TARGETED REINNERVATION

Yonatan Levi Moshayev

INTRODUCTION

Imagine living a life where even the simplest of tasks such as eating a grape or holding an egg required intense concentration and months of training. Until recently, this was the harsh reality for people with upper limb prostheses. Currently, the most common upper limb prosthetic technology being used is body powered. These devices capture remaining shoulder movements with a harness and transfer this movement through a cable to operate the hand, wrist, or elbow. With this control method, only one joint can be operated at a time. When the amputee has positioned one component, he or she can activate a switch that locks that component in place, and then he or she can operate the next component (Longe 2006; Miguelez et al. 2009; Edeer and Martin 2011). Until recently, this was the only technology available for someone using an upper limb prosthesis.

Over the past few years, myoelectric prostheses have been developed. These prostheses use electromyogram (EMG) signals (the electrical signals generated during muscle contraction) from remaining upper limb muscles to control motorized arm joints. Myoelectric signals are derived from the contraction of voluntary control muscles in the residual limb and are recorded by surface electrodes implanted in a prosthetic socket. Unfortunately, myoelectric prostheses are also restricted to one function at a time because of a lack of independent control signals (Longe 2006; Miguelez et al. 2009; Edeer and Martin 2011).

Current control strategies use the electromyogram signals from one or two agonist-antagonist remaining muscles to sequentially operate each function in the prosthesis. For example, an individual with transhumeral amputation uses the biceps and triceps muscles to control the elbow, wrist, and hand. For an individual with shoulder disarticulation the pectoralis major can be used to close the hand and supraspinatus to open it. The individual would then use a chin switch to toggle through the controls so that these same two muscles operate the wrist rotator and elbow. This type of operation is not always intuitive, because the residual muscles control physiologically unrelated movements (Longe 2006; Miguelez et al. 2009; Edeer and Martin 2011).

It is estimated that by the year 2020, the number of people in need of a prosthetic limb will reach 2.4 million (Nielsen 2002). Evident that prosthetic technology needed improvement to serve a growing demand and multitudes of frustrated patients, Todd A. Kuiken (2006) developed a better upper limb prosthetic alternative using a procedure called Targeted Reinnervation. The purpose of this paper is to assess the extent in which targeted reinnervations improve prosthetic functions, facilitate its use, and restore meaningful sensory feedback in patients.

With Targeted Muscle Reinnervation (TMR), it is possible to denervate regions of muscle that are not bio-mechanically functional in or near an amputated limb and transfer residual arm peripheral nerve endings to these muscles. Over time, the transferred nerves reinnervate these muscles. The surface electromyogram signals from the newly reinnervated muscles can be used as additional control signals for an externally powered prosthesis (Kuiken 2006; Hijjawi et al. 2006).

The amazing thing about using targeted muscle reinnervation to control prosthetic limbs is that it is intuitive. The patient thinks about closing his or her hand and it closes. This is achieved because the electromyogram signals from the reinnervated muscles are used to control

---

Yonatan Levi Moshayev, B.S. '13, majored in Biology. He hopes to attend a Master's program in Prosthetics and Orthotics.

functions in the artificial arm that the motor nerves naturally controlled before amputation. The motor nerve that usually sends the signal to close the hand contracts the reinnervated muscle. This produces a surface electromyogram signal that is processed and translated by the prosthesis and causes the prosthetic hand to close (Kuiken 2006; Hijjawi et al. 2006).

Even more impressive is that a similar procedure can be done for Targeted Sensory Reinnervation (TSR). With targeted sensory reinnervation, a section of skin near or overlying the targeted muscle reinnervation site is denervated and the remaining afferent sensory nerve fibers from the residual arm are transferred to it. Over time, the transferred nerves reinnervate this skin and can potentially provide meaningful sensations for amputee patients (Kuiken 2006; Kuiken et al. 2007a; Marasco et al. 2009).

In theory, targeted sensory reinnervation can offer patients a sense of texture, temperature, and pressure of the objects they touch with their prosthesis (Kuiken et al. 2007a; Marasco et al. 2009). If a patient touched a hot cup of tea, sensors in the prosthetic hand could process information about the texture, temperature, and pressure of the cup and use that information to apply proportional stimuli to the reinnervated skin. In theory, the patient should feel as if he/she were actually touching the cup with a normal hand.

METHODS

The data used for this research paper was compiled from, case studies, review articles, and proof of concept studies found in medical and scientific journals using the Touro College database. Several medical books and online sources were also used for data.

FIRST TARGETED REINNERVATION PATIENT (M1)

The first patient to undergo targeted reinnervation was a 54-year-old male working as a high-power lineman, who experienced severe electrical burns in May 2002 that resulted in bilateral shoulder disarticulation (Kuiken 2006). He was initially fitted with an externally powered prosthesis on the left side, that was controlled using touch pads in his shoulder socket and a chin switch, and a body-powered prosthesis on the right. The patient became relatively proficient operating his new prostheses after receiving extensive operational training (Kuiken 2006; Hijjawi et al. 2006).

The left limb was chosen for the targeted reinnervation procedure because that was the side of his externally powered prosthesis. Together, the patient and his medical team decided not to alter the operation of his right body-powered prosthesis because it worked very well for him (Kuiken 2006; Hijjawi et al. 2006).

The goal of surgery was to create four new physiologically appropriate myoelectric control inputs using the four major arm nerves from the brachial plexus. The left pectoralis major and minor muscles were denervated, and the proximal ends of the native nerves were ligated and sutured up under the clavicle to prevent them from reinnervating the pectoral muscles. The musculocutaneous, median, and radial nerves were transferred on to the clavicular head, the upper sternal head, and the lower sternal head. The pectoralis minor was moved out from under the pectoralis major and over to the lateral thoracic wall to serve as a fourth donor muscle segment for the ulnar nerve. In addition, this prevented the pectoralis minor electromyogram from interfering with the myoelectric signals from the other nerve transfers. All four of the residual plexus nerves were sewn onto the distal ends of the original pectoral muscle nerve fascicles and onto the muscle itself (Figure 1) (Kuiken 2006; Hijjawi et al. 2006).

Most of the pectoralis muscle’s subcutaneous fat was surgically removed to optimize surface myoelectric recordings. Once the fat was removed, the recording electrodes were as close as possible to the muscle regions with the strongest surface electromyogram signals and the least cross-talk from adjacent muscles (Kuiken 2006; Hijjawi et al. 2006).

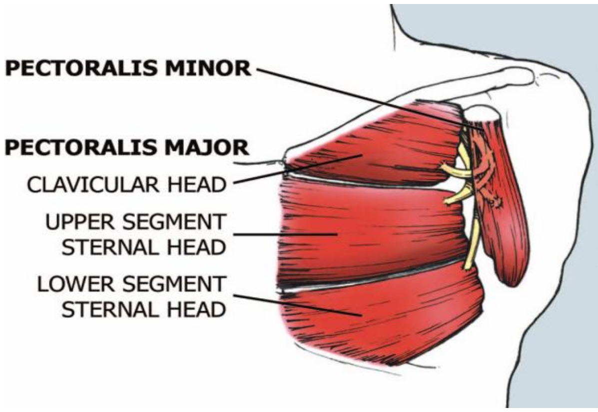


Figure 1: Diagram of first TR patient's surgical procedure. Source: Hijjawi et al. 2006

RESULTS

After five months of recovery, the patient was able to activate four different areas of his pectoralis major muscle when he tried moving his phantom hand or arm. Two distinct electromyogram signals could be identified in the mid-pectoral region where the median nerve was relocated. When the patient thought about closing his hand, a strong electromyogram signal could be identified on the lateral pectoral region. Surprisingly, when the patient tried to open his hand, an independent signal could be detected more medially. When the patient tried to flex his amputated elbow, it caused a strong contraction of the muscle just below the clavicle (Kuiken 2006; Hijjawi et al. 2006). This was consistent with musculocutaneous nerve reinnervation because the musculocutaneous naturally controls elbow flexion (Tortora and Grabowski 2003). Extension of his hand and elbow caused a substantial contraction of the lower pectoralis muscle, consistent with radial nerve reinnervation. Surprisingly, however, the transfer of the efferent ulnar nerve to the pectoralis minor was unsuccessful (Kuiken 2006; Hijjawi et al. 2006).

In addition to the motor reinnervation of the muscle, targeted sensory reinnervation occurred in the skin of the chest wall primarily over the musculocutaneous, median, and ulnar nerve transfers. When the patient's chest was touched in different places, he felt as though he was being touched on different points of his hand and arm. The patient acquired the sensation of touch, sharp/dull sensation, graded pressure sensation, and thermal sensation, all previously thought lost to him (Kuiken 2006; Kuiken et al. 2007a; Marasco et al. 2009).

He felt these sensations over an area 15 cm across × 17 cm high. The area was mapped using a cotton-tipped probe that indented the skin with 300 grams applied force (gAF) (Figure 2). He usually felt pressure in large areas of his hand when touched at a single point. These evoked sensations were localized to the palmar and dorsal aspects of his hand and forearm.

As seen in Figure 2, pressing the skin over the lateral ulnar nerve reinnervation site elicited sensations on the forearm, palm, digit four, and digit five. Pressing the skin over the superior median nerve transfer site stimulated sensations on the palm and first three digits. Similarly, pressing the skin over the inferior musculocutaneous and radial transfer sites generated sensations localized to the back of the hand and forearm. Such sensations corresponded well with the natural skin sensations provided by nerves in a normal hand (Figure 3).

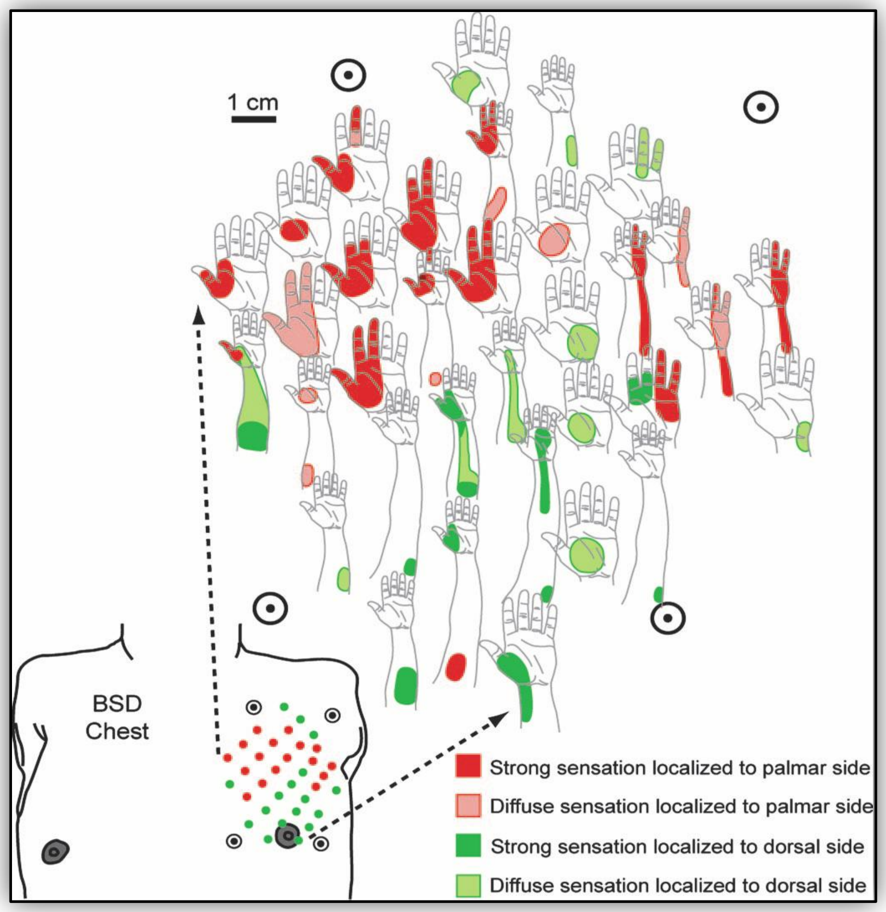


Figure 2: The reinnervated chest skin of patient M1 (BSD) showing sensations referred to the missing limb elicited by indentation of the skin by a cotton-tipped probe (300 gAF). Referred sensations localized to either the palm side (red) or the backside (green) of the missing limb. Circled points at the corners serve as registers to orient the diagram. Source: Kuiken et al. 2007a

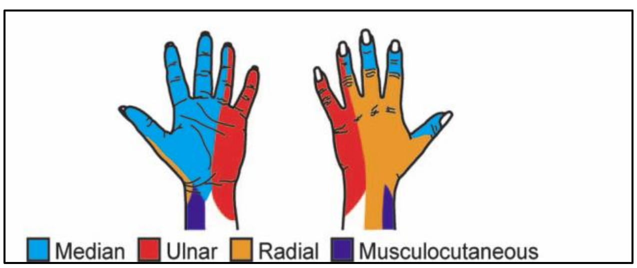


Figure 3: Diagrams of skin sensation provided by each nerve in the normal hand. Source: Kuiken et al. 2007a

The patient was fitted with an experimental 3 Degrees of Freedom (DOF) myoelectric prosthesis that consisted of a Griefer terminal device, a powered wrist rotator, a Boston digital arm, and a LTI-Collier Shoulder joint. An electronic lock also was added to the left shoulder joint, operated with a single touch pad in the apex of the left socket. The choice was made to use the three strongest electromyogram signals to control the experimental prosthesis (Kuiken 2006; Hijjawi et al. 2006).

The lateral hand close and wrist flexors portion of the median nerve reinnervation site was used to control hand closing, while the medial portion was used to control the patient's hand opening. The patient could then use a touch pad in the shoulder socket to switch from hook/hand function to wrist function and use the same electromyogram signals to rotate his wrist. The musculocutaneous reinnervation site was used for elbow flexion. The amount and speed that the prosthesis moved was dependent on the strength of the electromyogram signal controlled by the extent of muscle contraction. This type of control was preferred because it allowed the patient to operate his elbow and terminal device intuitively and simultaneously (Kuiken 2006; Hijjawi et al. 2006).

TESTING

Two tests were performed comparing the function of the patient's experimental myoelectric prosthesis with his old touch pad prosthesis. The first test, the box and blocks test, is a standardized, validated assessment in which the test subject moves 1-inch-square blocks between two boxes separated by a short wall. The subject has to move as many blocks as he can from one box to the other in a one-minute period (Mathiowetz et al. 1985). The test was slightly altered, allowing the patient two minutes of moving the blocks.

After using his original touch-pad prosthesis for 20 months, the patient was able to move 5.7 boxes, averaged over three trials. After seven months of recovery and just two months of training, the patient was able to move 14 boxes using his new myoelectric prosthesis. That's a 246% increase in speed with his experimental prosthesis (Kuiken 2006; Hijjawi et al. 2006).

A second test, called the clothespin test was developed that required use of the elbow, terminal device, and wrist rotator unit. The patient has to take clothespins off a horizontal bar, rotate the pins, and place them on a higher vertical bar. The goal is to see how long it takes the patient to move three clothespins. The patient's speed improved 26% on this test (Kuiken 2006).

It is also important to note, that the patient reported that he strongly preferred his new myoelectric prosthesis and was able to do things that he could not do with his old prosthesis (Table 1).

Things patient can do *better* with myoelectric prosthesis	*New things* patient can do with myoelectric prosthesis
Take out garbage Carry groceries Pick up yard Vacuum Dust mop Pick up toys Put on hat Put on glasses Wash driveway	Feed himself Shave Put on socks Weed in garden Water the yard Open small jar Use pair of handicap scissors Throw a ball

Table 1: Patient M1's self-report of improved function with nerve-muscle graft controlled prosthesis. Source: Kuiken 2006

The one issue the patient did have, was that the prosthesis made him too hot and caused him to sweat. When the prosthesis got wet, it did not function as well and had to be taken off to dry (Kuiken 2006).

FIRST FEMALE TARGETED REINNERVATION PATIENT (F1)

The first female patient to undergo targeted reinnervation was a 23-year-old woman with a very short transhumeral amputation at the left humeral neck. In her case, the ulnar nerve had been transferred to the medial region of the upper pectoralis muscle, the musculocutaneous nerve was transferred to the lateral region of the upper pectoralis muscle, the median nerve was transferred to the middle and lower pectoralis muscles, and the distal radial nerve was transferred to the serratus anterior muscle (Figure 4a). In addition, the supraclavicular cutaneous and intercostobrachial cutaneous nerves were cut and the distal ends were anastomosed to the ulnar and median nerves (Figure 4b).

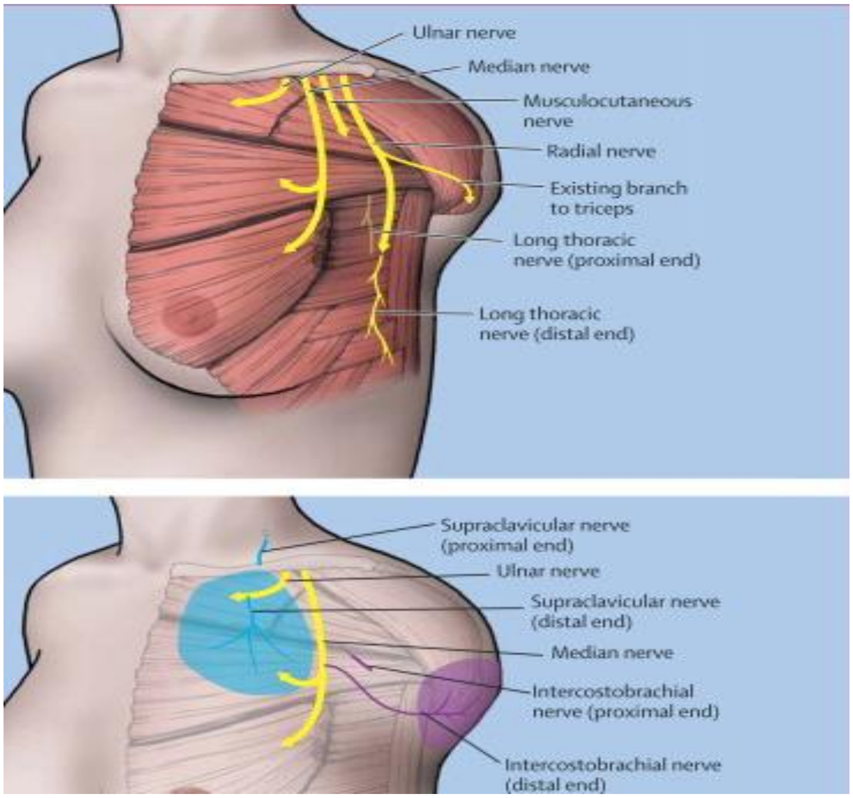
A
B


Figure 4: Diagram of first female patient's targeted reinnervation surgery (A) Targeted muscle reinnervation. The musculocutaneous, ulnar, and median nerves were transferred to separate segments of the pectoralis major muscle. The long thoracic nerve innervating the inferior three slips of serratus anterior was divided and the distal segment was coapted to the radial nerve. (B) Targeted sensory reinnervation. The supraclavicular cutaneous nerve was cut and the distal segment was coapted to the side of the ulnar nerve. The intercostobrachial cutaneous nerve was cut and the distal end was coapted to the side of the median nerve. Source: Kuiken et al. 2007b

A 4-cm diameter of subcutaneous fat was thinned over the clavicular head of the pectoralis muscle to enhance the surface electromyogram signal while not disfiguring the patient's breast. Similarly, a 4-cm circle of fat over the serratus muscle was removed through a separate incision (Kuiken et al. 2007b).

RESULTS

The targeted muscle reinnervation was successful, so a new experimental prosthesis was made comprising of a motorized elbow with a computerized arm controller, a motorized hand, and a motorized wrist rotator. Two pressure-sensitive pads were also mounted in the patient's socket, which were used to control her motorized wrist, allowing proportional, independent, simultaneous control of all three joints (Table 2).

	Control source	Nerve	Muscle
Elbow flexion	Electromyogram	Musculocutaneous	Lateral clavicular pectoralis major
Elbow extension	Electromyogram	Radial-triceps branch	Remnant triceps
Hand close	Electromyogram	Median	Sternal pectoralis major
Hand open	Electromyogram	Distal radial	Inferior serratus anterior
Wrist pronate	Anterior shoulder pressure button		
Wrist supinate	Posterior shoulder pressure button		

Table 2: Control pattern of targeted motor reinnervation prosthesis in this patient. Source: Kuiken et al. 2007b

Targeted sensory reinnervation was also successful. However, instead of feeling regular sensation the patient felt tingling in her arm in response to being touched on her target chest skin. With increased pressure, the patient felt an increased intensity of the tingling sensation. Her referred-touch sensation thresholds ranged from 0.4 to 300 gAF. In addition to graded pressure, the patient was also able to sense hot/cold sensations, distinguish between sharp and dull sensation, and was able to perceive vibration in her reinnervated skin (Figure 5). The patient was also able to perceive distinct sensation of each finger at different areas of the nerve transfer sites (Figure 6).

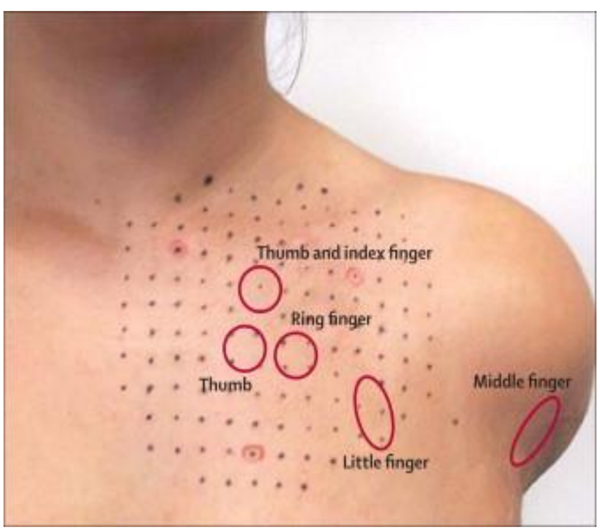


Figure. 5: The reinnervated chest skin of patient F1 (STH) showing sensations referred to the missing limb elicited by indentation of the skin by a cotton tipped probe (300 gAF). Red, referred sensation points localized to the palm side of the hand. Blue, points where a general diffuse feeling of pressure was felt within the hand. Circled points orient the diagram. P, proprioceptive sensation of fourth finger joint position. S, sensation of skin stretch. Double headed arrows, direction of stretch. Arrowheads, edge sensation. Source: Kuiken et al. 2007a

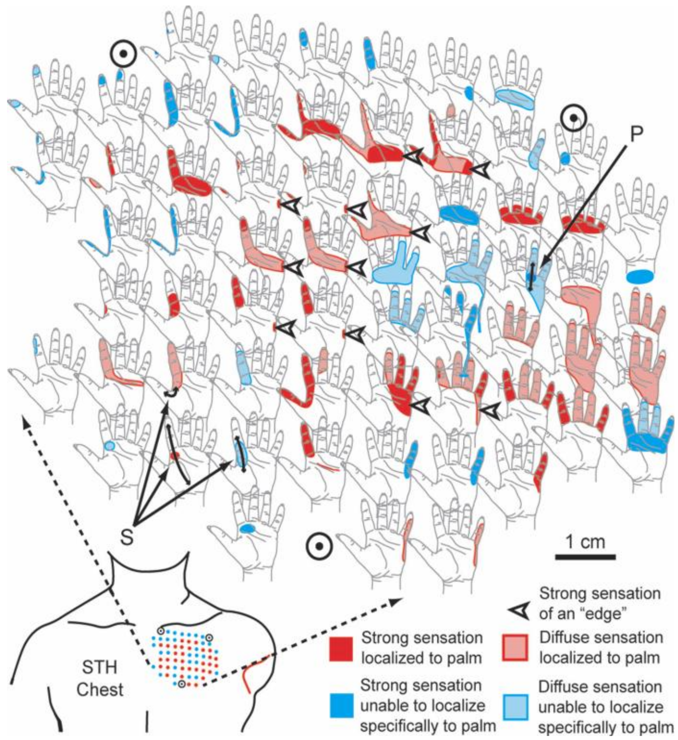


Figure 6: Map of areas that the patient F1 perceived as distinctly different fingers in response to touch. Source: Kuiken et al. 2007b

TESTING

Functional testing was done with her conventional myoelectric prosthesis, which she had been using for five months and then again with her new experimental prosthesis that she trained with for only seven weeks. A slightly modified box and blocks test was done, allowing the patient two minutes, instead of one minute, to move the blocks. The patient was allowed to practice for several minutes until she felt comfortable with the task. She then did the task three times with short breaks in between. With her old prosthesis, she moved an average of 4.0 blocks (SD-1.0). With her new prosthesis, she moved 15.6 (SD-1.5). That is almost a 400% increase in speed with her new prosthesis (Kuiken et al. 2007b).

The Assessment of Motor and Process Skills (AMPS) test was also done. The AMPS is an internationally recognized, occupational therapy–specific assessment of the quality of a client's activities of daily living performance (Merritt 2011) the test required the patient to do two tasks. For the old prosthesis, she had to prepare a peanut butter and jelly sandwich from beginning (gathering items) to end (returning items to appropriate storage) and iron a shirt from beginning to end. For the experimental prosthesis, she had to prepare a grilled cheese sandwich, and prepare and serve a tossed salad with four ingredients. For the old prosthesis, she got a single score of 0.30 for motor skill and 0.90 for process skills. For the new prosthesis, she got a score of 1.98 in both motor and process skill (Kuiken et al. 2007b).

ADVANCES IN PROSTHESIS DESIGN

In addition to being the first male targeted reinnervation patient, M1 was also chosen to try out advanced experimental prostheses. He was fitted with a 6 degree of freedom (DOF) prosthesis capable of shoulder flexion, humeral rotation, elbow flexion, wrist rotation, wrist flexion, and hand control (Table 3).

Location of input	Control input type	Controlled function
Median nerve transfer to middle pectoralis*	EMG	Hand open
Median nerve transfer to middle pectoralis*	EMG	Hand close
Musculocutaneous nerve transfer to superior pectoralis*	EMG	Elbow flexion
Radial nerve transfer to inferior pectoralis*	EMG	Elbow extension
Middle Deltoid	EMG	Internal humeral rotation
Latissimus Dorsi	EMG	External humeral rotation
Shoulder contact with anterior location of socket	Force sensing resistor	Wrist flexion/extension
Shoulder contact with posertior location of socket	Force sensing resistor	Wrist pronation/supination
Shoulder contact with superior location of socket	Digital rocker switch	Shoulder flexion/extension
EMG = electromyographic *Targeted reinnervation site		

Table 3: Location of targeted reinnervation sites and additional electromyographic and analog inputs used for control of the 6-DOF prosthesis. Source: Miller et al. 2008

The patient was able to independently operate all six of the prosthetic arm functions with good control. He was able to simultaneously operate 2 degrees of freedom of several different joint combinations with relative ease, and was also able to operate up to 4 degrees of freedom simultaneously, but with poor control. Overall, the patient's workspace was significantly increased and some of the timed tasks performed were faster with his new 6-DOF system (Miller et al. 2008).

Patient M1 was also fitted for a prosthetic arm with 7 degrees of freedom in January 2007. In addition Patients M1, F1, and one other patient where all fitted for a 10 degrees of freedom prosthesis in May, June, and July 2007 (Kuiken et al. 2009).

DISCUSSION

The cases presented show the successful use of targeted reinnervation in both men and women with different levels of upper limb amputation. The targeted sensory reinnervation procedure may possibly be utilized in lower limb amputations to provide patients with sensory perception of the floor they are walking on. Targeted muscle reinnervation can also provide the information necessary to control a powered joint in lower limb prosthesis.

However, despite such promising results, there is still much room for improvement and research. Further study is clearly needed to understand how long amputated nerves are viable.

Finding ways to provide more control signals is the key to operating more degrees of freedom. Using implantable myoelectric sensors (IMES) in place of surface electrodes can possibly enhance the amount and quality of control data collected from electromyograms (Merrill et al. 2010). By implanting the electrodes, crosstalk would be significantly reduced and the issue of sweat with patient M1 would be resolved. The size, weight, and battery life of advanced prostheses need to be improved in order to provide a more comfortable and practical experience for patients. Finally, a prosthesis that actually provides sensory feedback still needs to be developed.

The future for amputee patients seems more promising than ever. Who knows where this kind of technology might take us? Perhaps using targeted reinnervation, we can make prosthetic limbs so authentic, powerful, and efficient that even healthy people, with real limbs, will choose to wear them.

REFERENCES

Edeer D, Martin CW. 2011. Upper limb prostheses: a review of the literature: with a focus on myoelectric hands. WorkSafeBC Evidence-Based Practice Group.

Hijjawi JB, Kuiken TA, Lipschutz RD, Miller LA, Stubblefield KA, Dumanian GA. 2006. Improved myoelectric prosthesis control accomplished using multiple nerve transfers. Plastic and Reconstrive Surgery 118(7):1573-1578.

Kuiken TA. 2006. Targeted reinnervation for improved prosthetic function. Physical Medicine and Rehabilitation Clinics of North America 17:1-13.

Kuiken TA, Li G, Lock BA, Lipschutz RD, Miller LA, Stubblefield KA, Englehart KB. 2009. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. Journal of the American Medical Association 301(6):619-628.

Kuiken TA, Marasco PD, Lock BA, Harden RN, Dewald JPA. 2007a. Redirection of cutaneous sensation from the hand to the chest skin of human amputees with targeted reinnervation. Proceedings of the National Academy of Sciences of the United States of America 104(50):20061-20066.

Kuiken TA, Miller LA, Lipschutz RD, Lock BA, Stubblefield K, Marasco PD, Zhou P, Dumanian GA. 2007b. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. Lancet 369(9559):371-380.

Longe JL. 2006. Upper limb prostheses. The Gale Encyclopedia of Nursing and Allied Health. Detroit: Gale Group 2777-2780.

Marasco PD, Schultz AE, Kuiken TA. 2009. Sensory capacity of reinnervated skin after redirection of amputated upper limb nerves to the chest. Brain 132:1441-1448.

Mathiowetz V, Volland G, Kashman N, Weber K. 1985. Adult norms for the box and block test of manual dexterity. The American Journal of Occupational Therapy 39(6):386-391.

Merrill DR, Lockhart J, Troyk PR, Weir RF, Hankin DL. 2010. Development of an implantable myoelectric sensor for advanced prosthesis control. Artificial Organs 35(3):249-252.

Merritt BK. 2011. Validity of using the assessment of motor and process skills to determine the need for assistance. The American Journal of Occupational Therapy 65(6):643-650.

Miguelez J, Conyers D, Lang M, Gulick K. 2009. Upper extremity prosthetics. Care of the Combat Amputee. 607-617.

Miller LA, Lipschutz RD, Stubblefield KA, Lock BA, Huang H, Williams TW III, Weir RF, Kuiken TA. 2008. Control of a six degree of freedom prosthetic arm after targeted muscle reinnervation surgery. American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation 89(11):2057-2065.

Nielsen CC. 2002, May. Issues affecting the future demand for orthotists and prosthetists. Retrieved from: http://www.ncope.org/summit/pdf/Footnote3.pdf.

Tortora GJ, Grabowski SR. 2003. The spinal cord and spinal nerves: brachial plexus. Principles of Anatomy and Physiology. Hoboken: John Wiley & Sons 438- 441.