SCIENCE ROBOTICS | RESEARCH ARTICLE

PROSTHETICS

A highly integrated bionic hand with neural control and feedback for use in daily life

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Restoration of sensorimotor function after amputation has remained challenging because of the lack of human-machine interfaces that provide reliable control, feedback, and attachment. Here, we present the clinical implementation of a transradial neuromusculoskeletal prosthesis—a bionic hand connected directly to the user's nervous and skeletal systems. In one person with unilateral below-elbow amputation, titanium implants were placed intramedullary in the radius and ulna bones, and electromuscular constructs were created surgically by transferring the severed nerves to free muscle grafts. The native muscles, free muscle grafts, and ulnar nerve were implanted with electrodes. Percutaneous extensions from the titanium implants provided direct skeletal attachment and bidirectional communication between the implanted electrodes and a prosthetic hand. Operation of the bionic hand in daily life resulted in improved prosthetic function, reduced postamputation, and increased quality of life. Sensations elicited via direct neural stimulation were consistently perceived on the phantom hand throughout the study. To date, the patient continues using the prosthesis in daily life. The functionality of conventional artificial limbs is hindered by discomfort and limited and unreliable control. Neuromusculoskeletal interfaces can overcome these hurdles and provide the means for the everyday use of a prosthesis with reliable neural control fixated into the skeleton.

INTRODUCTION

The ability to interact with everyday objects and perform mundane and complex tasks is greatly damaged after the amputation of a hand. Upper-limb prosthetic devices aiming to restore function vary in their degree of anthropomorphism, from hooks and grippers to hand-like robotic devices matching the patient′s skin color. Prosthetic hardware aside, these assistive devices are only functionally useful provided that they can be controlled reliably. Moreover, prosthetic limbs are of limited use if patients cannot wear them comfortably and throughout the day, every day. Prosthetic attachment (mechanical interface) is a major source of problems for users (*1*, *2*). Likewise, reliable control of the prosthetic device ranks highly in priority for people with amputations (*3*, *4*), and in this case, the problem lies in the interface with the user′s sensorimotor system (control interface). The overall human-prosthesis interface is therefore crucial for the restoration of function.

Osseointegration allows for direct skeletal attachment of limb prostheses, overcoming the problems of socket suspension. Bone-anchored prostheses attached via osseointegration can be worn comfortably all day because there is no compression over the residual limb while also providing better transfer of mechanical loads. Although osseointegration has proven beneficial at different levels of amputation, its benefits are limited to the mechanical interface. Control over the prosthesis, on the other hand, is commonly coupled to the electrical activity of muscles remnant in the residual limb (in other words, myoelectric signals). In its most widespread form, myoelectric signals recorded by surface electrodes from an agonist-antagonist muscle pair are used to distinguish between two opposite movements (for example, hand open and close) and to proportionally control one of them at a time (*5*). More complex approaches, including pattern recognition classifiers (*6*–*9*) and parallel regressors (*10*, *11*), have demonstrated viable options to increase the number of simultaneously controllable movements.

Myoelectric signals recorded by surface electrodes are prone to disturbance and interference, thus rendering prosthetic control in daily life unreliable. Implanted electrodes have been found to provide reliable control signals (*12*–*16*) but impose an additional communication requirement, namely, that the signals must travel constantly from inside to outside the body (*17*). The same challenge is present in the opposite direction to restore somatosensation. Numerous laboratory experiments have shown that electrodes implanted in or around nerves can be used to elicit sensations in the missing hand triggered by sensors embedded in the prosthesis (*18*–*22*). However, the communication between implanted electrodes and external prosthetic components has been a long-standing problem preventing the use of implanted electrodes in bionic limbs ever since the first successful demonstrations of their utility for

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prosthetic control (*23*–*25*) and sensory feedback (*26*, *27*) more than 60 years ago.

A neuromusculoskeletal interface using an osseointegrated implant engineered to enable bidirectional communication between the prosthesis and implanted electrodes, in addition to skeletal attachment, can resolve the aforementioned problems (*28*, *29*). Here, we present the clinical implementation of this concept in a patient with below-elbow amputation, in whom surgical reconstruction of the residual limb was also performed to increase the number of myoelectric control sources and treat neuropathic pain (Fig. 1 and movie S1). As opposed to previously implanted neuroprosthetic systems used solely for research purposes, our implementation is self-contained; in other words, it requires no additional equipment, such as large batteries or processing units, to be worn by the patient, making it safe and reliable for unsupervised use in daily life. The patient has used it successfully in activities of daily living (ADLs) for more than 3 years and continues using it at present.

RESULTS

Prosthesis functionality

Postinterventional testing using the highly integrated neuromuscular interface (Fig. 2A) showed that the patient's prosthesis functionality increased compared with preintervention (Table 1 and Fig. 2, B and C). Assessment of Capacity for Myoelectric Control (ACMC) outcome scores improved from 68 to 77 and from 65 to 80 for the luggage and table tasks, respectively; both improvements are above the minimum detectable change (*30*). Similarly, the Southampton Hand Assessment Procedure (SHAP) score improved by 23%, from 56 to 69, after the intervention. Both evaluations demonstrate an improvement in prosthesis capability and functionality during the performance of ADLs. These tests were conducted using the same control scheme (two-site direct and proportional control) and therefore represent the difference between the conventional prosthetic interface (socket and surface electrodes) and the neuromusculoskeletal interface (osseointegration and implanted electrode).

Questionnaire outcomes

Perceived disability, problems faced during prosthesis use, and pain all decreased after the intervention, whereas the quality of life increased (Table 1 and Fig. 2, D to H). The EQ-5D-5L value improved by 0.4 [0.18 is the average minimal clinically important difference (MCID) for the EQ-5D-5L (*31*)], from 0.23 to 0.63. The Disabilities of the Arm Shoulder and Hand (DASH) score improved 9 points, from 43.3 to 34.3, after the intervention [MCID is 10 to 15 points (*32*)]. The Questionnaire for Upper Limb Amputation (Q-ULA) score was 42.7 before the intervention and improved to 15.5 after the intervention. Phantom limb pain intensity decreased from 5 to 3, and stump pain vanished entirely compared with 6 of 10 before the intervention. Interference with ADLs decreased by 2 scores, interference with work decreased from 9 to 5 of 10, and interference with sleep decreased by 6 points to be absent after the intervention. Table 1 shows the summary of the study outcomes, and Fig. 3 (A and B) and movie S1 show prosthesis use during ADLs and an exploratory demonstration of the sensory feedback.

Neuromusculoskeletal interface stability

The electrical impedance to each electrode contact was monitored over time to evaluate the stability of the interface with the patient's neuromuscular system (fig. S1). A very high or low impedance would indicate a broken or short-circuited connection, respectively, and both would represent a failure that prevents recording or stimulation. The implanted electrodes remained within working range (cuff: 8325 ± 2754 ohm; epimysial: 1419 ± 775 ohm; intramuscular: 985 ± 733 ohm), with temporal exceptions attributed to external connections (fig. S1).

Neurostimulation and perception thresholds

The neural electrode allowed for stimulation of afferent nerve fibers that resulted in tactile sensations perceived consistently in the missing hand corresponding to the dermatome associated with the ulnar nerve, where the cuff electrode was implanted (fig. S2). The perception thresholds (minimum charge required to elicit sensations) remained within conservatively safe stimulation parameters, with temporal exceptions (fig. S3). Overall, we were able to

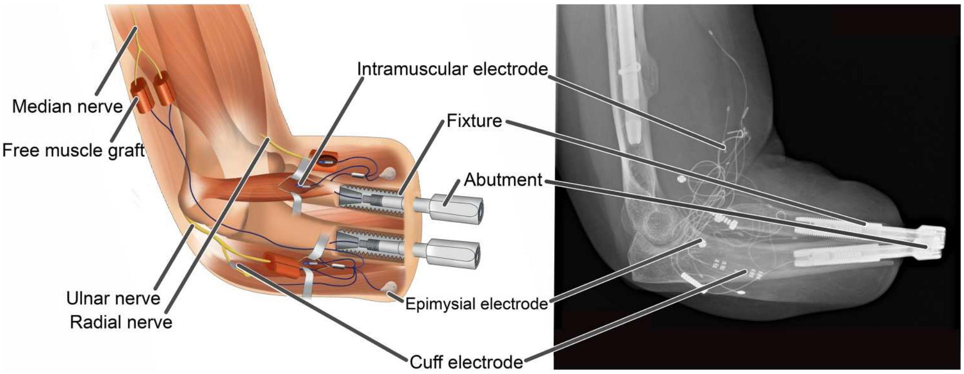

Fig. 1. Schematic illustration and x-ray of a highly integrated human-machine interface in a patient with transradial amputation. Four monopolar epymisial and four monopolar intramuscular electrodes were sutured on/in native residual muscles to provide myoelectric signals for prosthetic control. Furthermore, fascicles of the median, ulnar, and radial nerves were transferred into nonvascularized muscle graft to create additional myoelectric sites. Each nonvascularized muscle graft was instrumented with a monopolar intramuscular electrode. Part of the ulnar nerve was wrapped with a cuff electrode for sensory feedback. A titanium fixture was implanted into both the radius and the ulna bones and left to osseointegrate. In addition, a percutaneous abutment was installed into each fixture, allowing for skeletal attachment of a prosthetic hand. Feedthrough connectors allow for wired electrical communication from the proximal end of the fixtures (inside the body) to the distal end of the two abutments (outside the body), creating a bidirectional communication between the human and the prosthetic hand.

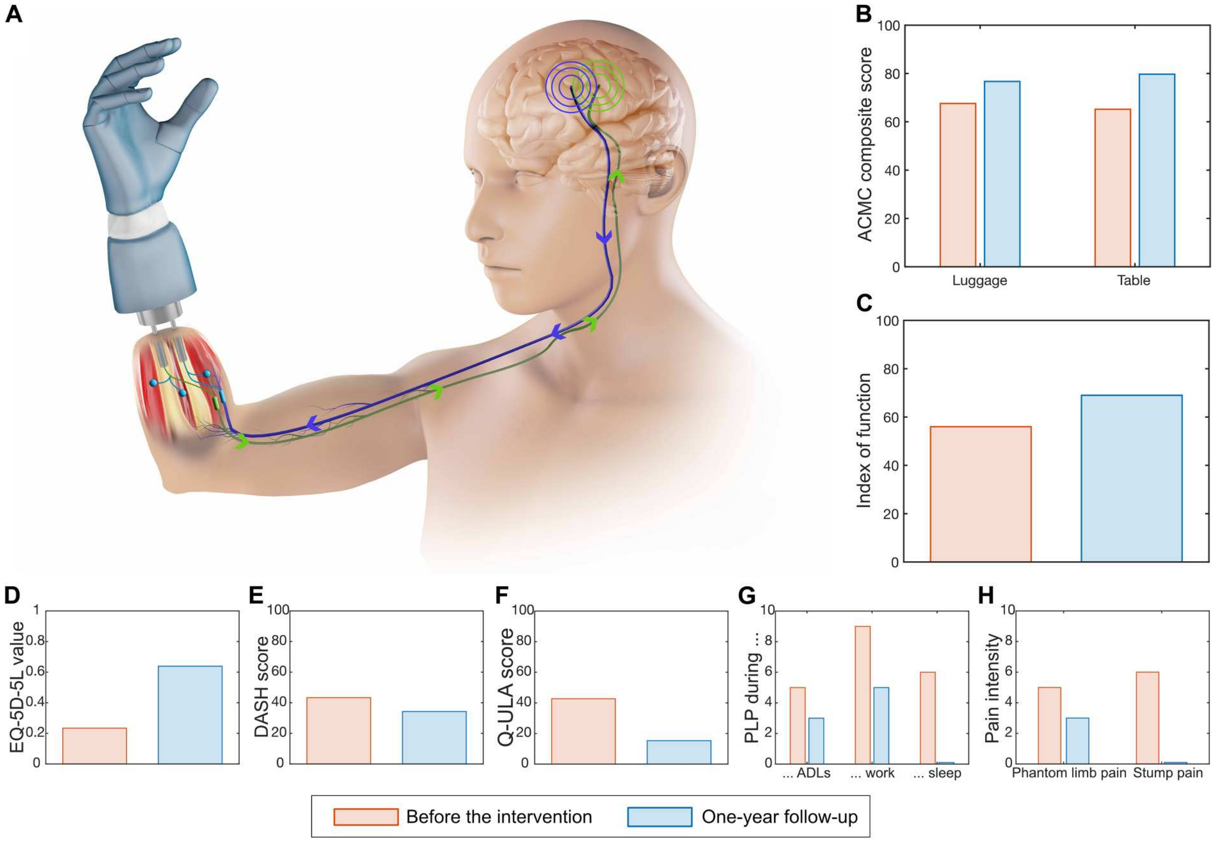

Fig. 2. Overview of outcomes comparing scores before the intervention with the scores 1 year after the intervention. (**A**) An illustration of the intervention, a bidirectional neuromusculoskeletal interface for people with transradial amputation. (**B**) The individual scores of the two ACMC tasks. (**C**) The index of function outcomes from the SHAP. (**D**) The outcomes of the EQ-5D-5L questionnaire. (**E**) The outcomes of the DASH questionnaire. (**F**) The outcomes of the Q-ULA questionnaire. (**G**) The perceived interference of phantom limb pain during ADLs, work, and sleep. (**H**) The reported perceived intensity of phantom limb pain and stump pain.

record myoelectric signals and elicit sensations via direct neural stimulation throughout the study.

Prosthesis control and signal quality

The signals from the native and newly created myoelectric sites allowed for the decoding of six phantom limb movements—equivalent to a 3–degrees-of-freedom (DoF) prosthesis—with a 100% completion rate in the Motion Test (fig. S4). In a separate Motion Test, the patient was able to control all five phantom fingers individually (5 DoF or 10 movements) with a completion rate of up to 95% (fig. S5). These findings illustrate the potential for further increasing prosthetic function using terminal devices with multiple DoF. The signal-to-noise ratio (SNR) calculated on the basis of data recorded for the Motion Test showed that, 2 years after the initial implantation, all epimysial electrodes (fig. S6), all except one intramuscular electrode in a native muscle (fig. S7), and all except one of the intramuscular electrodes in reinnervated free muscle grafts (fig. S8) featured a SNR higher than 10 dB. The muscular electrodes allowed for higher grip precision as measured by the minimum force applicable to an object, which was improved on average by 3.8 times (5.7 ± 4.7 N using surface electrodes and 1.5 ± 2.2 N implanted electrodes; fig. S9).

Osseointegration failure and reimplantation

The titanium fixture implanted in the radial bone failed to osseointegrate and was removed 5 months after implantation. No infection was detected, and the electrodes pertaining to this implant remained implanted (eight intramuscular electrodes). The implant system has a modular design with a series of connectors that allow for the electrodes or the titanium implants to be removed or exchanged without explanting the other components. The patient was allowed to continue using the prosthesis coupled to the ulna implant alone but with careful loading. Four months after explantation, to allow for healing of tissues, a new titanium fixture was implanted. The new titanium fixture had a larger diameter to ensure contact with cortical bone. Six months after the implantation of the new fixture, the weight of the prosthesis was loaded equally in both radial and ulna implants. The new fixture was not loaded immediately to allow for osseointegration to take place. Although the hand prosthesis could be electromechanically coupled to a single implant, distributing the weight to both implants reduces the risks of mechanical failures. Two fixtures also allow for a total of 16 electrode channels. The e-abutment screw of the ulna implant was replaced because of mechanical failure 3.5 years after implantation. A potential cause for said failure could be that this implant had to carry the full weight of the prosthesis alone for approximately 10

Table 1. Outcome scores of the functionality, quality of life, and pain assessments before the intervention compared with after the intervention. For the ACMC and SHAP, higher scores represent better function, and for the EQ-5D-5, higher scores represent increased quality of life. For the DASH, Q-ULA, and postamputation pain, lower scores indicated improved function, a decrease in problems faced during prosthesis use, and a decrease in pain and interference caused by pain, respectively. PLP, phantom limb pain.

Outcome	Before	After
Functional		
ACMC		
Luggage	68	77
Table	65	80
SHAP	56	69
Experiential		
EQ-5D-5L	0.23	0.63
DASH	43.3	34.3
Q-ULA	42.7	15.5
Pain		
PLP interference with ADLs	5	3
PLP interference with work	9	5
PLP interference with sleep	6	0
PLP intensity	5	3
Stump pain intensity	6	0

months, whereas the other implant was replaced and became ready to load weight.

DISCUSSION

Solutions for artificial limbs must be designed for use outside of research laboratories to confer real clinical benefit to people with limb loss. Here, we present the clinical implementation of a transradial neuromusculoskeletal prosthesis interfacing directly between the hand prosthesis and the nervous and skeletal systems of the user. Implanted electrodes with feedthrough connections through the titanium implant allowed for safe and stable acquisition of neuromuscular signals, resulting in bionic hand control that was suitable for long-term use in daily life.

After using the system at home for a year, the patient demonstrated a greater capacity for myoelectric control, specifically improving when gripping in different body positions, repetitive grasps and releases, and holding objects during motion (ACMC). This improved capacity suggests higher reliability and repeatability of the myoelectric signals acquired from the implanted electrodes compared with surface electrodes mounted in a socket (*14*, *28*, *29*). Tests stimulating the cuffed nerve also showed longitudinally stable percepts evoked on the palm and fingers of the phantom hand (Supplementary Materials), sensations that open the door for biomimetic feedback directly communicating tactile information from the sensorized bionic hand (*33*–*35*).

Experiential questionnaires suggest that quality of life improved as a result of using the neuromusculoskeletal prosthesis, with the EQ-5D-5L and Q-ULA both showing higher outcomes and the reduced DASH score suggesting lower perceived disability. Likewise, the patient reported reduced intensity of stump and phantom limb pain.

Human-machine interfaces requiring surgical interventions carry additional risks over noninvasive solutions. Risks associated with the surgery itself and the long-term potential risk of infections must be factored. Failed osseointegration in one implant was observed in this case and was resolved with a larger-diameter implant. The other implant required a change of the e-abutment screw after this broke in June 2022 (>4 years after implantation), potentially because of the fatigue experienced when the patient only used one implant to load the prosthesis. Compromised soft tissue and skeletal structures can complicate reconstruction procedures and the selection of suitable implants. All of these aspects should be weighed against the functional and psychosocial benefits of patients (*36*).

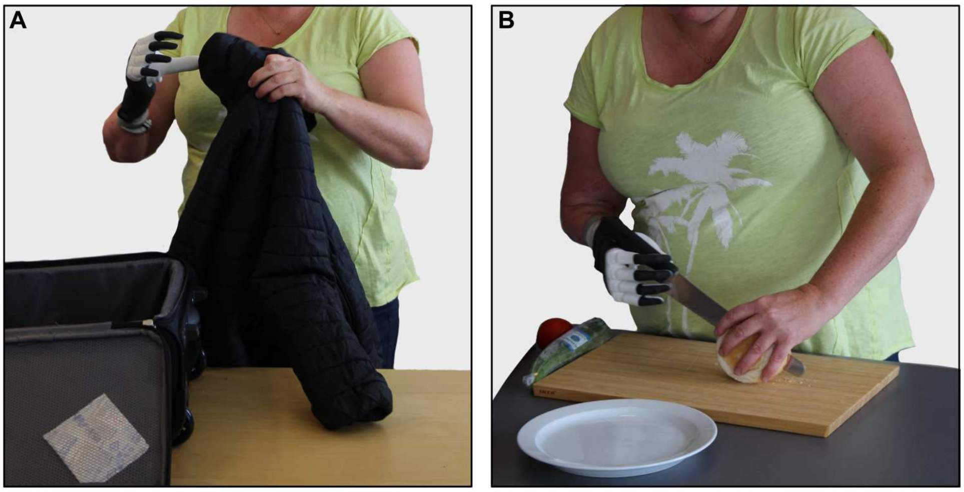

Fig. 3. The patient performs tasks representative of daily life. After a short fitting session where control parameters were fine-tuned, the participant was able to use the neuromusculoskeletal prosthesis to perform daily tasks, including packing a suitcase (**A**) and preparing food (**B**).

In this work, we prioritized research on prosthetic control over the provision of sensory feedback because the former has been reported to be of higher priority for patients (*36*). In addition, the implementation of sensory feedback in daily life requires robust and reliable sensors in the prosthesis, as well as analog and digital strategies to reduce the effect of stimulation artifacts interfering with myoelectric recordings (*37*, *38*). There was no commercially available multi-articulated hand prosthesis with embedded sensors that could be used for a reliable implementation of sensory feedback in daily life during this study. Our research priorities and the lack of readily available sensorized prosthetic hands have delayed the implementation of sensory feedback in daily life in this patient. However, we foresee that this will change in the coming years with the advent of commercially available, multi-articulated, and sensorized prosthetic hands. Overall, we demonstrated in one patient the long-term viability and utility of a transradial neuromusculoskeletal prosthesis and its ability to improve control over a bionic hand, along with improved quality of life for the user.

MATERIALS AND METHODS

Study design

This case study investigated the in-human implementation of a transradial neuromusculoskeletal prosthesis. The study objectives were to assess the safety and functionality of the neuromusculoskeletal interface (measured by functional assessments and engineering tests), as well as the effects on the quality of life of the patient after using the neuromusculoskeletal prosthesis in daily life (measured by questionnaires).

Patient

One patient (female, born 1973) took part in this study between September 2018 and April 2021. The patient sustained a traumatic injury leading to transradial amputation of the right hand. The study protocols were carried out in accordance with the Declaration of Helsinki and approved by the Regional Ethical Review Board in Gothenburg (Dnr. 12-769). Signed, informed consent was obtained before conducting the experiments.

Surgical procedures and neuromusculoskeletal interface

Osseointegrated implant

A skin flap was raised at the distal aspect of the residual limb, and both radius and ulna bones were identified and made even in length. For each bone, the medullary canal was opened and prepared for implantation using a procedure previously described (*39*). A fixture was then installed and soft tissues trimmed as described by Brånemark *et al.* (*40*). Lateral and medial access to the forearm allowed for drilling a 3.5-mm hole in each bone, about 2 cm proximal to the fixture. An e-central screw (e-CS), an e-abutment screw, and an abutment were installed within each fixture (Fig. 1). Through the cortical holes, both leads coming from the e-CS were retrieved, and one was passed into the dorsal and the other into the volar compartment of the forearm.

Electroneuromuscular constructs

All muscles in the proximal forearm were degenerated, and some of them could not be properly identified. On the dorsal surface, the interosseous nerve stump was isolated, and the end-neuroma was excised, making it available for transfer to a nonvascularized free muscle graft [also known as a regenerative peripheral nerve interface; (*15*)]. Motor nerve stimulation revealed relatively good muscle contraction for the extensor carpi radialis (ECR), the extensor digitorum communis (EDC), and the supinator muscles. One epimysial and one intramuscular electrode were implanted in the ECR, one intramuscular electrode in the supinator, and one epimysial electrode in the EDC.

On the volar surface, the end-neuroma on the ulnar nerve was excised, and the nerve was split in two fascicles: One fascicle was used to innervate a nonvascularized muscle graft, and one was wrapped with a cuff electrode for sensory feedback. Only the flexor carpi ulnaris (FCU) and the pronator teres (PT) muscles showed signs of active contraction after motor branch stimulation. One epimysial and one intramuscular electrode were implanted in the FCU and one epimysial electrode into the PT. The median nerve was identified proximal to the elbow joint. The large end-neuroma was removed, and the nerve was split in two fascicles, each of which was then transferred to a nonvascularized muscle graft. No muscle was deinnervated because only the distal nerve branches terminating in neuromas were used for reconstruction. The four nonvascularized muscle grafts were harvested from the vastus lateralis muscle on the right thigh with a dimension of 5 cm by 3 cm by 1.5 cm, and all of them were instrumented with intramuscular electrodes.

Neuromuscular electrodes

All muscular electrodes were unipolar. The intramuscular electrode contacts had a 1.27-mm diameter and a 2-mm length, and the epimysial electrode contacts had a 2.2-mm diameter. The neural electrode was a 4-mm diameter self-sizing spiral cuff with three central contacts of 1-mm diameter each in a mixed-tripole configuration (*41*). We used two types of muscular electrodes because of the nature of the targets. Epimysial electrodes are exposed to less mechanical stress and therefore are expected to remain operational for longer (*17*). In addition, the epimysial electrode contacts tend to have larger surface area, and, therefore, fibrous encapsulation is less detrimental than for intramuscular electrodes (*17*). On the other hand, intramuscular electrodes are more selective and less affected by cross-talk and thus preferable for signal source independence (*17*). We used epimysial electrodes in the native muscles prioritizing longevity, but the free muscle grafts were not vascularized and therefore depend primarily on blood diffusing from surrounding tissue for survival. An epimysial electrode on such a relatively small and nonvascularized muscle would compromise diffusion and thus survival. This is the reason for using intramuscular electrodes in such targets. In addition, mechanical stress is greatly reduced in small free muscle grafts in comparison with larger native muscles. Regarding the neural interface, we used an extraneural electrode primarily for safety and longevity (*17*, *42*, *43*). Neural electrodes have been used mostly to provide sensory feedback rather than for control (*18*–*22*). This is because of the much lower SNR obtained in comparison with muscular electrodes. Despite that, we have shown that our chronically implanted extraneural electrodes can be used to decode motor intention (*44*); this has not yet been implemented reliably in daily life owing to the SNR challenge.

Self-contained prosthesis

The self-contained prosthesis included a hand, an embedded controller, a wrist-shaped battery unit, and a mechatronic coupler connected to the neuromusculoskeletal interface. The patient was provided with a single-DoF hand (MyoHand Variplus Speed, Ottobock, Germany) and an advanced multi-DoF hand that allowed for different grasps (Mia Hand, Prensilia SRL, Italy) (*45*). The patient was free to use either prosthesis during daily life; however, the assessments to evaluate function were performed using the same single-DoF hand to avoid potential bias due to the end effector. Before the intervention, the patient used the single-DoF hand attached to her residual limb by a conventional socket and controlled by surface electrodes. She used the most common control scheme in which an electrode placed on the hand flexors and another one in the hand extensors were used to close and open the hand, respectively (two-site direct control). After the intervention, myoelectric signals from intramuscular electrodes in the ECR longus and FCU were mapped to open and close the prosthetic hand, respectively. A sustained open signal was used to switch between grasps when the multi-DoF hand was used. Preoperative assessments were conducted with this prosthetic system in which the socket and surface electrodes were replaced by the neuromusculoskeletal interface in the postoperative assessments. Mechanical attachment was then made via the osseointegrated implants, and control signals were recorded using the implanted electrodes. The same control scheme was maintained in the pre- and postoperative assessments.

Functionality, quality of life, and pain assessments

Prosthetic functionality was evaluated with the ACMC (*46*) and the SHAP (*47*). Changes in quality of life, perceived disability, problems faced during prosthesis use, and pain related to amputation were measured using the EQ-5D-5L questionnaire (*48*), the DASH questionnaire (*49*), the Q-ULA (*50*), and the questionnaire for Phantom Limb Pain Tracking (Q-PLPT) (*51*), respectively. These assessments were performed 6 weeks before and 123 weeks after the intervention.

The ACMC is an observational assessment evaluating a person's ability to perform predefined daily tasks, including packing a suitcase and setting a table. Twenty-two different aspects of prosthetic use (for example, grasping, holding, and releasing objects) are scored on a four-point rating scale with a maximum of 66 points attainable per task. A normed composite score between 0 and 100 can be obtained from the raw score via Rasch analysis, where a composite score above 57.2 is classified as "extremely capable." The SHAP consists of two parts: In the first, comprising 12 tasks, the participant grasps and relocates abstract-shaped objects (cylinders, tabs, spheres, etc.); in the second part, the participant performs 14 ADLs, such as turning a door handle, picking up coins, and moving containers. The execution times of all 26 tasks are used to calculate the global Index of Function, a normed score where 100 or higher is associated with normal hand function.

The EQ-5D-5L questionnaire assesses the quality of a patient's life within five categories: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. An EQ-5D score was obtained by norming the five responses ranging between "no problems" and "extreme problems" using the Danish value set (*52*), because there is no Swedish EQ-5D-5L value set available yet. The DASH measures physical functions based on 30 questions, each rated on a five-point Likert scale. The DASH score is a weighted sum of the questionnaire answers between 0 (no physical difficulties) and 100 (unable to perform physical functions with the arm/shoulder/hand). The Q-ULA assesses changes in and problems faced during prosthesis use. The Q-ULA score is a weighted average of 30 questions rated on a four-point Likert scale, where 0 means that the patient experiences no problems and 100 signifies extreme problems during prosthesis use and extreme reduction in quality of life. The Q-PLPT measures changes in phantom limb pain, stump pain, and how much the phantom limb pain interferes with daily life, each on a Likert scale between 0 (no pain/no interference) to 10 (extreme pain/full interference).

Throughout the duration of the study, the long-term electrical and functional stability of the implanted electrodes was periodically monitored by sending cathodic-first, rectangular, bipolar, asymmetric, charge-balanced, current-controlled pulses with known current and measuring the resulting voltage at each electrode via an oscilloscope, thereby calculating electrical impedance. In addition, sensory acuity to neural stimulation was documented via a manual psychometric procedure to identify stimulation thresholds, and perception stability was tracked via somatotopic maps drawn by the participant detailing where elicited sensations were felt on the phantom hand.

Supplementary Materials

This PDF file includes:
Supplementary Methods
Figs. S1 to S9
References (*53–61*)

Other Supplementary Material for this manuscript includes the following:
Movie S1

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