Characterization of evoked tactile sensation in forearm amputees with transcutaneous electrical nerve stimulation

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Abstract
Objective. The goal of this study is to characterize the phenomenon of evoked tactile sensation (ETS) on the stump skin of forearm amputees using transcutaneous electrical nerve stimulation (TENS). Approach. We identified the projected finger map (PFM) of ETS on the stump skin in 11 forearm amputees, and compared perceptual attributes of the ETS in nine forearm amputees and eight able-bodied subjects using TENS. The profile of perceptual thresholds at the most sensitive points (MSPs) in each finger-projected area was obtained by modulating current amplitude, pulse width, and frequency of the biphasic, rectangular current stimulus. The long-term stability of the PFM and the perceptual threshold of the ETS were monitored in five forearm amputees for a period of 11 months. Main results. Five finger-specific projection areas can be independently identified on the stump skin of forearm amputees with a relatively long residual stump length. The shape of the PFM was progressively similar to that of the hand with more distal amputation. Similar sensory modalities of touch, pressure, buzz, vibration, and numb below pain sensation could be evoked both in the PFM of the stump skin of amputees and in the normal skin of able-bodied subjects. Sensory thresholds in the normal skin of able-bodied subjects were generally lower than those in the stump skin of forearm amputees, however, both were linearly modulated by current amplitude and pulse width. The variation of the MSPs in the PFM was confined to a small elliptical area with 95% confidence. The perceptual thresholds of thumb-projected areas were found to vary less than 0.99 × 10⁻² mA cm⁻². Significance. The stable PFM and sensory thresholds of ETS are desirable for a non-invasive neural interface that can feed back finger-specific tactile information from the prosthetic hand to forearm amputees.

Keywords: evoked tactile sensation (ETS), transcutaneous electrical nerve stimulation (TENS), neural interface, sensory feedback, prosthetic hand, perceptual threshold, sensory modality

1. Introduction

There have been significant advances in the development of prosthetic hands or limbs to improve the quality of life for amputees [1–8]. More dexterous control of prosthetic hands has been achieved using neural signals directly recorded from populations of cortical neurons [9–12], from the peripheral nerves [13–15], or from a group of muscles in the stump [16–20]. However, the functionality of the prosthetic hand may be compromised due to lack of awareness in the amputees when contacting objects, since sensory feedback provides critical tactile information for hand grasp and manipulation [21–23]. Although substantial progress in sensory feedback for
prosthetic hands has been made with emerging neural interface technologies [13, 24–27], it still remains a significant challenge to achieve efficacious sensory feedback from the prosthetic device to the amputee.

Creating an intelligent prosthetic hand that can feel and act like a real hand is desirable to improve the dexterity of prosthetic device to the amputee. This requires providing physiologically appropriate tactile information via a natural afferent pathway from prosthetic fingers to the sensory cortex of amputees. Extensive efforts have been directed to provide near-natural tactile sensation through invasive neural technologies at various levels in the peripheral or central nervous system. It has been demonstrated in monkey [5, 28, 29] that it was possible to deliver an artificial tactile sense by direct electrical stimulation of the somatosensory cortex (S1). Studies have even found that S1 neural populations could accurately discriminate between different patterns of direct dorsal root ganglia stimulation across a wide range of stimulus pulse rates [30]. It is also promising to achieve natural sensory feedback by means of the ever-developing peripheral nerve interfacing technologies [15, 31–33]. A natural sensory feedback of graded, discrete touch sensation had been achieved by implanting electrodes within individual fascicles of peripheral nerve stumps in amputees [34]. Recently, Raspopovic et al [1] and Tan et al [6] demonstrated that the implanted peripheral nerve electrodes can provide relatively stable, near-natural sensory information to amputees, and can improve their ability to manipulate delicate objects with a more accurate grasping strength. Targeted muscle reinnervation (TMR), which rerouted the residual nerves of the amputees to innervate the chest muscles surgically, could also provide noninvasive sensory feedback in TMR-based prosthetics [25, 35, 36].

Mechanotactile stimulation can achieve sensory feedback non-invasively by a pusher or a vibrator [3]. Mechanotactile stimulation has been widely used to evoke the visual-tactile illusion in upper-limb amputees [37–40], and to transfer peripheral tactile pressure from a prosthetic hand to the forearm skin of amputees [41–44]. However, the neural mechanism of sensory illusion lacks a clear physiological afferent pathway compared to that of direct stimulation of the peripheral sensory nerves or cortex. Interestingly, most forearm amputees are able to perceive a ‘touch’ on the missing fingers when a mechanical ‘touch’ is applied to the stump skin [45, 46]. An fMRI study revealed that non-painful phantom finger perception elicited by mechanical stimulation of a specific stump skin area in forearm amputees produced a similar activation area [46] in the primary somatosensory cortex (S1) representing the finger in able-bodied subjects [47]. This appeared to suggest that the normal neural afferent pathway is evoked for the non-painful phantom finger sensation induced by mechanical touch in the stump skin.

Transcutaneous electrical nerve stimulation (TENS) of the peripheral sensory nerve (also referred to as electrocutaneous or electrotactile stimulation in the literature [49, 50, 52–54]) has been considered as a plausible non-invasive means to convey tactile information from the prosthetic device to amputees [48–51]. Evidence also suggested that TENS not only can reduce phantom pain or stump pain caused by amputation [55–57], but also can induce a sense of perceptual embodiment in able-bodied subjects with a visual-tactile illusion and in missing limbs of amputees with stimulation of sensory afferents [58, 59]. In this study, we hypothesize that TENS could evoke the similar tactile sensation as that of mechanical ‘touch’, but may provide more variety of sensory modalities and richer sensory information because of the involvement of more kinds of sensory receptors deeply located in the skin layer. This phenomenon is referred to as evoked tactile sensation (ETS) in this paper, since it requires an external stimulus to elicit it, as opposed to phantom limb sensation (PLS) [60, 61], which does not require any external stimulus.

The goal of the present study is to characterize the projected finger map (PFM) of evoked tactile sensation on the stump skin in the forearm of amputees induced by TENS, and to evaluate the legible sensory modalities and perceptual thresholds, as well as their anatomical and temporal stability over time. The main findings of this study revealed a map of hand-shaped projection on the stump skin of the forearm of amputees, which was more complete with more distal amputation. The sensory thresholds and anatomical locations of the projected finger areas were found stable over 11 months. These results indicate that the PFM on the forearm of these forearm amputees could serve as a non-invasive neural interface to restore a natural sensory feedback from a prosthetic hand. Characterization of the evoked tactile sensation in forearm amputees will allow for a non-invasive, ETS-based closed-loop control of prosthetic hands. Preliminary work was also reported in conference proceedings elsewhere [45, 62].

2. Materials and methods

2.1. Subjects

Eleven volunteers (seven men and four women; mean age \(\pm SD = 49 \pm 12\)) were randomly recruited as recommended to us by Shanghai Liankang Prosthetics and Orthotics Manufacturing Co. Ltd, Shanghai, China (see table 1). The inclusion criterion was a unilateral forearm amputation and healthy condition. Nine of them had forearm amputation, one had elbow amputation, and the other one had congenital limb deficiency at the elbow. No other tests were given at the time of recruitment. In addition to amputee subjects, eight healthy and able-bodied volunteers (four men and four women, mean age \(\pm SD = 24 \pm 2\)) were also recruited from Shanghai Jiao Tong University as control group for the perceptual attribute study. All experiments were conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Human and Animal Experiments of the Med-X Research Institute of Shanghai Jiao Tong University. All participants were informed about all experimental procedures, and signed the informed consent form before participating.
Two experimental setups were designed for this study. The first experimental setup was a stump fixture apparatus used to quantify the stability of the PFM of ETS on the stump skin of the forearm for a specific amputee over time (figure 1(a)). The apparatus body was made of hard foam, upon which a groove was carved to fit the shape of the stump of the specific amputee. The apparatus body was fastened with a hard plastic bracket, and two holes with a distance of 20 (mm) were drilled in the middle of the top transparent panel. A laser pointer was placed in each hole. The two laser spots were used to pinpoint the origin of a coordinate system and a separate point in the X coordinate on the forearm stump. A coordinate system was thus set up by defining the Y coordinate in the perpendicular direction (figure 1(c)), which was used for measurement of location of PFM on the forearm of the amputee.

The second experimental setup for TENS is shown in figure 2, which was used in evaluating their perceptual attributes in both forearm amputees (figure 2(a)) and able-bodied subjects (figure 2(b)). We used the Master-9 Pulse Stimulator with two isolators (Iso-Flex, A.M.P.I. Company, Israel) to produce a multi-pulse \((n = 5)\) train of biphasic, rectangular current pulses (figure 2(c)). The nominal stimulation parameters were as follows: current amplitude was 3.75 (mA), pulse width of 200 (μs) with an inter-pulse delay of 200 (μs), and frequency of 50 (Hz). Two non-woven surface electrodes (25 cm in diameter, Shanghai Kangren Medical Science Instrument Equipment Co. Ltd) were used as reference and stimulation electrodes. In forearm amputees, the stimulation electrode was positioned at one of the MSPs within the PFM (figure 2(a)). The reference electrode was placed in a selected site at 10 (cm) above the elbow crease of the same stump as far as possible away from the upper arm muscles. While for able-bodied subjects, the simulation electrode was placed opposite to the reference electrode (figure 2(b)).

ETS could be experienced if a mechanical ‘touch’ was applied to finger-projected areas of the forearm amputees’ stump [37, 45, 46]. The first experiment was aimed at identifying all possible ETS sites on the entire stump skin by mechanically ‘touching’ the skin using a stylus with a globular head of 2 mm in diameter (figure 1(b)), so as to obtain a complete distribution of ETS on the stump skin of the forearm in each amputee. We also tested the skin areas on their face and neck in each amputee, and asked them if they had the similar ETS on other parts of their body, such as trunk and contralateral limb. Ten of our amputees reported finger sensation only in the forearm stump skin, but not in other parts of the body.

The experimental protocol for identifying PFM of ETS was as follows: (1) The subject sat in a chair in a comfortable position with his/her stump placed in the assigned position, then the targeted skin area was cleaned with alcohol wipes; (2) A survey was conducted about subject’s history of amputation, phantom sensation (or pain) and use of prosthetic devices (see summary in table 1); (3) Then we used a test stylus with a globular head of 2 mm in diameter to touch the forearm stump skin between the tip of the stump and the elbow, as shown figure 1(b). The amputee responded to the touch by identifying which finger was felt. A contiguous outline of the whole ETS sites (from subject’s personal description) was marked with color pens, which corresponded to the sensation of specific fingers by stylus “touch”. The contiguous area of the whole ETS site was referred to as PFM, which consisted of the independent finger-projected areas. The MSPs of each finger-projected area was then labeled with a cross symbol. The PFM of Subject 6 was shown in figure 1(c). To eliminate the effect of vision, the subject’s eyes were covered with an eyeshade throughout the procedure of Step 3 in the experiment. (4) The subject was asked to reconfirm the PFM using the same stylus by his/her own contralateral hand. During this experiment, several
The objective of this psychophysical experiment was to identify typical sensory modalities evoked with TENS and to quantify corresponding thresholds and ranges of modulation on the MSPs of the PFM. Parameters modulated were current amplitude, pulse width and frequency. In general, six sensory modalities of ETS could be perceived with increasing stimulation intensity: touch, pressure, pressure and buzz, pressure and vibration, pressure and numbness, and tingling and pain.

The protocol of this experiment was as follows: (1) after the PFM was identified, the subject sat in a chair comfortably with his/her stump placed in the assigned position. The targeted skin area for stimulation electrodes was cleaned with alcohol wipes. (2) The stimulation electrode was attached to the MSPs of the selected finger-projected area, and the reference electrode to the assigned position on the upper arm as in figure 2(a). (3) Stimulation of each finger-projected area constituted one session of the experiment, in which only one kind of parameter, i.e., current amplitude, pulse width, or frequency, were adjusted respectively in a random order between zero and its maximal value, while the other two parameters remained at the nominal values. The maximal value was set at the level where tingling and pain sensation was perceived. The intervals of parameter change were determined according to the minimal-change psychophysical method [63], which were 0.125 (mA) for current amplitude, 5 (μs)–20 (μs) for pulse width, and 1 (Hz)–20 (Hz) for frequency. Variable interval was used in order to go through all sensory modalities. (4) With one set of selected parameters, the subject was stimulated for 3 s, and then asked to describe the sensory feeling produced by the stimulation. We recorded the matched modality, gradation levels and values of stimulation parameters.

In all stimulation trials, caution had been taken not to exceed the upper limit parameters of stimulation that produced tingling and pain sensations. Meanwhile, we were also careful not to induce any muscle contraction during stimulation at both stimulation and reference electrode sites. A 10–15 min intermittent break was given between two sessions of experiments to allow the subject to relax, and to avoid habituation of the receptors in the skin during repeated stimulation trials.

In this experiment, the measurement of thresholds of sensory modalities was repeated three times for each finger-projected area in nine forearm amputees (except for Subjects 7 and 11, see below for explanation). The threshold data of one sensory modality of all nine amputees were lumped to calculate a mean threshold value and a range of modulation for each finger-projected area of thumb, index, middle, ring, and little fingers. All sensory modality attributes with modulations of current amplitude, pulse width, and frequency were shown in form of boxplot (figure 4).

In order to compare perceptual attributes with TENS in normal skin, the same psychophysical experiment was performed on the upper arm normal skin of eight able-bodied subjects. The procedure described in above was followed. Sensory modalities in able-bodied volunteers were quantified similarly as in forearm amputees. But the tactile sensation produced in able-bodied subjects could not be associated to any specific fingers [62]. Perceptual thresholds of each
sensory modality with current amplitude, pulse width, or frequency modulations were averaged for all able-bodied subjects and forearm amputees. Two-way ANOVA analysis was performed to detect inter-block difference on the same sensory modality between able-bodied and amputee groups, followed by Bonferroni correction used for the post hoc pairwise comparisons (figure 5).

Amputee Subject 11, with congenital forearm loss, was excluded from all stimulation tests above due to lack of ETS. Amputee Subject 7, whose amputation was at the elbow joint, reported weak ETS for thumb and little finger with no distinctive sensory modality. Thus, data obtained in Subject 7 was also excluded in statistical analysis.

2.5. Stability evaluation for the ETS

The purpose of this experiment was to evaluate the stability of the ETS concerning the anatomical and perceptual threshold changes in the PFM over time. The stability evaluation experiment was conducted in five forearm amputees (Subjects 1, 4, 5, 6, and 9), who were willing to participate in this evaluation. The whole evaluation was performed bimonthly during a period of 11 months. The procedure of this experiment was as follows: (1) for stability evaluation of finger-projected area, a stump fixture apparatus described in experimental setup (figure 1(b)) was made specifically for the selected amputee. The PFM of the forearm amputee was identified using the protocol described in section 2.3. The MSPs of each finger-projected area was identified and marked with a cross. The coordinate system was determined using the two laser reference points in the specific apparatus. Then the inter-distance between any two of the MSPs, as well as the distances between each MSPs and the two laser reference points, was measured using a flexible tape with a minimum scale value of 1 mm. Each measurement was repeated three times, and an average value was used in the following calculation of coordinates. The multiple distance measurements between the MSPs and between the laser reference points were converted to the coordinate values by triangulation. The variability of the MSPs indicated the stability of PFMs over the course of 11 months (figure 6 and table 3). (2) Stability evaluation of sensory threshold was also evaluated bimonthly. In this evaluation, the protocol described in session 2.4 was followed, and the current perception threshold of six sensory modalities on the MSPs of thumb-projected area was measured with ten repetitions in each measurement. The averaged threshold values over the period of 11 months were used to assess the stability of perceptual thresholds (figure 7).

3. Results

3.1. Distribution of ETS on the stump skin of forearm amputees

The phenomenon ETS was tested in the entire stump skin area of 11 amputee subjects using mechanical ‘touch’ by a test stylus. We found that the finger-projected areas of thumb and little finger were always towards the radial and ulnar sides, lateral to the palmar side, as shown in figure 3. The projected areas of index, middle, and ring fingers were always on the palmar side. We did not find any clear finger-projected area on the dorsal side of the stump skin.
The perceptual intensity levels and distribution of independent finger-projected areas on the stump skin appeared to be related to the amputation level (or length) at forearm (see details in table 2). Representative PFM of the ETS were portrayed in figure 3. In seven of the subjects (1, 2, 4, 5, 6, 8, and 9), whose forearm stump lengths were relatively long, independently long-striped areas (∗) of projected thumb (I), index (II), middle (III), ring (IV), and little fingers (V) could be identified on their stump skin (see cross-section C-C in figure 3), except for Subject 2, whose projected area for the ring finger was not found on his stump skin. While in Subjects 3 and 10, whose residual stump lengths were relatively short compared to others, independent areas of projected index (II) and ring fingers (IV) were missing on their stump skin (see cross-section B-B in figure 3). In Subject 7, whose amputation was at the elbow joint, only two small circular areas (∗) of thumb (I) and little finger (V) could be identified with weak ETS (see cross-section A-A in figure 3). For subject 11, no ETS could be found on the entire stump skin.

It can be seen from figure 3, the more distal amputation level was, the more detailed representation of finger digits could be found in the PFM. Especially at cross-section C-C (close to wrist amputation), the most sensitive point of each finger-projected area was labeled by a cross, and this area was found to correspond to fingertip of the first digit indicated by ‘1’ with blue color. The second area (labeled with ‘2’) corresponded to the second digit of the finger with a reduced sensitivity, and the third area (labeled with ‘3’) corresponded to the third digit of the finger with a further reduced sensitivity. The digit specificity of ETS was preserved in those subjects with relative distal forearm amputation (signified with long forearm stump length). While for Subjects 3 and 10 with proximal amputation, their PFM consisted of discontinuous small circular area and they could only perceive ETS specific to fingers.
eight able-bodied subjects

six different kinds of sensory modalities between normal skin of

subjects. The lumped results are pre-

We evaluated the sensory modalities and perceptual thresh-

3.2. Perceptual attributes of sensory modalities with TENS

Figure 5. Results of two-way ANOVA test. The mean thresholds of six different kinds of sensory modalities between normal skin of eight able-bodied subjects (control group) and MSPs of nine forearm amputees in the finger-projected areas were compared. (a) Perceptual thresholds of different sensory modalities in current amplitude modulation. (b) Perceptual thresholds of different sensory modalities in pulse width modulation. (c) Perceptual thresholds of different sensory modalities in frequency modulation. N indicates the total number of subjects in each group. ‘#’ denotes that no significant difference is detected (P 0.05); ‘*’ indicates that significant difference is detected at 0.01 P < 0.05; and ‘**’ indicates highly significant difference at statistical level P < 0.01. The mean value and one standard deviation of threshold correspond to the height and the error of the bar.

3.2. Perceptual attributes of sensory modalities with TENS

We evaluated the sensory modalities and perceptual thresholds of ETS with TENS in nine forearm amputees on the most sensitive points of their PFM. The lumped results are presented in figure 4 with the form of boxplot, in which two of the subjects did not have projected area for the index finger (n = 7) and three of them were without projected area for the ring finger (n = 6).

In general, six sensory modalities can be perceived by forearm amputees in the order of touch, pressure and buzz, pressure and vibration, pressure and numb, and tingling and pain with modulation of current amplitude, pulse width, or frequency (figure 4). It is shown that current amplitude and pulse width modulations yielded a proportionally increasing threshold order with increasing stimulus strength and a uniform range of modulation (figures 4(a) and (b)). However, frequency modulation appeared to have a wider range of threshold distribution (figure 4(c)). All subjects could clearly distinguish the first four sensory modalities. The ‘touch’ was perceived by amputees as an intermittent ‘light touch’, and the ‘pressure’ was perceived as a continuous touch with a pressing force. A couple of subjects had a very high tolerance to ‘pressure and numb’ and ‘tingling and pain’ sensations, so that the thresholds of these two kinds of modalities could not be determined at maximal capacity of the stimulator.

Perceptual threshold comparison of six kinds of sensory modalities between the most sensitive finger-projected areas in forearm amputees and normal skin in able-bodied subjects was presented in figure 5. The able-bodied subjects perceived the similar six kinds of sensory modalities by modulating the same three types of stimulation parameters of TENS as well as forearm amputees. However, the perceptual thresholds of normal skin were generally lower than those at the most sensitive finger-projected areas of forearm amputees. Two-way ANOVA test results confirmed that the mean thresholds between normal skin on able-bodied subjects and finger-projected areas of forearm amputee were significantly different (**) for all sensory modalities, but with no significant differences (#) for ‘touch’ with current amplitude modulation (figure 5(a)). With pulse modulation, the mean thresholds were significantly different in all sensory modalities (figure 5(b)). However, there were no significant differences
in the mean thresholds of ‘pressure and buzz’ and ‘pressure and vibration’ with frequency modulation (figure 5(c)).

3.3. Anatomical and threshold stabilities of ETS over time

Anatomical locations of projected finger maps and threshold attributes of ETS were monitored to evaluate their changes over time in five forearm amputees. Anatomical changes of the five most sensitive points representing five independent finger-projected areas were monitored bimonthly over a period of 11 months to verify the stability of the projected finger map. Typical variations in anatomical position of the five most sensitive points in the thumb-projected area relative to the two fixed reference points (O1, O2) for Subject 6 were presented in figure 6. Eleven-month measurements indicated that anatomical positions of the five most sensitive points were confined within an area defined by the 95% confidence ellipses, which had a maximal long axis of about 10 mm. Variations of the five most sensitive points for all five participants (subject 1, 4, 5, 6, and 9) were summarized in table 3. Anatomical changes of each finger-projected point were described with the major and minor axes of the corresponding confidence ellipse. It can be seen that the maximum variations in the major and minor axes were 10.7 mm for index-projected area and 7.1 mm for thumb-projected area of Subject 9, respectively.

The perceptual thresholds of six kinds of sensory modalities on the most sensitive point of thumb-projected area in five forearm amputees were monitored bimonthly over a period of 11 months. The results were presented in figure 7 for each subject, respectively. For all amputee subjects, the maximal error bar (one standard deviation) in threshold measurements was quantified to be 0.043 \( \times 10^{-2} \text{ mA cm}^{-2} \) in current density with ten repetitions. For each forearm amputee, the overall variation in threshold of each sensory modality was relatively small, maintained within a narrow range over the course of 11 months (table 4).

4. Discussion

This study evaluated and characterized the phenomenon of ETS on the palmar and lateral (radial and ulnar) sides of stump skin in forearm amputees using TENS. TENS has long been considered as a non-invasive way to establish a communication between prosthetic rehabilitation devices and human \([48–51, 56]\). TENS can generate touch and proprioceptive sensations in missing limbs of amputees and rubber hand illusion in able-bodied subjects \([51, 55, 58, 59]\). The number of stimulation pulse and specific stimulation sites on the forearm could be used to encode the opening of prosthetic hands and finger position in able-bodied subjects through imagery association, respectively \([54]\). Usually, subjects can

Figure 7. Perceptual threshold variability of the most sensitive point of the thumb-projected area over time. The thresholds of six kinds of sensory modalities were monitored using current amplitude modulation in 5 forearm amputees (1, 4, 5, 6 and 9) over a period of 11 months at a bimonthly interval.
be trained to interpret the information encoded in the cutaneous stimulation with high spatial acuity, but relatively low temporal resolution, because of limited bandwidth of information transmission. The variable skin impedance on different subjects would also add to perceptual fluctuation of stimulation under different skin conditions [50]. Particularly for refined sensory feedback in a prosthetic hand, transmitting specific tactile information from a specific finger requires encoding separate channels ofelectrocutaneous stimulation. This requires quantification of thresholds of sensory modalities and training to discriminate the encoded information in TENS for an amputee. In this study the perceptual attributes obtained in nine forearm amputees (figure 5) provides the essential information to guide the choice of stimulation parameters for TENS.

The characterization of ETS is significant in that it strongly demonstrates the plausibility of establishing a finger-specific communication between prosthetic hands and forearm amputees. In the study, we found that the skin area around the palmar and lateral (radial and ulnar) sides of the forearm stump (close to wrist) had five independent finger-projected areas related to the anatomical distribution of actual hand fingers as shown in figure 3(c). On each finger-projected area, both mechanical ‘touch’ and TENS could produce a natural sense of the corresponding missing finger of the forearm amputee. The ETS induced by TENS could further distinguish finger digits by these forearm amputees with more distal amputation to the wrist. The projected finger map on forearm stump skin was found related to amputation level and residual stump length (figure 3 and table 2). Seven of our subjects (1, 2, 4, 5, 6, 8, and 9) with relatively long stump lengths (table 1) showed a relatively complete projected finger map with five independent finger-projected areas, except for Subject 2 having no ring finger sensation. For Subjects 3 and 10, who had shorter stump lengths (table 1), only three finger-projected areas for thumb, middle and little fingers could be identified. The ETS for index and ring fingers could not be elicted by stimulating stump skin. For Subject 7, who had a near elbow amputation, only slight sensation of thumb and little finger remained with TENS. Interestingly, Subject 11, who had congenital forearm deficiency, showed no evidence of ETS, which is in accordance with the conclusions in the literature [61, 64]. This projected finger map of ETS forms a non-invasive interface for transmitting finger-specific tactile information in a subpopulation of forearm amputees who possess this somatotopic formation of ‘hand’ on the forearm stump skin.

The results of long-term evaluation over 11 months (figures 6 and 7, tables 3 and 4) indicated that the finger-projected area is stable in its somatotopic location on the stump skin and in perceptual thresholds of sensory modalities. The finding is corroborated by neurophysiological evidence that suggests reinnervation of the stump skin receptors by sensory fibers supplying the original hand fingers [65–67]. This implies that ETS and the formation of projected finger map on the stump skin are likely due to sprouting of the peripheral nerve that originally innervated the missing hand into stump skin receptors after amputation. Navarro et al [67] illustrated that transected peripheral nerve fibers could sprout into and reinnervate a target organ.

**Table 2. ETS in amputee subjects.**

| Forearm Stump lengtha (cm) | Thumb | Index | Middle | Ring | Little | Anatomical projection levelsb and shapec |
|---------------------------|-------|-------|--------|------|--------|----------------------------------------|
| Subjects                  | (I)   | (II)  | (III)  | (IV) | (V)    |                                        |
| 1                         | √(++) | √(+)  | √(+  ) | √(+  ) | √(+  ) | 2(★)                                  |
| 2                         | √(++) | √(+)  | √(+  ) | √(+  ) | ×      | 2(★)                                  |
| 3                         | √(++) | ×     | √(+  ) | ×     | √(+  ) | 1(*)                                  |
| 4                         | √(++) | √(+)  | √(+  ) | √(+  ) | √(+  ) | 2(★)                                  |
| 5                         | √(++) | √(+)  | √(+  ) | √(+  ) | √(+  ) | 2(★)                                  |
| 6                         | √(++) | √(+)  | √(+  ) | √(+  ) | √(+  ) | 2(★)                                  |
| 7                         | √(++) | ×     | ×      | ×     | ×      | 0                                     |

a Forearm stump length of a forearm amputee that was used to signify his (her) amputation level (how distal or proximal to the missing hand) was referred to distance from elbow joint to stump terminal in centimeter.

b √ denotes whole finger-projected area; ‘1’ denotes whole finger representation in the finger-projected area; ‘2’ denotes digit specific representation in the finger-projected area (see figure 3).

c × denotes PFM consisting of discontinuous small circular area; ‘★’ denotes PFM consisting of long-striped finger-projected area (see figure 3).
This may explain why the projected finger map on the forearm stump skin (figure 3(c)) is stable in its anatomical location over time (figures 6 and 7, table 4), and has the similar sensory modalities as those at the normal skin (figure 5). The stable nature of ETS in the stump skin may, therefore, be suitable to serve as a site of noninvasive interface to provide sensory feedback from prosthetic hand to amputees.

Currently, TENS is mainly used to reduce phantom pain or stump pain due to amputation [55–57], or induce a sense of perceptual embodiment in able-bodied subjects or amputees [58, 59]. To our knowledge, this is a pioneer study to quantify multisensory modalities on normal skin and PFM in the stump skin. The multisensory modalities of ETS with TENS below pain threshold could be useful in encoding different aspects of sensory information for prosthetic hands. It is clear from figures 4–6, that sensory information could be reliably encoded using three modes of modulation, i.e., current amplitude, pulse width, and frequency. Since sensory intensity is more linearly correlated with current amplitude and pulse width, a discernable parameter range with these modulation modes can be easily programmed in TENS. In the sensation produced by TENS, a large range of pressure sensation is mixed with other sensation modalities, such as buzz, vibration, and numb. The mixed modality of sensation may be possibly caused by simultaneous recruitment of a variety of skin receptors with small receptive field under the same electric field of TENS. Perhaps, a finer electrode array together with the combination of the three modes of modulation could be utilized to achieve more selective activation of skin receptors, so as to minimize the compounding effects of sensation. However, the multiple modalities of sensation quantified in this study may be useful to encode multiple aspects of sensory information. For example, touch and pressure is critical for the amputee to detect whether prosthetic fingers are in contact with external objects. In addition, the sensation of buzz and vibration could be used for encoding slip information that is critical to maintain grasp of an object.

The ETS requires an external physical stimulus to elicit. It is a different sensation from the phantom limb sensation (PLS) [60, 61], which requires no physical stimulus, and is often accompanied by phantom pain. These two types of sensation may also have different origins that affect the somatosensory cortex [60, 68–72]. Results presented here support the hypothesis that ETS is caused by activation of peripheral sensory nerves that originally innervated the specific fingers before amputation. This unique nature of ETS allows us to develop a feedback system using TENS to convey external tactile information from prosthetic fingers via the finger-projected area to the sensory cortex of the amputees, so that the tactile information coming from specific fingers can be discriminated. We have recently developed an multichannel ETS-based prototype system for sensory feedback [73] to test multichannel effects. Preliminary tests in amputee subjects indicated that the amputees could perceive which fingers were being touched with a high degree of accuracy. This result is encouraging for future development of an ETS-based sensory feedback for a subpopulation of forearm amputees. Furthermore, a multichannel electrode array will be designed to achieve the high spatial resolution in tactile sensory feedback for the ETS-based prosthetic hand.

| Subjects | Thumb | Index | Middle | Ring | Little |
|----------|-------|-------|--------|------|--------|
|          | major axis (mm) | minor axis (mm) | major axis (mm) | minor axis (mm) | major axis (mm) | minor axis (mm) | major axis (mm) | minor axis (mm) | major axis (mm) | minor axis (mm) |
| 1        | 9.7   | 6.2   | 9.3    | 5.8  | 9.1    | 6.0    | 8.9    | 5.2  | 9.5    | 5.5   |
| 4        | 9.6   | 5.9   | 10.6   | 5.6  | 9.0    | 5.5    | 7.5    | 5.8  | 8.4    | 7.0   |
| 5        | 9.6   | 5.7   | 8.8    | 5.2  | 9.7    | 4.8    | 8.8    | 4.5  | 7.7    | 4.5   |
| 6        | 10.5  | 6.2   | 10.4   | 6.1  | 9.5    | 6.1    | 9.4    | 5.4  | 9.5    | 6.7   |
| 9        | 9.5   | 7.1   | 10.7   | 4.6  | 8.9    | 4.5    | 10.2   | 6.0  | 9.2    | 6.8   |

Table 3. Summary of anatomical variations* of the MSPs*. To our knowledge, this is a pioneer study to quantify multisensory modalities on normal skin and PFM in the stump skin. The multisensory modalities of ETS with TENS below pain threshold could be useful in encoding different aspects of sensory information for prosthetic hands. It is clear from figures 4–6, that sensory information could be reliably encoded using three modes of modulation, i.e., current amplitude, pulse width, and frequency. Since sensory intensity is more linearly correlated with current amplitude and pulse width, a discernable parameter range with these modulation modes can be easily programmed in TENS. In the sensation produced by TENS, a large range of pressure sensation is mixed with other sensation modalities, such as buzz, vibration, and numb. The mixed modality of sensation may be possibly caused by simultaneous recruitment of a variety of skin receptors with small receptive field under the same electric field of TENS. Perhaps, a finer electrode array together with the combination of the three modes of modulation could be utilized to achieve more selective activation of skin receptors, so as to minimize the compounding effects of sensation. However, the multiple modalities of sensation quantified in this study may be useful to encode multiple aspects of sensory information. For example, touch and pressure is critical for the amputee to detect whether prosthetic fingers are in contact with external objects. In addition, the sensation of buzz and vibration could be used for encoding slip information that is critical to maintain grasp of an object.

The ETS requires an external physical stimulus to elicit. It is a different sensation from the phantom limb sensation (PLS) [60, 61], which requires no physical stimulus, and is often accompanied by phantom pain. These two types of sensation may also have different origins that affect the somatosensory cortex [60, 68–72]. Results presented here support the hypothesis that ETS is caused by activation of peripheral sensory nerves that originally innervated the specific fingers before amputation. This unique nature of ETS allows us to develop a feedback system using TENS to convey external tactile information from prosthetic fingers via the finger-projected area to the sensory cortex of the amputees, so that the tactile information coming from specific fingers can be discriminated. We have recently developed an multichannel ETS-based prototype system for sensory feedback [73] to test multichannel effects. Preliminary tests in amputee subjects indicated that the amputees could perceive which fingers were being touched with a high degree of accuracy. This result is encouraging for future development of an ETS-based sensory feedback for a subpopulation of forearm amputees. Furthermore, a multichannel electrode array will be designed to achieve the high spatial resolution in tactile sensory feedback for the ETS-based prosthetic hand.

| Subjects | Touch | Pressure | Pressure & buzz | Pressure & vibration | Pressure & numb | Tingling & pain |
|----------|-------|----------|----------------|---------------------|----------------|---------------|
| 1        | 0.33 ± 0.01 | 0.43 ± 0.01 | 0.56 ± 0.01 | 0.63 ± 0.01 | 0.73 ± 0.01 | 0.90 ± 0.02 |
| 4        | 0.19 ± 0.01 | 0.23 ± 0.01 | 0.33 ± 0.01 | 0.45 ± 0.01 | 0.64 ± 0.02 | 0.92 ± 0.01 |
| 5        | 0.19 ± 0.01 | 0.25 ± 0.02 | 0.33 ± 0.01 | 0.43 ± 0.01 | 0.66 ± 0.03 | 0.98 ± 0.01 |
| 6        | 0.19 ± 0.01 | 0.25 ± 0.01 | 0.35 ± 0.01 | 0.46 ± 0.01 | 0.55 ± 0.01 | 0.73 ± 0.01 |
| 9        | 0.16 ± 0.01 | 0.23 ± 0.02 | 0.37 ± 0.02 | 0.50 ± 0.02 | 0.73 ± 0.03 | 0.99 ± 0.02 |

Table 4. Mean threshold of six sensory modalities over 11 months in five forearm amputees. This may explain why the projected finger map on the forearm stump skin (figure 3(c)) is stable in its anatomical location over time (figures 6 and 7, table 4), and has the similar sensory modalities as those at the normal skin (figure 5). The stable nature of ETS in the stump skin may, therefore, be suitable to serve as a site of noninvasive interface to provide sensory feedback from prosthetic hand to amputees.
5. Conclusion

The ETS induced by TENS on the finger-projected areas of forearm amputees was characterized and evaluated in this study. The projected finger map on the palmar and lateral (radial and ulnar) sides of the skin of relative long forearm stump can provide detailed sensation with respect to distinct fingers or digits. The projected finger map was found to be stable in anatomical location and perceptual threshold within a period of 11 months. The similar sensory modalities evoked with TENS as those of stimulating normal skin indicate that forearm amputees may learn to discern the contents of encoded feedback information through proper training. The non-invasive nature of this approach may potentially be advantageous for providing a neural interface for engineering a natural sensory feedback from prosthetic hand to forearm amputee. Future studies may be directed to establish and integrate the ETS-based sensory feedback system for closed-loop control of prosthetic hands, and to further understand the central and peripheral neural mechanisms of ETS.

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