interface that will be used to improve device design.

One approach will be to treat the surface of the titanium in various ways to provide a porous surface that might enhance cell adhesion.[10] Anodization of the titanium to produce a porous oxide, coating the surface with powder that could be sintered to different degrees of porosity is one possibility. Another is the use of various mechanical surface-roughening treatments. We have devised a novel method to rapidly produce thin films of titanium and its alloys, with which we can control the chemistry, grain size, and morphology of the metal surface. Experiments are under way to determine the stability of these surfaces under in vitro physiologic conditions. We have also started initial testing of these surfaces and have set up quantitative fluorescent assays to measure cell number, cell adhesion, and cell morphology. These approaches will facilitate rapid and quantitative screening of a large array of surface chemistries and morphologies to identify those that are optimal for cell attachment.

To validate a finite element analysis model, we also have begun mechanical testing of whole human skin to determine its viscoelastic and biomechanical properties. For these tests, small circular biopsies of discarded tissue are loaded into one of several mechanical testing devices: a rheometer, a new torsional wave device to measure the viscoelastic properties of skin, and a uniaxial tester (Instron, Norwood, MA) to measure the breaking strength of skin. These data will be incorporated into a first-generation finite element analysis model to examine the unique load conditions present at the percutaneous portion of the osseointegration device. This model will facilitate the design of a more effective percutaneous abutment that resists epidermal regression, infection, and device failure.

Development of Neural Control Interfaces

Advances in microelectronic devices and our understanding of neural plasticity suggest that, in the foreseeable future, linkages will be made between nerve tissue and robotic prostheses. Our investigations in this area focus on the use of microelectronic devices and the development of mathematical algorithms to translate complex patterns of neural activity into control outputs for prosthetic devices.

Sensory and motor information is represented in patterns of electrical signals in the nervous system. This understanding has paved the way for the development of closed-loop brain-machine interfaces (BMIs), which have the promise of enabling bidirectional interaction between machines and the human nervous system. The application of BMI neurotechnology has the potential to restore lost neurologic function to disabled people and to provide relatively precise control of physical devices, including prosthetic limbs or semiautonomous robots. Our research will develop the key elements of advanced BMI technology with integrated microscale signal processors, innovative broadband optical telemetry and powering, and miniaturized processors. In addition, we are working on new mathematical models for representing and decoding human neural coding to allow two-way communication between machines and the nervous system. Finally, we are using this technology to establish the nature of control signals required for humans to control complex devices. Our goal is to develop both control algorithms and user interfaces that would enable human performance of robot navigation tasks or other complex interactions under neural control, and to apply these advances to robotic limbs.

Decoding is the task of transforming complex neural patterns into a meaningful control signal that can drive physical or biologic devices. The challenges that exist for decoding are the ability to develop a mathematical neural translator, real-time implementation of this translator, and automated set-up and calibration. Substantial progress has been made in decoding motor signals that provide a real-time hand-motion control signal. We have developed and tested a series of well-defined mathematical algorithms that can convert motor cortex spike activity into a continuous reconstruction of hand position (linear regression methods[11]) or that can classify patterns of motor cortex activity into discrete choices.[12,13] These include maximum likelihood, Bayesian inference techniques, Kalman filtering for linear models, and particle filtering for nonlinear models.[14,15] These techniques provide a principled basis for progress from our present ability to generate simple motion signals to the production of more complex ones.

Most previous work has explored simple scenarios in which the decoding of hand motion either is in one of a fixed number of directions or is a continuous reconstruction of hand trajectory. However, realistic scenarios for a prosthetic arm, for mobile and dexterous robots, or for rich assistive technologies are more complex. In particular, tasks such as manipulating, grasping, pushing, and gesturing involve the composition of more primitive motions. For example, even a simple action such as picking up a block may be composed of a preparation phase, a ballistic hand transport motion, manipulator positioning using visual servoing, and finally a grasping motion. Our goal is to develop a prosthetic device under neural control that is capable of executing such compositional actions. Achieving this goal will require basic scientific and engineering advances to determine the full extent of information available from spike trains.

An additional challenge is that decoders may be required to function adaptively to deal with changes in the system that can arise from instabilities in the sensors or in the biologic system. For example, the neurons available may change over time as the sensor moves in the tissue. We will develop a variety of adaptive filters that will be tested in online experiments in which monkeys will use these filters to perform a variety of actions. For development purposes, we can simulate more complex actions on a computer screen, where we can readily control the properties of a wide range of devices. This knowledge will set the stage for the development of actual devices that can serve real-world interactions, such as navigation in complex environments or control of multidimensional manipulators requiring dexterous finger, hand, and arm movements of an artificial device.

Improvement of Limb Lengthening Techniques

Short residual limbs present particular difficulties with prosthesis fitting, resulting in compromised function and inability to use prosthetic devices. Proximal transfemoral amputations can adversely affect sitting balance and may require functional hip disarticulation prostheses. Short residual proximal tibias may not allow fitting with a below-knee prosthesis and may require extension of the prosthesis to the thigh, forcing the user to function as an above-knee amputee. Similar problems exist in the upper extremity for both above-elbow and below-elbow prostheses. Heavier, more awkward proximal prostheses increase the energy cost of movement. In the lower extremity, the metabolic costs of walking, as well as functional outcomes, are directly related to the length of the residual limb and the number of usable joints preserved.[16]

Distraction osteogenesis and bone transport have been applied to the problem of short residual limbs, and several case reports have been published. Although not necessarily exhaustive, a review of this literature has revealed 15 reports of bone lengthening in both the upper and lower extremities, describing lengthening of short residual limbs in 6 femurs, 7 tibias, 11 below-elbow amputations, and 30 digits and phalanges. When amputation of the upper extremities is performed for trauma, salvage of length is even more crucial than in the lower extremity. When more than one joint needs to be replaced, the prosthesis becomes increasingly heavy and cumbersome to operate.[16] In the upper extremity, lengthening of digital amputations by 1 mm per day has been achieved with a mean length of 3 cm.[17] In phalanges, the reported mean gain in length is 7 mm.[18] Lengthening of short residual forearms 5 to 6 cm has been reported.[19-21] Lengthening also has been successful in the lower extremity;[22-24] a mean gain in length of 7 cm has been reported.[25,26] In one patient, bone transport techniques were used to convert the level of amputation from hip disarticulation to above-knee, with a gain in length of 9 cm.[27] Limb lengthening with distraction osteogenesis can convert a proximal level of amputation to a more distal one. Problems that have been encountered are long consolidation times, pin infections, inadequate skin coverage, and joint stiffness. Issues that may be related to these complications, and that therefore may permit reduction in their frequency, are vascularity and tissue oxygenation, nutritional status, and immunocompromise.

Augmentation of distraction osteogenesis has been attempted by application of physical agents, notably electromagnetic fields (EMFs) and ultrasound. In one controlled clinical trial, application of EMF had no effect on the rate of bone consolidation but significantly ($P < 0.0001$) reduced bone loss in distal segments, suggesting that EMF may have an important role in preventing the risk of fracture.[28] In a subsequent experimental study on rabbits, EMF increased bone consolidation and torsional strength of the healing callus.[29] A controlled clinical study of ultrasound in distraction osteogenesis demonstrated faster callus formation and a decrease in treatment time in the ultrasound-treated group.[30] Callus density measured radiographically was greater, and mean time until docking and time to removal of the external fixator was significantly ($P < 0.05$) shorter, in the ultrasound group. Bone grafting of the consolidation site may enhance healing and also shorten the time to removal of the external fixation device.[16] These studies collectively suggest that distraction osteogenesis can be accelerated by changes in the biologic environment. Both EMF and ultrasound have been shown to change gene expression for structural skeletal proteins and increase local growth factor synthesis. They may also affect local vascularization. Distraction osteogenesis may be modifiable by other tissue engineering strategies, as well.

Our studies of the biomechanical and physical properties of distraction osteogenesis have demonstrated that tensile properties of lengthened bone increased with time after lengthening but that they remained 50% weaker than did control bone 3 months after lengthening.[31] A series of studies was undertaken to assess the effects of progressive weight bearing on the biology of distraction osteogenesis in an attempt to optimize consolidation and healing of the lengthened segments.[32,33] These studies collectively demonstrated that matrix formation and calcification occurred earlier in animals with distraction osteogenesis that were permitted graded weight bearing compared with non–weight-bearing animals. Weight bearing also has been shown to stimulate new blood vessel formation during distraction osteogenesis. These studies suggest that early regenerate bone is augmented by mechanical loading and support the concept of early weight bearing after limb lengthening.

Eberson et al[34] studied changes in mineralization in distraction osteogenesis caused by low-intensity ultrasound stimulation. Radiographically, healing of the ultrasound-treated bones preceded that of control bones by approximately 1 week. The bone volume fraction was significantly ($P < 0.05$) higher in the ultrasound-treated animals. The ultrasound-treated femurs were 20% stiffer and 33% stronger than the control femurs.

Summary

The long-term goals of our center are to create biomimetic prostheses, optimized control systems for prostheses, and optimized human-prosthesis interfaces using both limb lengthening and osseointegration techniques. An ankle-foot prosthesis currently under development in our center uses muscle-like actuation, biomimetic control, and peripheral neural sensory information to directly measure user intent. Our program to optimize control systems for prostheses focuses on the application of brain-machine interface neurotechnology that may potentially restore lost neurologic function. We are developing advanced brain-machine interface technology to assist disabled people and to provide novel control of physical devices, including prosthetic limbs or semiautonomous robots. Finally, our program to optimize human-prosthesis interfaces is investigating the extent to which distraction osteogenesis may be modifiable by electromagnetic fields as well as by other tissue engineering strategies. Our studies of the biomechanical and physical properties of distraction osteogenesis have demonstrated that the tensile properties of lengthened bone increase with time after lengthening. Also, to improve the soft-tissue interface with osseointegrated prostheses, we are determining the optimal surface chemistry and morphology of titanium for the attachment of epidermal keratinocytes and dermal fibroblasts, and we are developing a finite element analysis model to understand the mechanics of the skin-prosthesis interface.

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