Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study

Todd A Kuiken, Laura A Miller, Robert D Lipschutz, Blair A Lock, Kathy Stubblefield, Paul D Marasco, Ping Zhou, Gregory A Dumanian

Summary

Background The function of current artificial arms is limited by inadequate control methods. We developed a technique that used nerve transfers to muscle to develop new electromyogram control signals and nerve transfers to skin, to provide a pathway for cutaneous sensory feedback to the missing hand.

Methods We did targeted reinnervation surgery on a woman with a left arm amputation at the humeral neck. The ulnar, median, musculocutaneous, and distal radial nerves were transferred to separate segments of her pectoral and serratus muscles. Two sensory nerves were cut and the distal ends were anastomosed to the ulnar and median nerves. After full recovery the patient was fit with a new prosthesis using the additional targeted muscle reinnervation sites. Functional testing was done and sensation in the reinnervated skin was quantified.

Findings The patient described the control as intuitive; she thought about using her hand or elbow and the prosthesis responded appropriately. Functional testing showed substantial improvement: mean scores in the blocks and box test increased from 4.0 (SD 1.0) with the conventional prosthesis to 15.6 (1.5) with the new prosthesis. Assessment of Motor and Process Skills test scores improved from 0.30 to 1.98 for motor skills and from 0.90 to 1.98 for process skills. The denervated anterior chest skin was reinnervated by both the ulnar and median nerves; the patient felt that her hand was being touched when this chest skin was touched, with near-normal thresholds in all sensory modalities.

Interpretation Targeted reinnervation improved prosthetic function and ease of use in this patient. Targeted sensory reinnervation provides a potential pathway for meaningful sensory feedback.

Introduction

Improving the function of artificial arms remains a challenge, especially for amputations at the elbow or higher, where the disability is greatest. Motorised hooks, hands, wrists, and elbows are available, but existing methods of control are inadequate. Currently, most powered artificial limbs are controlled with the surface electromyogram (myoelectric signals) from a remaining pair of agonist-antagonist muscles in the amputated limb.1 This method allows only a single motion to be controlled at a time; operation of the prosthetic elbow, wrist and hand, or hook must be done sequentially. Furthermore, current methods of myoelectric control do not have a natural feel because proximal muscle functions (eg, shoulder, bicep, or triceps muscles) are not normally used to direct wrist or hand movements. Thus, these methods are frustratingly slow and awkward. Furthermore, current prostheses have no intrinsic sense of touch and provide little sensory feedback to the user. They are instead operated only with visual feedback.

We developed a new biological neural machine interface for individuals with amputations, called targeted reinnervation. Targeted muscle reinnervation (TMR) uses the residual nerves from an amputated limb and transfers them onto alternative muscle groups that are not biomechanically functional since they are no longer attached to the missing arm. During the nerve transfer procedure, target muscles are denervated so that they can be reinnervated by the residual arm nerves that previously travelled to the arm before amputation. The reinnervated muscles then serve as biological amplifiers of the amputated nerve motor commands.2,3 Subcutaneous tissue is removed so that surface myoelectric signals are optimised for power and focal recording. TMR thus provides physiologically appropriate electromyogram control signals that are related to previous functions of the lost arm. For example, transferring the median nerve to a segment of pectoralis muscle provides a hand-close myoelectric signal. The patient thinks about closing his or her hand and the median nerve reinnervated segment of the pectoralis muscle contracts. The myoelectric signal from this reinnervated muscle segment is then used to provide a control input to close the motorised hand. By transferring multiple nerves, TMR myoelectric signals allow intuitive, simultaneous control of multiple joints in an advanced prosthesis. TMR was first done in a man with bilateral shoulder disarticulation,4 increasing his performance on standardised function tests by as much as 250%. Two men with long transhumeral amputations had successful targeted reinnervation surgery with similar functional results. Surgery was unsuccessful in a fourth man, because of nerve injuries discovered during the surgery.

Similarly, targeted sensory reinnervation (TSR) might potentially be used to provide the amputee a sense of touch in the missing limb. With this technique, a segment of skin near or overlying the TMR site is denervated and the regenerating afferent nerve fibres...
from the residual hand nerves are enabled to reinnervate this area of skin. As a result, when this skin is touched, the amputee feels as if their hand is being touched. We call this transfer sensation, and it is an exciting mechanism to potentially provide meaningful sensation to the amputee. For example, sensors in the prosthetic hand could quantify pressure, temperature, and texture of objects, and actuators over the reinnervated skin could apply proportional pressure, thermal, and shear stimuli back to the skin of the TSR site, so that the amputee seems to feel what he or she is touching. TSR developed unexpectedly in our first patient. By removing subcutaneous fat, his skin was denervated and afferent nerve fibres regenerated through his pectoral muscles to reinnervate his chest skin.

After the initial success with our first male patient we sought to improve our techniques in subsequent surgeries and address new challenges for female patients. Specifically, we would not be able to remove much subcutaneous tissue in female patients (ie, give them a mastectomy) to optimise surface myoelectric recordings as we did in the male patient. For this reason, surgical techniques were developed to work above and to the side of the breast. Additionally, a new technique was developed to purposefully apply targeted sensory reinnervation without subcutaneous tissue removal. We describe the application of targeted muscle and sensory reinnervation in a young woman with a very proximal transhumeral amputation.

**Methods**

**Patient**

The patient was a 24-year-old woman who had a traumatic transhumeral amputation in May, 2004, due to a motorcycle accident. She had severe phantom limb pain (9 out of 10 Likert scale) that abated with treatment over 6 months. Since only 3 cm of her humerus remained, the patient was fitted with a shoulder disarticulation level prosthesis. She received her first conventional myoelectric prosthesis in October, 2004, in a different city; the device...
consisted of a passive shoulder, a motorised elbow, a passive wrist rotator and a motorised hand. She used myoelectric signals from her pectoral and remnant triceps muscles to sequentially operate the prosthetic elbow and hand. She was trained to use the device in weekly occupation therapy sessions that lasted 3 months, starting in January, 2005.

**Procedures**

Targeted reinnervation surgery was done in August, 2005, with ethics committee approval and written informed consent from the patient. The risks of the procedure included permanent paralysis of the target muscles, recurrence of phantom limb pain, and development of painful neuromas, in addition to standard risks of elective surgery. Surgery was done under general anaesthesia and without muscle relaxation (figures 1–6). The patient’s previous amputation incision was reopened. The musculocutaneous, median, ulnar, and radial nerves were all identified by their branching pattern and cut back to normal appearing fascicles. A branch of the radial nerve leading to a triceps remnant was identified using a nerve stimulator and carefully preserved. All fat and scar tissue over the remnant triceps muscle was excised to optimise the surface myoelectric signal of this muscle. Inspection of the inferior aspect of the clavicular head of the pectoralis revealed two separate motor nerves entering this muscle segment. Two large (1·5 mm diameter) motor nerves were found innervating the sternal head of the pectoralis major, and the motor nerve to the pectoralis minor was also identified. These motor nerve branches were all divided a few mm from where the motor nerve

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**Figure 3**: Coaptation of nerves to pectoralis major

1. Ulnar nerve. 2. Median nerve. 3. Coaptation of musculocutaneous nerve to clavicular head of pectoralis major. 4. Coaptation of median nerve to sternal portion of pectoralis major. 5. Coaptation of musculocutaneous nerve to clavicular head of pectoralis major.

**Figure 4**: Healthy fascicles of ulnar nerve

**Figure 5**: End-to-side neurorrhaphy of intercostal brachial cutaneous nerve coapted to median nerve

**Figure 6**: Final appearance

Lower incision marks area from which fat was removed from over serratus muscle.
entered the muscle segments. The proximal ends of these nerves were resected and mobilised away from the chest wall so that they could not reinnervate the target muscles.

We then did four brachial plexus nerve transfers (figure 7A). The ulnar nerve was sewn to the motor nerve of the medial half of the clavicular head of the pectoralis major and the musculocutaneous nerve was sewn to the lateral motor nerve of the same muscle segment. The median nerve was divided in half lengthwise along its inner epineurium, and the split nerve endings were coapted to each of the two motor nerves of the sternal head of the pectoralis major. These large brachial plexus level nerves completely covered the areas where the small motor nerves entered the muscle segments. The radial nerve was sewn end-to-end to the long thoracic nerve for reinnervation of the distal slips of the serratus anterior muscle.

We did two sensory nerve transfers (figure 7B). The supraclavicular sensory nerve was located through a 4-cm disk of fat over the serratus anterior muscle. The long thoracic nerve for reinnervation of the distal slips of the serratus anterior was divided and the distal segment was coapted to the side of the median nerve. The intercostobrachial cutaneous nerve was identified and divided, and the distal segment was coapted in similar fashion to the median nerve.

The subcutaneous fat was thinned in a 4-cm diameter region over the clavicular head of the pectoralis muscle to enhance the surface electromyogram while not disfiguring the patient. Similarly, a 4-cm disk of fat over the serratus muscle was excised through a separate incision. A drain was placed, the surgical field was well irrigated, and the wounds were closed in layers. The drain was removed 2 days after the operation, and the patient returned to her home 4 days after the operation. She was monitored for wound problems, pain, and the initial development of reinnervation with telephone calls about once every 2 weeks.

When the patient was enrolled into our study in May, 2005, functional testing was done with her conventional myoelectric prosthesis control. At this time, she had had the prosthesis for 8 months, and had been regularly using it for 5 months. A box and blocks test was done, in which the patient moves 2.5-cm square blocks from one box, over a 10-cm wall, and into another box. The test was modified slightly, allowing the patient 2 min, instead of 1 min, to move blocks. The patient was allowed to practise each test for several minutes until she felt comfortable with the task. She then did the task three times with rest breaks of several minutes in between. The Assessment of Motor and Process Skills (AMPS) test was done by an occupational therapist certified in this validated, single-subject testing method. For testing with the patient’s conventional prosthesis, the two tasks were: preparation of a peanut butter and jelly sandwich, including gathering items, preparing, cutting the sandwich in half, serving, cleaning up, and returning items to appropriate storage; and ironing a shirt, including setting up an ironing board, hanging the shirt on a hanger, safely storing the iron, and folding up the board. The patient was also asked to keep a diary of how much she used her prosthesis, recording changes in sensation, and documenting her impressions.

After the experimental surgery, the patient was instructed to try to use all aspects of her missing arm (elbow, wrist, hand, and fingers) daily in an attempt to activate pathways and strengthen muscle as soon as reinnervation occurred. In March, 2006, she was brought to our facility for 2 weeks to fit her with the new experimental prosthesis, train her in its use, and participate in studies. We did extensive surface electromyogram testing. A grid of 128 monopolar surface electrodes was placed over the muscles of interest in the patient’s anterior chest, lateral chest, and shoulder. Monopolar myoelectric signals were recorded as the patient attempted to open her hand, close her hand, flex her elbow, and extend her elbow, following a video demonstration. Ten trials of each movement were recorded with a BioSemi Active II system (BioSemi, Amsterdam, www.thelancet.com Vol 369 February 3, 2007
Netherlands) sampled at 2 kHz. The spatial electromyogram activity for each movement was characterised by contour plots where the average root mean square value of each channel’s electromyogram was represented by different colours. Surface electrodes were mounted in the patient’s prosthetic socket at the points corresponding to the maximum surface amplitude for each elbow and hand movement. During this 2-week period, the patient had training every day with the experimental prosthesis. On completion of this fitting and training period she went home and used her prosthesis for 5 weeks. She then returned to our facility for 1 week of testing and other experiments. The blocks and box test was repeated. The AMPs test was repeated with two different tasks: preparation of a grilled cheese sandwich, including preparation in a pan on the stove using butter, cutting the sandwich in half, and serving it with a beverage, opening and closing the container, returning items to the refrigerator, and cleaning of surfaces; and preparation and serving of a tossed salad with four ingredients, including peeling and slicing, getting out items and returning them to the refrigerator, pouring dressing, covering and storing leftovers, and cleaning up. The patient’s subjective opinions of the new prosthesis were also obtained.

In the assessment of sensory reinnervation, the patient was asked to point to the areas of her chest where the transfer sensation for individual digits was most prominent. The positions of the points were recorded on a schematic diagram of her chest with a representative grid. The character of the sensory reinnervation was quantified for each type of sensory percept. Light touch thresholds were determined with Semmes-Weinstein monofilaments (North Coast Medical, Morgan Hill, CA, USA). Sharp and dull sensibility was determined at 20 selected points distributed across the transfer site with a hand-held neurotip neurometer (Owen Mumford, Marietta, GA, USA). Ability to detect vibration was assessed by pressing a C128 tuning fork to various points on the chest. Temperature thresholds were assessed at two positions over the transfer site with a TSA II NeuroSensory Analyzer (Medoc, Ramat-Yishai, Israel). The patient’s normal contralateral chest and right thenar eminence served as control sites.

Role of the funding source
The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
Postoperatively, the patient’s phantom limb pain returned to a lesser degree (6 out of 10 Likert scale) but it resolved.
with treatment within 4 weeks. No other complications occurred. The surgery caused no disfigurement (figure 8). An area 11 cm wide by 9 cm high became insensate on the patient’s anterior superior chest (figure 8). On her lateral chest wall, only a narrow band around her surgical wound site became numb.

The patient had the first indication of muscle reinnervation about 3 months after the surgery. She could feel the muscles of her chest twitching when she tried to close her hand or bend her elbow. By 5 months, strong muscle contractions could be seen and palpated. Extensive electromyogram testing was done 6 months after surgery following full muscle reinnervation; signals were recorded from all the nerve transfer sites (figure 9). A new experimental prosthesis was made (figure 10) consisting of a motorised elbow with a computerised arm controller (Liberating Technologies, Holliston, MA, USA), a motorised wrist rotator, and a motorised hand (Otto Bock,

**Figure 9:** Map of surface electromyogram amplitude for four different movements

A Placement of electrodes
B Elbow flexion
C Elbow extension
D Hand closure
E Hand opening

These contour plots were built using monopolar high density surface electromyogram recordings. Distinct surface electromyogram distributions are evident for different movements.
Minneapolis, MN, USA). The prosthesis had passive shoulder components. The computerised arm was programmed to use the myoelectric inputs from the TMR muscles to control the motorised hand and elbow. Two pressure-sensitive pads were mounted in the patient’s socket that she used to control her motorised wrist, allowing independent, proportional, simultaneous control of all three joints (table 1).

With training, the patient became proficient in use of the prosthesis within a few days. She was able to operate the hand, wrist, and elbow simultaneously. She reported that operation of the hand and elbow was very intuitive: when she thought of opening the hand, closing the hand, bending the elbow, or straightening the elbow, the prosthesis responded accordingly. The patient was able to operate the wrist rotator with the pressure sensitive buttons at the same time as moving the hand and elbow; however, she rarely did so, because the cognitive burden of controlling all three joints simultaneously was high.

At the time of pre-operative testing the patient had been using her conventional prosthesis for 7 months. Testing with her conventional prosthesis showed poor function, as is typical with this level of amputation (table 2). Her functional outcomes were improved in all areas 7 weeks after beginning the fitting and training of the TMR-controlled experimental prosthesis. Webmovie 1 shows the patient undertaking the blocks and box test (left side is with conventional myoelectric control; right side is using TMR controlled prosthesis); she was almost four times as fast with TMR control, compared with the conventional prosthesis. AMPS testing showed substantial improvement in both motor and process scores. Webmovie 2 shows the patient undertaking daily living tasks with the experimental prosthesis.

The patient was very satisfied with the cosmetic result of the surgery and enthusiastic about the improvement in her limb control. Although she initially tried to use her original conventional prosthesis on a regular basis, she said that it was very frustrating and difficult to operate. Her use of the conventional prosthesis decreased to only 1–2 times per month, when the device was worn mainly for cosmetic reasons. She reported that her experimental prosthesis was much easier and more natural to use than was the conventional prosthesis. She described operation of her hand and elbow as: “I just think about moving my hand and elbow and they move.” Perhaps her most telling statement was: “My original prosthesis wasn’t worth wearing—this one is.” At time of writing the patient used her new TMR prosthesis for an average of 4–5 h a day (up to 16 h), 5–6 days per week for many functional tasks including cooking, putting on makeup, carrying things, eating, house cleaning and laundry, as well as for cosmetic purposes.

The patient had the first indication of sensory reinnervation at 3 months after the surgery. She reported a tingling sensation in her missing hand when her anterior

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Table 1: Control pattern of targeted motor reinnervation prosthesis in this patient

<table>
<thead>
<tr>
<th>Control source</th>
<th>Nerve</th>
<th>Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbow flexion</td>
<td>Electromyogram</td>
<td>Musculocutaneous</td>
</tr>
<tr>
<td>Elbow extension</td>
<td>Electromyogram</td>
<td>Radial-triceps branch</td>
</tr>
<tr>
<td>Hand close</td>
<td>Electromyogram</td>
<td>Median</td>
</tr>
<tr>
<td>Hand open</td>
<td>Electromyogram</td>
<td>Distal radial</td>
</tr>
<tr>
<td>Wrist pronate</td>
<td>Pressure button</td>
<td></td>
</tr>
<tr>
<td>Wrist supinate</td>
<td>Pressure button</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Functional outcome comparing conventional myoelectric prosthesis with experimental TMR-controlled prosthesis

<table>
<thead>
<tr>
<th></th>
<th>Conventional prosthesis (5 months’ use)</th>
<th>Experimental TMR prosthesis (7 weeks’ use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blocks and box test, mean block number (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three trials</td>
<td>4·0 (1·0)</td>
<td>15·6 (1·5)*</td>
</tr>
<tr>
<td>AMPS test, single score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td>0·30</td>
<td>1·98</td>
</tr>
<tr>
<td>Process</td>
<td>0·90</td>
<td>1·98</td>
</tr>
</tbody>
</table>

Testing with conventional device occurred 14 months after amputation and 5 months after prosthetic training was started. Experimental prosthesis testing occurred 8 months after TMR surgery and 7 weeks after starting training.

See Online for webmovies 1 and 2
chest was touched. By 5 months, any stimulus applied to
the previously insensate anterior chest skin was perceived
as being in her missing hand. After about 6 months, she
developed a relatively faint percept of her middle finger on
the lateral chest wall.

The supraclavicular cutaneous nerve was anastomosed
end-to-side to the ulnar nerve and a percept of the fourth
and fifth fingers was expected in the reinnervated anterior
chest skin. However, the anterior chest skin was clearly
reinnervated by both median and ulnar afferents. The
perceptive fields of touch were quite complex; when the
patient was touched at a single point she often perceived
sensation in contiguous or disjoint areas of different digits
and her palm. Figure 11 shows the spots that the patient
identified as the primary points where she perceived
sensation in just one digit.

All modalities of cutaneous sensation were present;
however, the percept of tingling in response to touch of the
target skin persisted (rather than a more normal pressure
sensation). The lowest threshold at which light touch could
be perceived in the reinnervated region was 0·4 g; the
thresholds at most points in this area were under 4 g,
compared with a threshold of 0·4 g at the same location on
the right side and a light-touch threshold of 0·16 g on the
right index finger. With increased pressure the patient felt
an increased intensity of the tingling sensation—ie, she
was able to feel graded pressure. She had appropriate
thresholds for warm and cold sensation within her
reinnervated region. The average threshold for perception
of cold was 29·1°C in her reinnervation area, 29·9°C on
the contralateral chest, and 33·2°C in her right hand,
indicating that sensitivity to cold was slightly increased in
the reinnervated skin. The average threshold for perception
of warmth was 35·2°C in the reinnervated region, 34·7°C
on the contralateral chest, and 33·2°C in the right hand,
indicating that sensitivity to an increase in temperature
was slightly reduced in the reinnervated skin. At 19 of the
20 selected points across the transfer site, the patient was
able to correctly differentiate between sharp and dull
sensation, and was also able to perceive vibration in the
reinnervated skin. Stimulation of each of the aforementioned types of percept modalities within the
reinnervation region was interpreted by the patient as
occurring in her missing hand.

Discussion

Targeted reinnervation surgery was successful in this
young woman. Four independent myoelectric sites were
created that allowed improved control of a motorised
artificial arm. Transfer sensation also developed; when the
patient was touched on her reinnervated chest skin, she
perceived the sensation to be in her missing hand.

A great need exists for neural-machine interfaces that
can enable people with disabilities to interact with their
environment. An effective interface should extract neural
command signals to operate devices that overcome a
person’s motor impairment, provide sensory feedback to
the person with a disability, or both. Research in brain-
machine interfacing is developing new communication
and control technology for people with severe motor
disorders such as paralysis, stroke, cerebral palsy, and
spinal cord injury. The possibilities of extracting
information from the peripheral nervous system with
nerve-cuff electrodes, sieve electrodes, and penetrating
arrays have also been examined. To date, the cochlear
implant is the most clinically successful neural-machine
interface, and has improved the hearing of thousands of
people by interfacing with the auditory neural system.

Targeted reinnervation is a new neural-machine inter-
face for individuals with amputations. TMR rewires
peripheral nerves and uses available surface muscles as
biological amplifiers to develop rich new sources of motor
command signals. After TMR our patient found that her
prostheses was much easier and more natural to use,
because she was using physiologically appropriate neural
pathways to operate her artificial arm. The function of her
prosthesis improved substantially, as shown by an increase
in speed and efficiency of motion. This system has other
distinct advantages: it is relatively simple to implement; no
hardware is implanted in the body that could break,
necessitating additional surgery; and the technique can be
used with existing myoelectric prosthetic technology.

Our patient tried to use her conventional prosthesis for
several months, but became frustrated with the device and
then wore it rarely. This problem is typical of shoulder
disarticulation amputees, since the prostheses have such
limited function and are quite heavy (our patient’s
prostheses weighed just over 6 kg) and the harnessing is
uncomfortable. The improved control led to improved
satisfaction and wear time—the new device had similar
weight and harnessing. The 4–5 h of use per day by the
patient is judged to be heavy use for a unilateral proximal
amputee. However, the prosthesis is still a tool that the
patient uses when needed and takes off for comfort.
Hopefully, improvements in arm prostheses will make

![Figure 11: Map of areas that the patient perceived as distinctly different fingers in response to touch](image-url)
them lighter and more comfortable, thus increasing the time for which they can be comfortably worn.

We faced a substantial challenge with this patient, in that her breast covered much of the primary target muscle—her pectoralis major muscle. It was helpful that a remnant of her humerus preserved the insertion of the pectoralis, holding the sternal head in its normal anatomical position, up and across the chest, allowing electromyogram detection over at least the upper portion of the muscle. With a complete shoulder disarticulation, the pectoralis retracts medially and inferiorly, thus less muscle would have remained above the breast. The long thoracic nerve and distal serratus anterior muscle were successfully used to develop an additional surface electromyogram control site not covered by the breast.

In this study, we used a commercially available prosthesis with simple algorithms based on the magnitude of the surface electromyogram to control only the elbow and a one degree-of-freedom hand. However, the residual nerves of the arm contain all the control commands for complex movement of the elbow, wrist, thumb, and fingers. Much of this information is transferred to the TMR muscle; thus the potential exists for further improvement in control, dexterity, and function of artificial arms. Advanced signal processing algorithms have been used to extract more information from the residual limbs in transradial amputees, showing improved, intuitive control of wrist rotation, wrist flexion, and hand movements. Research is in progress to clinically implement these algorithms in advanced artificial arms that promise further improvement in control and function. Another developing technology that could benefit TMR is implantable myoelectric systems.

Telemetry of intramuscular myoelectric signals could increase access to muscles under subcutaneous fat, breast tissue, and deeper muscles. They might improve information content and stability, compared with surface myoelectric signals, and increase the robustness of this neural-machine interface.

In this study we showed that targeted sensory reinnervation can be purposefully implemented to provide a discrete region of transfer sensation—ie, a sensation of touch in the missing limb. The target skin is an excellent transducer for cutaneous sensory input into the nervous system. We hypothesise that the skin provided the environment for the amputated afferent axons to find appropriate end organs that yielded appropriate sensory perception. This patient’s transfer sensation had high fidelity, in that all the cutaneous sensory modalities were present and the thresholds of perception were close to normal.

The clinical implications of TSR are exciting. The potential exists to provide meaningful light touch, graded pressure, texture, edge detection, and thermal feedback to amputees in an intuitive manner. For the patient, there is much to be gained with even a single point of pressure feedback. For example, the perception of simply touching an object can provide goal confirmation in grasping, and graded force feedback relates to how hard the user is squeezing an object; both have great functional value. This patient had a somatotopic organisation, in that different regions of the TSR skin felt like different fingers or her thumb. This occurrence might allow useful sensory feedback for multiple regions of the hand; sensors could be placed in each prosthetic digit and have the sensory feedback applied to the corresponding regions of reinnervated skin. Perhaps the most important aspect of TSR is psychological. Enabling patients a perception of feeling what they are touching could help them to incorporate their prosthesis into their self image in a more positive manner, and to better connect with their physical and social environments.

The sensory somatotopic organisation that developed differed from what we expected. In surgery, the distal segment of the intercostobrachial nerve was transferred to the median nerve and median sensation was anticipated on the lateral chest. Only a faint median percept developed, probably because the skin innervated by the intercostobrachial nerve was amputated with the arm leaving nothing for the median afferents to reinnervate. The distal segment of the supraclavicular nerve was transferred to the ulnar nerve, and ulnar sensation alone was expected on the anterior chest. However, a strong percept and large area of median nerve reinnervation were noted. The robustness of the median nerve sensory reinnervation was surprising. The median nerve afferents had to regenerate through the pectoralis major muscle and through a layer of subcutaneous tissue that was more than 1 cm thick while in competition with the regenerating ulnar afferents. Further study is clearly needed to better understand what guides, promotes, or impedes sensory axon regeneration. Research is also needed to assess the skin-receptor densities and receptor types and to characterise afferent-receptor interaction in this hyper-reinnervation model, in which a large excess of sensory afferents are competing to reinnervate a limited skin region.

The primary sensory cortex is able to undergo substantial change after amputation and nerve transfer. Neural plasticity could be detrimental to the outcome of the TSR if the sensory cortex was to integrate the hand percepts into a chest body image. However, this problem has not happened in 4 years with our first patient or in 1 year with this second patient. Additionally, the motor pathways seem to be equally robust. In fact, targeted reinnervation shows the endurance of dormant central pathways. The time of complete non-use for these central pathways was at least 18 months in this patient (time from amputation to reinnervation), yet motor commands were readily elicited and complex transfer sensation developed. However, whether longer periods of dormancy might affect the viability of these pathways is unclear. Another interesting possibility associated with neural plasticity is that the sensory cortex might develop a more functional somatosensory representation of the TSR site with use and
time. For example, repeatedly touching a spot of reinnervated skin that contains some thumb afferents in correlation to touching an object with the prosthetic thumb might cause the brain to interpret that skin spot more clearly as representing a thumb.

A key question for the application of targeted reinnervation is how long do amputated nerves remain viable? Voluntary signals can be recorded from motoneurons many years after amputation and stimulating a nerve decades after amputation will produce a perception of sensation in the missing limb. Some axons are lost with time, but estimates of the time taken vary greatly. Furthermore, targeted reinnervation uses hyper-reinnervation of the target muscle and skin. The proportion of viable axons that are needed is unknown, but a large excess of both motor and sensory axons are transferred. The procedure can probably be undertaken successfully many years after the initial amputation.

This patient and our other three patients represent early application of targeted reinnervation technique. Whether the improved function is enough to keep these patients wearing their devices in years to come, or whether they adapt to their new control even better and show greater functional gains, remains to be seen. Long-term follow-up is also needed to see how our patient’s transfer sensation evolves. We need to ascertain whether the sensation persists unchanged or whether the character, localisation, and somatotopic organisation of the sensation are altered with time and use.

Contributors

T Kuiken participated in all the aspects of this article, including project management, surgery, data collection, and manuscript writing. L Miller, R Lipschutz, and B Lock participated in fitting of the prosthetic limb, data collection, and manuscript writing. K Stubblefield participated in the patient’s training, data collection, and manuscript writing. P Marasco participated in data collection and manuscript writing. G Dumanian participated in the surgery, data collection, and manuscript writing. P Zhou participated in collection and analysis of electromyogram data. All authors saw and approved the final manuscript.

Conflict of interest statement

We declare that we have no conflict of interest.

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This work was done in collaboration with Liberating Technologies, a company that manufactures and distributes prosthetic components. As a fee-for-service, they sold us the Boston Digital Elbow and modified the onboard computer controller to allow use of the targeted reinnervation myoelectric signals and the ability to do simultaneous control of the three prosthetic joints. We thank Jules Dewald and Levi Hargrove for their participation in the patient's training, data collection, and manuscript writing. G Dumanian participated in the surgery, data collection, and manuscript writing. P Zhou participated in collection and analysis of electromyogram data. All authors saw and approved the final manuscript.

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