MEDICAL ROBOTS

Long-term implant of intramuscular sensors and nerve transfers for wireless control of robotic arms in above-elbow amputees

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Targeted muscle reinnervation (TMR) amplifies the electrical activity of nerves at the stump of amputees by redirecting them in remnant muscles above the amputation. The electrical activity of the reinnervated muscles can be used to extract natural control signals. Nonetheless, current control systems, mainly based on noninvasive muscle recordings, fail to provide accurate and reliable control over time. This is one of the major reasons for prosthetic abandonment. This prospective interventional study includes three unilateral above-elbow amputees and reports the long-term (2.5 years) implant of wireless myoelectric sensors in the reinnervation sites after TMR and their use for control of robotic arms in daily life. It therefore demonstrates the clinical viability of chronically implanted myoelectric interfaces that amplify nerve activity through TMR. The patients showed substantial functional improvements using the implanted system compared with control based on surface electrodes. The combination of TMR and chronically implanted sensors may drastically improve robotic limb replacement in above-elbow amputees.

INTRODUCTION

Robotic arm replacement in above-elbow amputees is challenging (*1*). Cumbersome control, poor and unreliable myosignal quality, as well as uncomfortable and mechanically unstable sockets determine the high rates of prosthesis abandonment reported in upper limb amputees (*2*, *3*). The success of targeted muscle reinnervation (TMR) (*4*) and the development of multiple degree-of-freedom (DOF) prosthetic devices have highlighted the limitations of the current man-machine interface (*5*, *6*). Prosthetic hardware, including multiarticulating hands, is more advanced than the available strategies to control these mechatronic devices (*7*).

Prosthetic arms are clinically controlled by surface electromyographic (EMG) signals recorded by electrodes placed on the skin overlying remnant muscles above the amputation (*8*, *9*). With this approach, only superficial muscles in the residual limb can be used for prosthetic control. Moreover, the surface EMG signal quality depends on loading of the prosthesis, causing soft tissue displacement, changing contact pressure, and movement between the skin surface and the electrodes, and is influenced by environmental conditions, skin texture, and perspiration. In addition, in TMR patients with up to six myoelectric sites, surface EMG recordings are susceptible to myoelectric cross-talk that reduces the number of independent control sites (*10*).

Despite the limitations of surface EMG as source of control signals, the increased number of EMG sites achieved by TMR surgery using selective nerve transfers enables prosthetic control in a more intuitive manner than with naturally innervated muscles alone (*11*). The functional benefit of TMR in above-elbow amputees compared with conventional myoelectric or body-powered prostheses has been previously shown (*1*, *4*, *12*). Yet, it is well known that prosthetic control is challenging in these patients, even after TMR (*1*). Therefore, the rate of abandonment of prostheses in above-elbow amputees is particularly high.

To improve the man-machine interface in above-elbow amputees, a direct skeletal attachment penetrating the skin has been proposed (*10*, *13*). With this attachment, wires can pass through the percutaneous port of an osseointegrated system (*10*). Although some of these solutions are promising, percutaneous interfaces disturb the skin barrier, resulting in the risk of superficial and deep infections as well as wire breakage, unstable connectors, and possible subsequent need for surgical intervention (*10*, *14*).

Here, we establish a man-machine interface for robotic arm control in above-elbow amputees based on a wireless implantable myoelectric sensor (IMES) system originally developed by Weir and colleagues (*15*) and then by the Alfred Mann Foundation (California, USA) (*16*). IMESs are implants with a ceramic housing of cylindrical shape, 16-mm long and 2.5 mm in diameter, and metal end caps acting as electrodes for recording intramuscular EMG (*16*). The IMESs wirelessly transmit EMG data to the prosthesis and are powered by inductive coupling using an external coil integrated into the prosthetic socket. Despite the potential high impact of IMES for man-machine interfacing in robotics, so far, there has been only one case report of their use in humans (*16*). This previous study reported on the use of IMES in a below-elbow amputee using naturally innervated EMG signals (*16*). In this study, we present the long-term implant of IMES in conjunction with TMR and in above-elbow amputees, for whom recovery of function is much more challenging than in below-elbow amputees. The aim was therefore to evaluate whether long-term implants of intramuscular sensors can pick up and transmit neural information after selective nerve transfers for establishing natural prosthetic control in the limited space available in above-elbow amputees.

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We provide clinical outcome results over a period of >2.5 years for an implanted wireless system after selective nerve transfers in a case series of three above-elbow amputees.

RESULTS

IMES and TMR surgery

In the three patients, implantation of the IMES combined with TMR surgery was successfully performed 1.03 ± 0.50 years after the amputation. Depending on the number of available target muscles, five to six IMESs were used.

For TMR surgery, our standard nerve transfer matrix (Table 1) was used in all three patients (*5*). Because of the short length of the residual stump, the brachioradialis muscle was not present in one of the patients (patient II), and thus, only five instead of six individual myosignals could be established. The nerve coaptation was performed between 1.5 and 2.5 cm from the epimysium. An IMES was implanted in each targeted muscle as well as available natively innervated muscles. Therefore, six IMESs were implanted in patients I and III and five IMESs were implanted in patient II. In this way, patients I and III had a distinct muscle with an implanted sensor for each prosthetic function (Table 1). Patient II distinguished between pronation and supination using low or high contraction force of the brachialis muscle.

The IMESs were placed intramuscularly near the motor entry point of the targeted muscle. At the end of the surgery, a communication test verified proper function of each sensor. The position of each IMES was evaluated with x-rays in the anterior/posterior and lateral axis. Immediate and 1-year postoperative x-ray showed no migration or axial rotation of the sensors (Fig. 1, A and B).

Myosignals

During the time of reinnervation of the targeted muscles, the patients were able to use the natively innervated long head of the biceps and the long/medial head of the triceps as myosignals for prosthetic control. Once the postoperative soft tissue swelling had resolved and stump circumference measures were stable, patients were fitted with a telemetry test socket using the two natively innervated EMG signals. The circumference was measured at the midway between the axillary fold and the distal stump end. Preoperatively, the three patients showed a mean circumference of 31.5 cm. Eight weeks after surgery, the soft tissue swelling had resolved, and the stump circumference measures (in mean, 32.67 cm) had almost returned to preoperative levels. These measures were stable afterward, except from patient I, where body weight changes led to stump volume changes. Over time, as the new signal sites emerged, they were progressively integrated into the control algorithm. The final prosthetic fitting with small socket adjustments was completed at 20, 12, and 10 months postoperatively in the three patients, respectively. The longer time in patient I was due to weight changes of the patient and resulting stump volume changes. Because of this socket issue, patient I missed two of five scheduled outcome measurements.

The first TMR myosignals were detected via IMES 3 months postoperatively, whereas surface EMG electrodes provided useful signals only after 6 months. Between 3 and 4 months postoperatively, all newly established myosignals could be detected in all patients with the IMES. At 5 months, all implanted sensors could actively be integrated for prosthetic control. Prosthetic control was based on the direct association between myosignals and prosthetic DOF (direct control). The gains of the IMES were adjusted during the first 6 months only. All other adjustments (threshold values and speed of prosthetic movement) were performed during the prosthetic fitting and never retuned. The procedure used for optimizing control was the same regardless of technology used for EMG recording, IMES, or surface electrodes.

The rehabilitation started immediately after surgery with training of posture and mirror therapy. As soon as the first new myosignals were detected, a previously described rehabilitation program was initiated to improve control of the individual TMR signals (*17*).

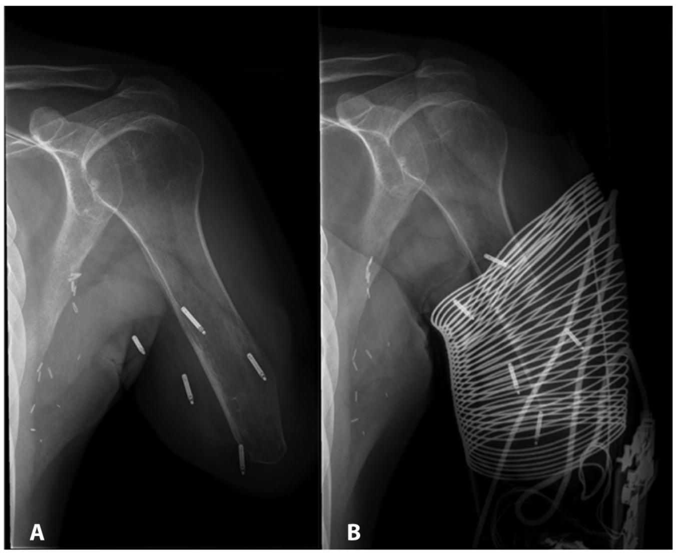

Fig. 1. Implants and magnetic coil. (**A**) X-ray of patient II with five IMES sensors implanted. (B) X-ray of patient II with telemetry socket (magnetic coil laminated within the socket) and the prosthetic device.

Table 1. TMR nerve transfer matrix for the above-elbow level of amputation.

Targeted muscles	Nerves	Prosthetic function	Innervation
M. biceps caput longum	N. musculocutaneous	Elbow flexion	Original
M. biceps caput breve	N. ulnaris	Hand close	Transferred
M. brachialis	N. medianus	Pronation	Transferred
M. triceps caput longum/mediale	N. radialis	Elbow extension	Original
M. triceps caput laterale	Split ramus prof. N. radialis	Hand open	Transferred
M. brachioradialis	Split ramus prof. N. radialis	Supination	Transferred

Table 2. Functional outcome using SHAP, BBT, CPRT, and AC. NA, not available.

Patient	SHAP			BBT			CPRT			AC	
	Pre	IMES	Surface	Pre	IMES	Surface	Pre	IMES	Surface	IMES	Surface
1	39	45	27	12	12	11	86.98	26	43.33	2.83	2.33
2	36	44	23	9	10	3.33	49.38	42.06	NA	2.95	2.22
3	24	52	45	2	15	6.67	117.00	14.67	37.58	3	2.33
Mean	33.00	47.00	31.67	7.67	12.33	7.00	84.45	27.58	40.46	2.93	2.29
SD	7.94	4.32	11.72	5.13	2.52	3.85	33.88	13.76	4.07	0.09	0.06

Table 3. Patient demographics.

Patient	Age at amputation	Side of amputation	Dominant hand before amputation	Years from amputation to surgery	Follow-up from surgery (years)	Time from surgery to evaluation (years)	Nature of loss	Number of IMES implanted
1	15.92	Right	Right	1.08	3.00	3.00	Traffic accident	6
2	31.42	Left	Right	1.50	2.75	2.00	Motorcycle accident	5
3	47.17	Right	Right	0.50	2.50	1.92	Machine accident	6
	31.50			1.03	2.75	2.31		
	15.63			0.50	0.25	0.60		

This process is essential for any patient having received selective nerve transfers (*17*). The three patients received 15, 22, and 28 hours of specific TMR rehabilitation within the complete follow-up process after surgery. At the last follow-up visit at 3, 2.75, and 2.5 years postoperatively, all IMES showed reliable communication. In addition, no events of disconnection between the sensors and the prosthetic device were reported by the patients or were identified during functional assessments.

Functional outcomes

The most effective way of testing man-machine interfacing systems for robotic limb control is through clinical tests that provide direct functional measures of outcome (*18*). We therefore mainly focused on clinical functional tests for assessing the performance of the system and its clinical impact. The functional outcome scores are summarized in Table 2. Final functional outcome measurements took place 2.31 ± 0.60 years after TMR and IMES surgery (Table 3 and movie S1). These evaluations were performed on two consecutive days. In the first day, the telemetric IMES prosthesis was used, whereas in the second day the surface EMG control was tested, as a reference. In addition, all patients were tested preoperatively with their standard two-signal surface EMG prosthetic device, and these results were used as baseline measurements. The patients showed improvements in Southampton Hand Assessment Procedure (SHAP) of 15.4, 22.2, and 116.7% using TMR signals and implantable electrodes compared with the baseline measurements. However, patients I and II showed declines in performance of 30.8 and 36.1% using TMR signals and surface electrodes compared with the baselines (surface electrodes and no TMR), whereas patient III showed an improvement of 187.5% with TMR and surface electrodes. With respect to baselines, the times needed to complete the Clothespin-Relocation Test (CPRT) decreased by 70.1, 8.3, and 87.4% with TMR and IMES, but only by 50.2 and 67.9% with TMR and surface electrodes, with respect to baselines. Patient II could not perform the test when using TMR and surface electrodes. The numbers of transferred blocks in the Box and Blocks Test (BBT) increased in patients II and III by 11.1 and 650% but decreased by 5.6% in patient I using TMR and IMES compared with baselines. Using TMR and surface electrodes, the transferred blocks decreased by 8.3 and 63.0% in patients I and II and increased by 233.5% in patient III compared with baselines. In addition, using surface electrodes, the accuracy test (AC) decreased by 17.3, 24.7, and 22.3% compared with the use of TMR signals with implanted electrodes (movie S2). During the rehabilitation process, longitudinal assessments were performed on the patients. Figure 2 documents the learning curve in SHAP, CPRT, BBT, and AC within this time.

DISCUSSION

The use of implantable intramuscular sensors enables the extraction and transmission of neural signals after selective nerve transfers in above-elbow amputees, resulting in intuitive and dexterous control of robotic arms. Because of the intramuscular placement, signals are independent of loading and position of the prostheses. For the same reason, these signals can be detected early after nerve transfer surgery with significant decrease in rehabilitation time. Here, we have reported on the long-term use of an implanted wireless system for dexterous and intuitive prosthetic control in three above-elbow amputees after TMR surgery. The results showed improvement in prosthetic function using the combination of implantable electrodes together with nerve transfers with respect to the current clinical state of the art. As a necessary first step in showing the potential of the muscle implanted technology, the study was limited by the number of participants

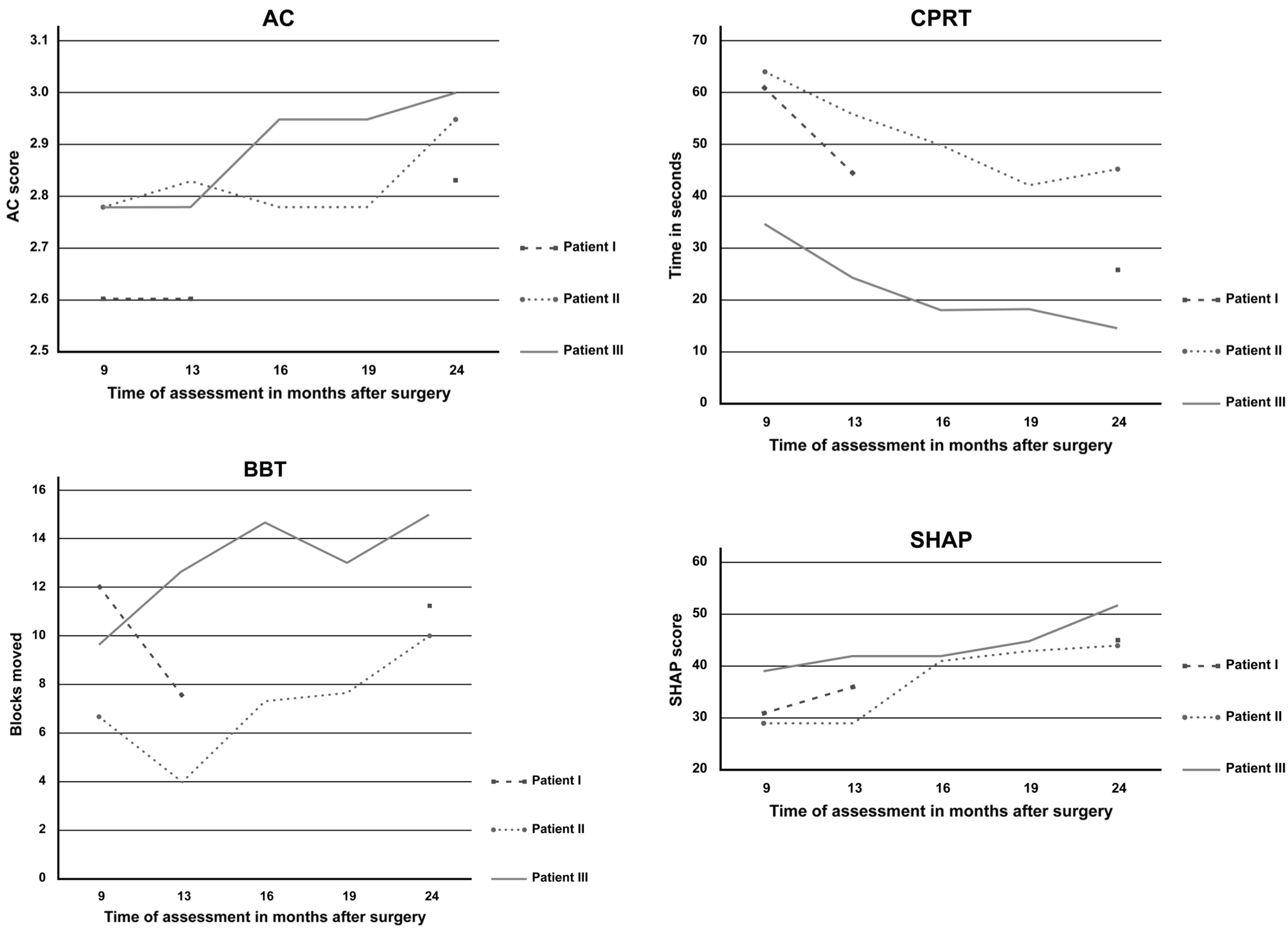

Fig. 2. Learning curves for SHAP, CPRT, BBT, and AC during the rehabilitation when using IMES for control.

and sessions, which hindered the possibility of statistical analyses and provided descriptive results. This limitation is common to previous studies testing implantable systems. Nonetheless, the clinical impact of these results is evident and paves the way to further research on larger clinical samples.

As opposed to below-elbow amputees, in above-elbow amputees, there are no naturally innervated muscles for the control of hand function. However, in these patients, the neural signals for hand and arm function are still available and thus can be manifested within the targeted muscles after nerve transfers. The challenge is the limited space for electrode location and signal cross-talk. Therefore, standard surface electrodes provide poor control signals for prosthetic control in this patient population (*10*). Moreover, in classic myocontrol by surface electrodes, and especially in TMR patients with multiple signal sites, finding the best location for surface EMG sensors is difficult and time consuming. Incorrect placement of the surface electrodes substantially influences the control performance. In addition, contact loss due to limb movement or loading of the socket can result in malfunction of the robotic device. As a consequence, threshold values are used to discriminate between volitional EMG signals and background noise and artefacts. The use of a threshold determines the need for relatively strong muscular contractions, which limits the accuracy in proportional myoelectric control and may result in fatigue (*10*, *19*). The fact that two of three patients within this study showed higher SHAP scores using conventional two-signal control preoperatively compared with TMR and surface electrodes postoperatively indicates that a greater number of myosignals are only useful if signal recording and transmission are accurate and precise. In most of the tasks of the SHAP, patients only need to control one DOF; therefore, they do not need to change control between the different prosthetic joints. The advantage of TMR is more noticeable in the CPRT, where all patients improved after TMR surgery. In BBT, the patients did not use the prosthetic elbow most of the time at the baseline assessment. Thus, the improvement after TMR was limited. There was a positive learning curve in the different assessments showing the success of rehabilitation after TMR surgery using telemetric signals. Still, at the end of the rehabilitation process, functional outcomes showed remarkable improvements using IMES compared with surface electrodes tested on two consecutive days.

The housing of the IMES sensor was previously used in an implantable microstimulation device (the BION) for poststroke hemiplegic patients with shoulder subluxation (*20*). The BIONs showed no migration over long periods of time and were well tolerated (*21*). This was also confirmed in this study with a follow-up of 2.75 ± 0.25 years.

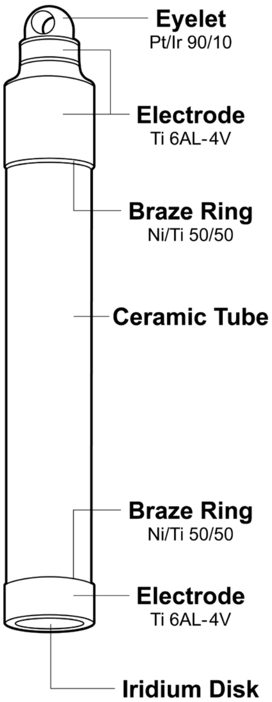

Fig. 3. Schematic drawing of the IMES sensor.

Continuous use of the prosthetic device requires constant signal transmission, resulting in increased power support (*7*). To optimize energy consumption, the IMES sensors were placed close to each other in the longitudinal axis to decrease the width of the coil. Because the IMESs were implanted directly at the reinnervation sites, they recorded EMG signals with high sensitivity immediately after reinnervation. The nerve coaptation was performed between 1.5 and 2.5 cm from the epimysium, and the first myosignals were detected already at 3 months after surgery. The early signal detection allowed starting the rehabilitation program earlier and therefore reducing the time from surgery to fully functional control of the prosthesis. Whereas the time from surgery to the final fitting using surface electrodes is about 1 year (*5*), prosthetic fitting and control of three DOFs was achieved after only 5 ± 1 months in the three patients of this study.

The implanted sensors have originally been designed to be placed using an ultrasound-guided minimal invasive technique. However, because the TMR surgery changes the muscle and nerve anatomy and all relevant structures are identified during this procedure, in this study, the implantation was performed during the TMR surgery. Thus, the IMES could be placed intramuscularly near the motor entry point of the targeted muscle. This would also be valid for regenerative peripheral nerve interfaces, where the information of single-nerve fascicles could potentially be used for prosthetic control (*22*).

Recent control systems for TMR patients based on pattern recognition algorithms showed significantly improved performance with respect to direct control and have the potential to be further improved (*23*). Pattern recognition is mostly needed because of unreliable control with surface EMG. In patients with IMES, however, the signal quality from the implanted sensors is superior to that from surface systems and allows for direct simultaneous and proportional control without retraining (*23*, *24*). The use of implantable sensors will have future impact on the surgical procedure of TMR, because these sensors can record from deep and small muscles that can become new targets for nerve transfers.

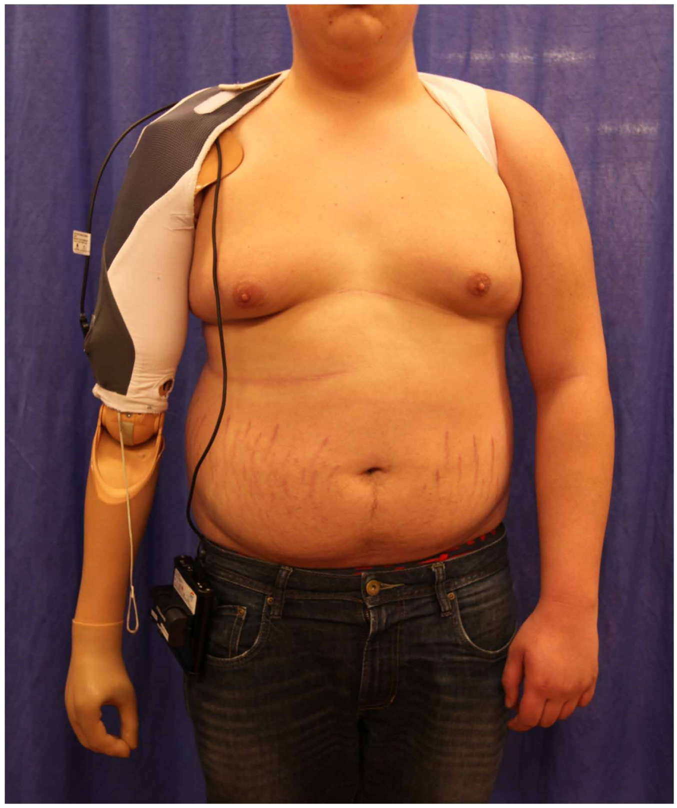

Fig. 4. Patient I wearing the IMES system.

Implanted sensors in muscles have been used for prosthetic control in chronic applications by wired transmission through the percutaneous metal implant of an osseointegrated prosthesis (*10*). The proposed combination of TMR and IMES does not include a percutaneous interface, making it a safe procedure without the constant risk of infection. Moreover, an alternative approach to extracting neural control signals is to establish a direct nerve interface (*25*). However, wireless and stable transmission of nerve signals for control has not been achieved yet. Moreover, reinnervation of severed nerves is necessary in most cases to remove neuromas (*10*), and once a target muscle is innervated, the muscle signals provide information on the nerve activity with greater signal-to-noise ratio and stability than a nerve interface. Last, high-density surface EMG systems have been proposed to decode nerve activity from reinnervated muscles (*26*). These systems have the potential to increase the information transfer for the man-machine interface (*27*) but have the same limitations as classic bipolar surface EMG electrodes in terms of robustness to change in shape of the soft tissue with respect to the underlying muscles. An implanted version of high-density EMG systems may provide in the future a further improvement in prosthesis control (*28*).

The current IMES system is not compatible with metal implants at the stump region. Thus, surgical procedures such as angulation osteotomy or osseointegration cannot be currently combined with the implantable system used in this study. In addition, because the coil has to be placed circumferentially around the stump, short above-elbow amputations or shoulder disarticulations cannot be treated with the current system. Furthermore, currently, no more than six IMESs, corresponding to direct control of three DOFs of the prosthetic device, can be used concurrently, with low transmission rate

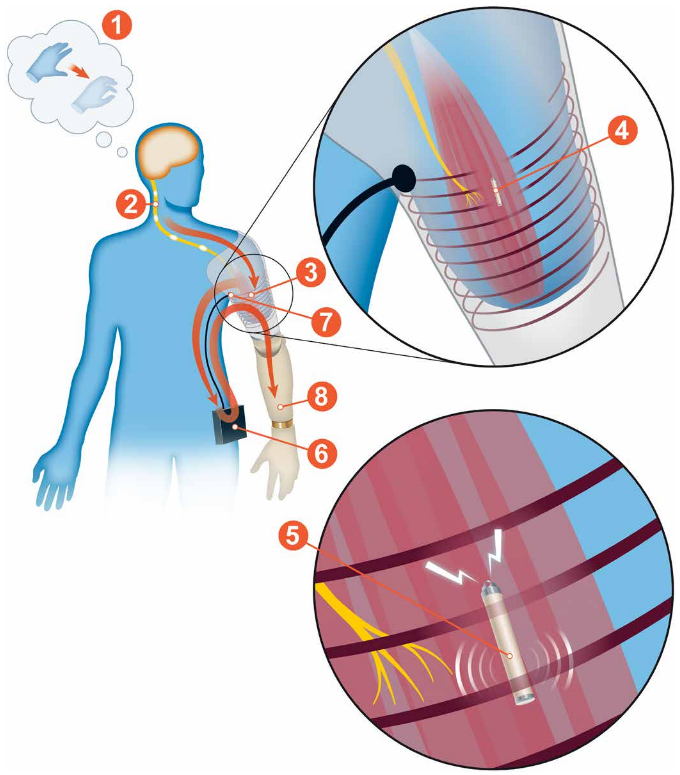

Fig. 5. Schematic signal pathway. To perform a specific motion of the prosthetic arm, the patient is thinking of this movement (1). This creates an impulse along the responsible nerve (2) and leads to a contraction of a specific muscle belly (3). The produced EMG signal is then recorded, rectified, and integrated within the IMES sensor (4). Via telemetry using a magnetic coil around the stump, these signals are transferred to the control unit, and forward telemetry is used to transmit power and configuration settings to the sensors (5). Within the belt-worn control unit, the preprocessed rectified EMG data (6) of the IMES are sent to the prosthesis (7), and the desired movement of the prosthetic device is performed (8).

that imposes the transmission of rectified and averaged EMG rather than the raw signals. This limits the use of the current system for future pattern recognition technologies that may require feature extraction from raw EMG signals. Thus, this study focused on the clinical prosthetic performance of the patients. In addition, because the sensors are passive devices, it is currently not possible to use them for stimulating to enable sensory feedback.

The combination of an implanted wireless system with TMR surgery, reported here for long-term clinical applications, represents a major milestone in prosthetic control. It eliminates some of the major reasons for prosthetic abandonment, such as cumbersome control and unreliable signal uptake. Moreover, IMES placement can be done at the time of the TMR surgery, with no need for an additional intervention and can provide excellent results after brief rehabilitation periods, as shown in this study. Yet, clinical challenges remain, such as the mechanical attachment of the prosthetic device or the establishment of a sensory feedback, for which current solutions are not yet optimal (*10*, *29*–*32*).

MATERIALS AND METHODS

Study design

Three patients were implanted with IMES while undergoing routine TMR surgery to demonstrate functional benefits and stability over time of intramuscular recorded EMG for prosthetic control. This prospective, self-controlled, nonrandomized interventional study was approved by the Austrian Agency for Health and Food Safety (approval no. TH-IMES 040714) and the local institutional review board (EK-number 1320/2014) as well as registered at clinicaltrials.gov (NCT03644394). All three patients gave written informed consent to take part in this study. Surgery in all three cases was performed by the senior author (O.C.A.).

The inclusion criteria were unilateral, above-elbow limb loss of half or greater residual upper arm length as determined by the contralateral side, age 16 or older, who were current users of a myoelectric prosthesis and qualified for TMR surgery. In addition, the patients had to be within the governmental insurance system and live within 3 hours from the study center. Potential patients were excluded because of an active implant (e.g., pacemaker, implanted cardiac defibrillator, neurostimulator, and drug infusion device), any metal implants located within the residual upper limb (e.g., screws, plates, and nails), or visual impairments or if they did not qualify for TMR surgery (*1*, *5*).

Three consecutive patients who met all inclusion criteria were referred from a local prosthetic technician. They suffered a traumatic above-elbow amputation at the ages of 16, 31, and 47 years. All were male. Limb loss of the dominant right arm ($n = 2$) and nondominant left arm ($n = 1$) was due to high-velocity traffic accidents ($n = 2$) or a work-related injury with a hydraulic press ($n = 1$) (Table 3).

Materials

Each IMES (Alfred Mann Foundation, California, USA) is about 2.5 mm in diameter and 16-mm long, can be inserted into a muscle during the TMR surgery, and acts as an independent differential amplifier consisting of custom electronics housed within a biocompatible, hermetically sealed ceramic cylinder with titanium end caps (*16*, *33*). The end caps serve as electrodes for picking up EMG activity during muscle contraction. Each sensor detects EMG signals in a frequency band between 4.4 and 2200 Hz (Fig. 3). The signals are then rectified and integrated (10-Hz cutoff frequency) within the IMES, and the resulting EMG envelope is digitized at a sampling rate of 72 samples per second. The latency from detection of the EMG signal to telemetry controller output is 100 ms. Reverse telemetry (via a coil around the arm) is used to transfer data from the implanted sensor, and forward telemetry is used to transmit power and configuration settings to the sensors. The coil and associated electronics are housed within the socket of the prosthesis. A control system, the prosthetic control interface that sends the preprocessed rectified data of the IMES associated with muscle contraction as inputs of the prosthesis, is housed in a belt-worn, battery-powered device. A cable attaches the control unit to the prosthetic socket. One IMES is implanted into each targeted muscle during the TMR surgery and used to control one function of the prosthetic arm. Therefore, two IMESs are needed for each DOF (Figs. 4 and 5).

All three patients of this study were fitted with DynamicArm Plus, Electric Wrist Rotator, and SensorHand Speed (Otto Bock HealthCare GmbH, Germany), resulting in three DOFs (elbow, wrist, and hand). This prosthetic arm was used on a daily basis by the three patients during the entire study period using the signals from the implanted electrodes for control.

TMR and implantation surgery

The implantation of the IMES was performed under general anesthesia during TMR surgery. Through a medial approach, the median, ulnar, and musculocutaneous nerve were prepared and dissected. The motor branches to the medial and lateral head of the biceps and to the brachial muscle were identified. Dissection and separation of the different branches are important, and stimulation of the different branches should only provoke twitches in the targeted muscles selectively. Once the target muscles with their branches were identified, the short head of the biceps muscle was detached from its origin at the coracoid process to displace it to the medial distal aspect of the stump and separate it clearly from the long head of the biceps. The donor nerves have to be neurotomized at least to a level of palpable healthy fascicles. Through a second incision on the radial aspect of the above-elbow stump, blunt dissection between the triceps heads was performed to displace the lateral head and further dissect its muscle branch and the distal radial nerve until it ends in the distal neuroma. In patients I and III, with long stumps and the presence of the brachioradialis muscle, the distal radial nerve could be split along the fascicles in two parts, one to reinnervate the lateral head of the triceps and one to reinnervate the brachioradialis muscle to achieve separate signals for hand open and supination of the prosthetic device. The motor branches of the targeted muscles were transected close to the muscle to achieve a short regeneration time. The proximal part of the motor branches was transected a few centimeters back and buried deep to prevent it from reinnervating the targeted muscles. All nerve transfers were performed under loupe magnification in an end-to-end fashion using 8-0 or 9-0 ethilon sutures. The distal neuromas were not excised, because this would have implied additional dissection in regions of no interest. The nerve transfers and the corresponding prosthetic functions are reported in Table 1.

After the nerve transfers had been performed, a small incision (about 5 mm) was made into the epimysium and a probe was inserted. A cannulated dilator was advanced over the probe to reach the target implant position within the muscle. The implant depth was 46.25 ± 6.19 mm from the epimysium. The dilator and probe were then removed, leaving the sheath in place. A piece of absorbable suture was threaded through the eyelet end of the IMES to pull the sensor out in case of inappropriate placement. The IMES was then inserted into the muscle with a trocar. One resorbable suture was made to close the epimysium. The IMES should be aligned in parallel to the axis of the humerus for efficient signal and energy transmission between the coil and the IMES. However, a deviation of up to 45° to the humerus can be tolerated and does not limit signal transmission. Immediately after wound closure, a communication test with a test coil placed over the residual limb was performed to determine proper function of all implanted sensors.

Functional outcome measurements

Global upper extremity function was evaluated using SHAP (*34*), CPRT, (*4*), and BBT (*35*), which monitor hand and extremity function closely related to activities of daily living. The SHAP has been validated for assessment of pathological and prosthetic hand function, where normal hand function is regarded as equal to or above 100 points (*34*). For the CPRT, the time is recorded as the patient moves three clothespins from a horizontal to a vertical bar. The mean of three repetitions is calculated. The BBT measures unilateral gross manual dexterity. It is made up of a wooden box divided into two compartments, one filled with 100 blocks. The BBT score is equal to the number of cubes transferred from one compartment to another in 1 min (*35*). To evaluate the accuracy of the intended movement/myosignal, we asked the patient to execute a series of tasks with the activation of the three DOFs separately. Each task was repeated three times (*16*). The patient scored three points when the intended movement was observed without any additional unintended movement, two points when additional movements were observed, and only one point when unintended movements were observed but not the intended one. Therefore, the maximum score was three.

The tests used for evaluating performance of the system have been selected because they provide a direct clinical information on functional gains. Other offline tests or tests in virtual reality environments were excluded because they have been shown to be poorly associated to the recovery of function (*18*). The results of the study provide a clinical evaluation of muscle implants for robotic arm control and indicate achievements superior to the current clinical state of the art.

Before IMES and TMR surgery, the patients were tested with their prosthetic device using a two-signal control with biceps and triceps and standard surface EMG electrodes. Nine months after the final fitting of the telemetry socket, a standard prosthesis with surface electrodes using the TMR signals was also created for comparison with the control system based on IMES. At this time, prosthetic functional outcome was evaluated in the three patients using both surface and implantable electrodes.

All outcome measures (SHAP, CPRT, BBT, and AC) were assessed by the same experienced physical therapist for all participants. The different outcomes measures were performed within one visit to the clinical laboratory. Assessment started with the SHAP, because this is the most time-consuming test, and was continued with the other measures after a break of 15 to 30 min. In case of fatigue, the patients had the opportunity to take a break at any time during the entire assessments. A randomization of the measurements was not performed.

SUPPLEMENTARY MATERIALS

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Movie S1. SHAP and CPRT of patient II.

Movie S2. Accuracy test of patient III with six myosignals and surface electrodes compared with implanted electrodes.

REFERENCES AND NOTES

1. G. A. Dumanian, J. H. Ko, K. D. O'Shaughnessy, P. S. Kim, C. J. Wilson, T. A. Kuiken, Targeted reinnervation for transhumeral amputees: Current surgical technique and update on results. *Plast. Reconstr. Surg.* **124**, 863–869 (2009).
2. T. W. Wright, A. D. Hagen, M. B. Wood, Prosthetic usage in major upper extremity amputations. *J. Hand Surg. Am.* **20**, 619–622 (1995).
3. D. Datta, J. Kingston, J. Ronald, Myoelectric prostheses for below-elbow amputees: The Trent experience. *Int. Disabil. Stud.* **11**, 167–170 (1989).
4. T. A. Kuiken, G. A. Dumanian, R. D. Lipschutz, L. A. Miller, K. A. Stubblefield, The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee. *Prosthet. Orthot. Int.* **28**, 245–253 (2004).
5. S. Salminger, A. Sturma, M. Herceg, O. Riedl, K. Bergmeister, O. C. Aszmann, Prosthetic reconstruction in high amputations of the upper extremity. *Orthopade* **44**, 413–418 (2015).
6. S. M. Tintle, M. F. Baechler, G. P. Nanos, J. A. Forsberg, B. K. Potter, Traumatic and trauma-related amputations: Part II: Upper extremity and future directions. *J. Bone Joint Surg. Am.* **92**, 2934–2945 (2010).
7. M. Ortiz-Catalan, R. Brånemark, B. Håkansson, J. Delbeke, On the viability of implantable electrodes for the natural control of artificial limbs: Review and discussion. *Biomed. Eng. Online* **11**, 33 (2012).
8. A. D. Roche, H. Rehbaum, D. Farina, O. C. Aszmann, Prosthetic myoelectric control strategies: A clinical perspective. *Curr. Surg. Rep.* **2**, 44 (2014).
9. D. Farina, O. Aszmann, Bionic limbs: Clinical reality and academic promises. *Sci. Transl. Med.* **6**, 257ps12 (2014).
10. M. Ortiz-Catalan, B. Håkansson, R. Brånemark, An osseointegrated human-machine gateway for long-term sensory feedback and motor control of artificial limbs. *Sci. Transl. Med.* **6**, 257re6 (2014).
11. O. C. Aszmann, H. Dietl, M. Frey, Selective nerve transfers to improve the control of myoelectrical arm prostheses. *Handchir. Mikrochir. Plast. Chir.* **40**, 60–65 (2008).

12. K. D. O'Shaughnessy, G. Dumanian, R. Lipschutz, L. Miller, K. Stubblefield, T. Kuiken, Targeted reinnervation to improve prosthesis control in transhumeral Amputees: A report of three cases. *J. Bone Joint Surg. Am.* **90**, 393–400 (2008).
13. J. A. Hoffer, G. E. Loeb, Implantable electrical and mechanical interfaces with nerve and muscle. *Ann. Biomed. Eng.* **8**, 351–360 (1980).
14. J. Tillander, K. Hagberg, Ö. Berlin, L. Hagberg, R. Brånemark, Osteomyelitis risk in patients with transfemoral amputations treated with osseointegration prostheses. *Clin. Orthop. Relat. Res.* **475**, 3100–3108 (2017).
15. R. F. Weir, P. R. Troyk, G. Demichele, D. Kerns, Technical details of the implantable myoelectric sensor (IMES) system for multifunction prosthesis control. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **7**, 7337–7340 (2005).
16. P. F. Pasquina, M. Evangelista, A. J. Carvalho, J. Lockhart, S. Griffin, G. Nanos, P. McKay, M. Hansen, D. Ipsen, J. Vandersea, J. Butkus, M. Miller, I. Murphy, D. Hankin, First-in-man demonstration of a fully implanted myoelectric sensors system to control an advanced electromechanical prosthetic hand. *J. Neurosci. Methods* **244**, 85–93 (2015).
17. A. Sturma, M. Herceg, B. Bischof, V. Fialka-Moser, O. C. Aszmann, Rehabilitation following targeted muscle reinnervation in amputees, in *Replace, Repair, Restore, Relieve—Bridging Clinical and Engineering Solutions in Neurorehabilitation*, W. Jensen, O. K. Andersen, M. Akay, Eds. (Springer, 2014), pp. 169–177.
18. I. Vujaklija, A. D. Roche, T. Hasenoehrl, A. Sturma, S. Amsuess, D. Farina, O. C. Aszmann, Translating research on myoelectric control into clinics—Are the performance assessment methods adequate? *Front. Neurorobot.* **11**, 7 (2017).
19. C. Almström, P. Herberts, L. Körner, Experience with Swedish multifunctional prosthetic hands controlled by pattern recognition of multiple myoelectric signals. *Int. Orthop.* **5**, 15–21 (1981).
20. A.-C. D. Salter, S. D. Bagg, J. L. Creasy, C. Romano, D. Romano, F. J. R. Richmond, G. E. Loeb, First clinical experience with BION implants for therapeutic electrical stimulation. *Neuromodulation* **7**, 38–47 (2004).
21. R. Davis, O. Sparrow, G. Cosendai, J. H. Burridge, C. Wulff, R. Turk, J. Schulman, Poststroke upper-limb rehabilitation using 5 to 7 inserted microstimulators: Implant procedure, safety, and efficacy for restoration of function. *Arch. Phys. Med. Rehabil.* **89**, 1907–1912 (2008).
22. M. G. Urbanchek, T. A. Kung, C. M. Frost, D. C. Martin, L. M. Larkin, A. Wollstein, P. S. Cederna, Development of a regenerative peripheral nerve interface for control of a neuroprosthetic limb. *Biomed. Res. Int.* **2016**, 5726730 (2016).
23. D. C. Tkach, A. J. Young, L. H. Smith, E. J. Rouse, L. J. Hargrove, Real-time and offline performance of pattern recognition myoelectric control using a generic electrode grid with targeted muscle reinnervation patients. *IEEE Trans. Neural Syst. Rehabil. Eng.* **22**, 727–734 (2014).
24. L. J. Hargrove, B. A. Lock, A. M. Simon, Pattern recognition control outperforms conventional myoelectric control in upper limb patients with targeted muscle reinnervation. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **2013**, 1599–1602 (2013).
25. S. Micera, J. Carpaneto, S. Raspopovic, Control of hand prostheses using peripheral information. *IEEE Rev. Biomed. Eng.* **3**, 48–68 (2010).
26. D. Farina, H. Rehbaum, A. Holobar, I. Vujaklija, N. Jiang, C. Hofer, S. Salminger, H.-W. van Vliet, O. C. Aszmann, Noninvasive, accurate assessment of the behavior of representative populations of motor units in targeted reinnervated muscles. *IEEE Trans. Neural Syst. Rehabil. Eng.* **22**, 810–819 (2014).
27. T. Kapelner, N. Jiang, A. Holobar, I. Vujaklija, A. D. Roche, D. Farina, O. C. Aszmann, Motor unit characteristics after targeted muscle reinnervation. *PLOS ONE* **11**, e0149772 (2016).
28. K. D. Bergmeister, I. Vujaklija, S. Muceli, A. Sturma, L. A. Hruby, C. Prahm, O. Riedl, S. Salminger, K. Manzano-Szalai, M. Aman, M.-F. Russold, C. Hofer, J. Principe, D. Farina, O. C. Aszmann, Broadband prosthetic interfaces: Combining nerve transfers and implantable multichannel EMG technology to decode spinal motor neuron activity. *Front. Neurosci.* **11**, 421 (2017).
29. S. Salminger, A. Gradischar, R. Skiera, A. D. Roche, A. Sturma, C. Hofer, O. C. Aszmann, Attachment of upper arm prostheses with a subcutaneous osseointegrated implant in transhumeral amputees. *Prosth. Orth. Int.* **42**, 93–100 (2016).
30. P. Svensson, U. Wijk, A. Björkman, C. Antfolk, A review of invasive and non-invasive sensory feedback in upper limb prostheses. *Expert Rev. Med. Devices* **14**, 439–447 (2017).
31. D. W. Tan, M. A. Schiefer, M. W. Keith, J. R. Anderson, J. Tyler, D. J. Tyler, A neural interface provides long-term stable natural touch perception. *Sci. Transl. Med.* **6**, 257ra138 (2014).
32. S. Raspopovic, M. Capogrosso, F. M. Petrini, M. Bonizzato, J. Rigosa, G. di Pino, J. Carpaneto, M. Controzzi, T. Boretius, E. Fernandez, G. Granata, C. M. Oddo, L. Citi, A. L. Ciancio, C. Cipriani, M. C. Carrozza, W. Jensen, E. Guglielmelli, T. Stieglitz, P. M. Rossini, S. Micera, Restoring natural sensory feedback in real-time bidirectional hand prostheses. *Sci. Transl. Med.* **6**, 222ra19 (2014).
33. R. F. Weir, P. R. Troyk, G. A. DeMichele, D. A. Kerns, J. F. Schorsch, H. Maas, Implantable myoelectric sensors (IMESs) for intramuscular electromyogram recording. *IEEE Trans. Biomed. Eng.* **56**, 159–171 (2009).
34. P. J. Kyberd, A. Murgia, M. Gasson, T. Tjerks, C. Metcalf, P. H. Chappell, K. Warwick, S. E. M. Lawson, T. Barnhill, Case studies to demonstrate the range of applications of the Southampton Hand Assessment Procedure. *Br. J. Occup. Ther.* **72**, 212–218 (2009).
35. V. Mathiowetz, G. Volland, N. Kashman, K. Weber, Adult norms for the Box and Block Test of manual dexterity. *Am. J. Occup. Ther.* **39**, 386–391 (1985).

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