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Towards a tactile artificial hand

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A hand prosthesis has an important role in reducing the negative effects of an amputation. However, a prosthetic hand can never replace the human hand. The lack of sensory feedback is one important factor that still is missing. The overall aim of this work was to further develop and implement a non-invasive concept for sensory feedback in hand prostheses. The feedback is transferred via the phantom hand map on the skin of the forearm.

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Towards a tactile artificial hand

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Ulrika Wijk

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DOCTORAL DISSERTATION

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Abstract

Amputation of a hand is a life-changing event, and the loss of motor and sensory functions leads to disability and has devastating effects on the individual. What is normally performed using two hands must be solved with only one, and the loss also affects body balance and body posture. In addition, amputation of a hand has psychological effects, and has an influence on social life, participation, and identity. A hand prosthesis has an important role in reducing the negative effects of an amputation. However, rejection of the prosthesis is common, due to expectations that are too high to be fulfilled and limitations in technical solutions, with possible overuse of the remaining hand as a consequence.

The overall aim of this work has been to further develop and implement a non-invasive concept for sensory feedback in hand prostheses. Specific aims were to explore forearm amputees' views of prosthesis use and perception of sensory feedback, to investigate the sensory qualities of phantom hand maps (PHMs) in amputees, to determine whether it is possible to learn to associate sensory stimuli on the forearm skin to specific fingers in healthy non-amputee volunteers, and lastly to evaluate a non-invasive sensory feedback system for a prosthetic hand in the everyday lives of forearm amputees.

Initial findings indicated that today's myoelectric hand prostheses allow the wearer to experience agency—the experience of controlling one's own motor acts—but the lack of sensory feedback appears to limit achievement of a sense of body ownership of the prosthesis.

A PHM on the residual limb is a phenomenon seen in many amputees, and when it is touched it generates a perception of touch on the hand that no longer exists. The neurobiological basis of the phenomenon is not fully understood, but it probably originates from plastic changes within the brain following amputation and also changes in peripheral nerves. We have demonstrated that the PHM has better discriminative sensibility than the corresponding skin area on the uninjured arm. Thus, the PHM is an ideal target for a non-invasive concept to achieve sensory feedback in prostheses. Given that not all amputees have a PHM, it was also found that it is possible to learn to associate stimuli on the skin of the forearm with specific fingers, i.e. it is possible to create a PHM. An evaluation of the non-invasive sensory feedback system based on the PHM in a prototype prosthesis during four weeks of use at home was also performed. The participants experienced the sensory feedback as being real, which gave a strong feeling of being complete, linked to body ownership. However, this was not verified by the quantitative measurements.

This thesis shows that the PHM may be a possible target for non-invasive somatotopically matched sensory feedback systems in hand prostheses. The fact that it is possible to learn to associate sensory stimuli on the skin of the forearm to specific fingers also appears promising for future development of sensory feedback systems, e.g. for congenital amputees or amputees who do not experience a PHM.
The long-term goal is that this non-invasive concept for sensory feedback will be applicable to several types of hand prosthesis, for various levels of amputation.

Key words: amputation, upper limb, phantom hand map, sensory feedback, referred sensation, hand prosthesis, body ownership, tactile sensation

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“As far as we know there is no limit to the power of the human mind
in designing its unique patterns of wisdom and love.”
Marian Diamond

Table of Contents

Abstract

Amputation of a hand is a life-changing event, and the loss of motor and sensory functions leads to disability and has devastating effects on the individual. What is normally performed using two hands must be solved with only one, and the loss also affects body balance and body posture. In addition, amputation of a hand has psychological effects, and has an influence on social life, participation, and identity. A hand prosthesis has an important role in reducing the negative effects of an amputation. However, rejection of the prosthesis is common, due to expectations that are to high to be fulfilled and limitations in technical solutions, with possible overuse of the existing hand as a consequence.

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List of papers

I. **Forearm amputees' views of prosthesis use and sensory feedback.**
Wijk U, Carlsson I.
Journal of Hand Therapy. 2015, 28 (3); 269-277.

II. **Sensory qualities of the phantom hand map in the residual forearm of amputees.**
Björkman A, Wijk U, Antfolk C, Björkman-Burtscher I, Rosen B.
Journal of Rehabilitation Medicine. 2016, 48 (4): 365-370.

III. **Touch on predefined areas on the forearm can be associated with specific fingers: Towards a new principle for sensory feedback in hand prostheses.**
Wijk U, Svensson P, Antfolk C, Carlsson I K, Björkman A, Rosén B.
Journal of Rehabilitation Medicine. 2019, 51(3): 209-216.

IV. **Sensory feedback in hand prostheses: a prospective study of everyday use.**
Wijk U, Carlsson I K, Antfolk C, Björkman A, Rosén B. Submitted.

Permission to reprint the articles has been granted by the publishers.

Thesis at a glance

Paper I. Forearm amputees' views of prosthesis use and sensory feedback.

There is a need to further investigate amputees’ experiences of prosthesis use and the lack of sensory feedback in today’s hand prostheses.

Methods: Thirteen individuals with unilateral congenital or traumatic forearm amputation participated in the study. The transcribed text from the semi-structured interviews was subjected to qualitative content analysis.

Results: The results could be divided into four main categories: Activity and participation, Perception of the “hand”, Body image, and Future expectations. Prostheses both facilitated and limited occupational performance. In some situations, when good sensibility was important, being without the prosthesis was preferred. Appearance was felt to be important for one’s identity and for integration into society. There was a feeling of agency regarding the prosthesis, but not of body ownership. There were future expectations concerning improved mobility, cosmetics, and sensory feedback.

Conclusion: There is a complex relationship between a prosthetic device and the wearer. Prostheses allow the wearer to experience agency, but it appears that the lack of sensory feedback limits achievement of a feeling of body ownership of the prosthesis.

Overview of the main categories and subcategories

Main category	Subcategory
Activity and participation	Prosthesis as a facilitating factor Prosthesis as a limiting factor
Perception of the ”hand”	Sensibility through prosthesis Grip control Compensation with vision/hearing Phantom phenomena
Body image	Proprioception Balance Appearance and symmetry Social interaction Body ownership Identity
Future expectations	Mobility Sensibility Appearance

Paper II. Sensory qualities of the phantom hand map in the residual forearm of amputees.

This was an evaluation of the sensory qualities of the phantom hand map (PHM), which is one aspect of referred sensations—specifically, the experience of touching the lost hand when touching specific areas of the skin on the residual arm.

Methods: Ten individuals with acquired unilateral transradial amputation and PHM participated. Touch threshold and discriminative touch were assessed in the phantom hand map on the residual arm, and compared with those in the contralateral arm. In addition, magnetic resonance imaging (MRI) was performed in two participants to evaluate the occurrence of neuromas relative to the PHM.

Results: Similar touch thresholds were seen in the phantom hand map and in the contralateral arm, but tactile discrimination was significantly better in the phantom hand map. No neuromas, individual cutaneous nerve branches, or sprouts were identified close to the PHM.

Conclusion: The superior tactile discrimination seen in the phantom hand map was interpreted as being based on adaptation within the brain, but this should be investigated further.

Touch threshold and discriminanitive touch in the PHM and at control sites on the contralateral arm

	PHM (median)	Contralateral arm (median)
SWM, g	0.008	0.008
2PD, mm	25 (10–40)	45 (12–60)
Localization, %	95%	

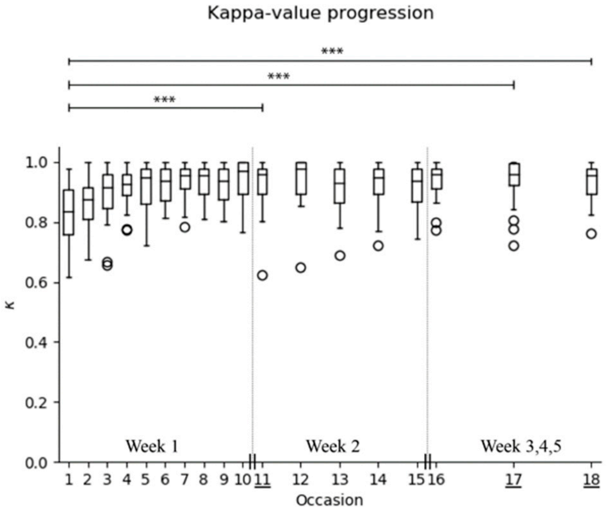
Paper III. Touch on predefined areas on the forearm can be associated with specific fingers: Towards a new principle for sensory feedback in hand prostheses

This was a study of whether touch on predefined areas on the forearm can be learned to be associated with specific fingers; i.e. can a “phantom hand map” be induced?

Methods: Thirty-one individuals with no neurological or physiological deficits were included. They underwent a computer-based sensory training period of two weeks, with follow-ups after one and two weeks of no training.

Results: Agreement between the stimulated areas and the individual’s response was high, with an improvement up to the third training occasion. The kappa score was stable at a high level for the rest of the period, and at follow-ups.

Conclusion: It is possible to learn to associate stimuli on the skin of the forearm to specific fingers, after a two-week training period. This may be important in the development of sensory feedback systems in hand prostheses.



Kappa-value progression
The box plot shows improvement (median kappa-values, 95% CI) in learning during the training period, on 18 occasions. The improvement was statistically significant between baseline and follow-ups on occasions 11, 17, and 18. ***$p < 0.001$.

Paper IV. Sensory feedback in hand prostheses: a prospective study of everyday use.

A prosthesis prototype including a non-invasive sensory feedback system was evaluated following use in daily life over 4 weeks.

Methods: Seven individuals with acquired unilateral transradial amputation were included. A mixed method was used, with subjective and objective assessments, and also semi-structured interviews that were subjected to directed content analysis.

Results: The results of the interviews showed that the sensory feedback was experienced as being real and gave a strong feeling of completeness, linked to body ownership. However, this was not verified in the quantitative measurements. There appeared to be no difference regarding performance during activity. Phantom pain was alleviated in four out of five patients who suffered from it.

Conclusion: The participants had positive subjective experiences, but this was not reflected by the quantitative measurements.

Abbreviations

2PD	Two-point discrimination
ACMC	Assessment of myoelectric control
ADL	Activities of daily living
CNS	Central nervous system
EMG	Electromyography
ICF	International Classification of Functioning, Disability, and Health
M1	Primary motor cortex
PHM	Phantom hand map
PLP	Phantom limb pain
PNS	Peripheral nervous system
S1	Primary sensory cortex
SWM	Semmes-Weinstein monofilament
TMR	Targeted muscle re-innervation
TSR	Targeted sensory re-innervation
VAS	Visual analogue scale

Introduction

A solution for non-invasive sensory feedback in hand prostheses, that aims to provide a perception of touch as close as possible to physiologically natural perceived sensation, has been on the agenda at the Department of Hand Surgery in Malmö for a long time. Over the years, interdisciplinary research has been undertaken under the leadership of Professor Göran Lundborg. The goal is having a true perception of touch that provides a conscious sensibility that approaches a feeling of body ownership of the prosthesis. The technical solution would preferably be non-invasive, simple, and durable, and should not interfere with the myoelectric, mechanical, or aesthetic functions of the prosthesis. A solution has been presented that employs a conscious sensory feedback system that goes beyond having an intrinsic loop only between sensors and motors in the prosthesis (3).

This PhD project has both technical and clinical aspects, and is a step towards achieving sensory feedback in hand prostheses that would be of importance in rehabilitation after amputation of the hand or arm.

The tactile hand

The hand is a sense organ, transferring tactile information about our surroundings to the brain. The hand is also an advanced tool with the ability to execute difficult tasks. The interaction between sensory and motor functions is the foundation for the functioning and skilfulness of the hand. The well-developed sensory and motor functions of the hand make it possible for it to make strong power grips and also to have delicate fine motor functions. With our hands, we can express ourselves, our identity, and our state of mind—so the hand is partly the basis of social interaction and communication between people (91).

The glabrous (hairless) skin of our hands is specialized in providing information to the brain so that high-definition neural images of what is being manipulated can be created (119). Hands in activity depend on functional sensibility, also called *haptics*, which refers to active exploration and recognition through touch (77). The ability to interpret and identify an object or a structure by just touching or manipulating it is termed stereognosis (119) or tactile gnosis (94).

The human nervous system

Anatomically, the nervous system consists of the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS includes the spinal cord and the brain. The brain comprises the *cerebrum*, the *corpus callosum*, the *cerebellum*, and the *brain stem*. It is in the grey matter in the outer layer of the brain—the *cortex*—that the cognitive abilities are based. Underneath the cortex is the white matter, which is mainly made up of myelinated axons that communicate with different brain regions. Deep inside the brain, in the mid-brain, is where the *thalamus* is located. The thalamus consists of grey matter, and functions as a relay station that processes tactile information before sending it on to the cortex (76).

The cortex can be divided into different regions depending on function. The primary sensory cortex (S1), where the processing of afferent sensory information takes place, is located in the gyrus postcentralis. The primary motor cortex (M1) is located close to S1, on the other side of sulcus centralis, in the gyrus precentralis. These two areas are closely connected, both anatomically and functionally (76) (*Figure 1*).

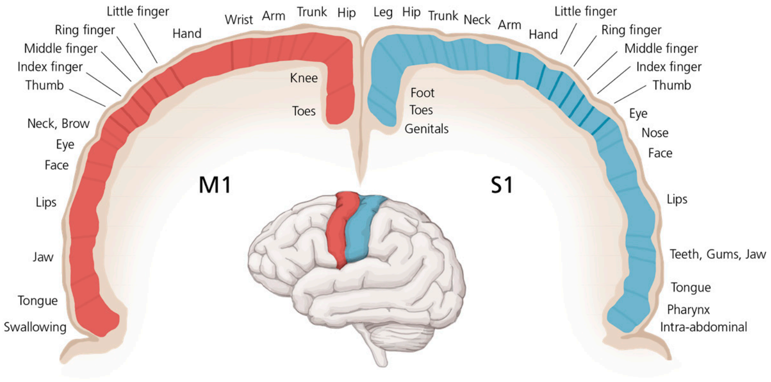


Figure 1. Cortical representation in M1 and S1, where the hand has a large representational area.
Illustration: Frida Nilsson, Media-Tryck.

The PNS consists of the receptors in the skin, peripheral nerves, and dorsal root ganglia located adjacent to the spinal cord. In the skin, four different types of mechanoreceptors register touch. Each type of receptor is used for registration of different types of touch: Merkel receptors (edges, points), Meissner receptors (lateral motion), Pacinian receptors (vibration), and Ruffini receptors (skin stretch, static stimulation). The mechanoreceptors differ in their response to stimuli, and slowly adapting receptors (Merkel and Ruffini) continue to respond to stimuli, whereas rapidly adapting receptors (Meissner and Pacinian) respond at the onset and cessation of stimulation. Due to these differences, both static and dynamic stimulation can be perceived. The receptive field of the mechanoreceptors varies in different parts of the body, and the smaller the receptive field the better the sensory perception. The fingers, toes, and lips are innervated with many mechanoreceptors that have small receptive fields—as compared to the forearm and back, where the mechanoreceptors have relatively large receptive fields. In the skin, there are also nerve fibres that do not end in a special receptor; these are referred to as free nerve endings, which are important for the sensation of pain and temperature (51, 76, 119), and even pleasant touch (146). Four different modalities of sensation have been defined: touch, temperature, nociception, and proprioception (76, 119).

From the mechanoreceptors in the skin, afferent impulses are mediated by the peripheral nerves to the sensory neurons in the dorsal root ganglia. From here, the tactile information is transferred in the dorsal columns to the medulla. Here, the axons decussate and the tactile information is sent further to the ventral posteriolateral nuclei of the thalamus. In the thalamus, the sensory signals are processed and sent on to the primary somatosensory cortex (S1). In S1 and higher order centres in the brain, the afferent impulses from the body become conscious perceptions. Other brain areas such as the secondary somatosensory cortex (S2) and the posterior insular cortex are also involved in processing some aspects of sensory information. Sensory information from the right hand is processed in the left, contralateral, hemisphere and vice versa (76, 119).

The S1 is subdivided into four regions called Brodmann’s area (BA) 3a, 3b, 1, and 2, and each area contains a representation of the body surface (somatotopy). BA 3b and BA 1 receive information from receptors in the skin and BA 3a and BA 2 receive proprioceptive information from muscles and joints, but there are extensive interconnections between the areas in processing afferent information. The number of neurons in S1 that process sensory information from a specific area of the skin is not proportional to the actual size, but rather to the amount of mechanoreceptors contained in that particular area or part of the body. This means that some areas of the skin are supplied with a very large number of neurons, i.e. have a large area in the cortex, whereas other areas are supplied with few neurons. The hand and face are supplied with a very large number of neurons, which is reflected in the fine sensibility in these areas. To illustrate the proportions of neurons supplying different areas of the skin, a “homunculus” (little man) picture has been created (51, 119) (*Figure 2*).

Illustration: Frida Nilsson, Media-Tryck.

Figure 2. The homunculus illustrates the sensory representation of body parts as proportions, corresponding to the amounts of neurons that handle sensory information in S1.

In contrast to the processing of sensory information, which is mainly done in S1 and S2, control of voluntary movement involves a large number of different areas of the brain, the motor network. This network involves the prefrontal areas, the premotor cortex, the primary motor cortex (M1), S1, the visual cortex, the basal ganglia, and the cerebellum to form a voluntary movement. A voluntary movement can be described as a set of sequential stages. It starts with deciding on the purpose or goal of the movement, e.g. grasping a glass of water. A motor plan is set based on information from memory, motor programs, vision, and proprioception—and finally the motor signal is sent, mainly from M1. The efferent signal is sent from the brain via the pyramidal tracts of the medulla oblongata in the brain stem, where it decussates to the contralateral side. It travels through the spinal cord and synapses to motor neurons in the ventral horn. From there, the signal is sent to motor terminal recipients—the muscles—and the glass of water is grasped (76, 119). Tactile information from the glass of water (shape, surface, weight, and the temperature of the glass) balances the grip forces that are adjusted instantaneously as required, due to rapid and continuous interaction between the hand and the brain.

The sense of touch is crucial for motor performance and motor learning (76). However, to execute a voluntary movement and to learn how to improve performance we use not only the sense of touch, but several senses. For example, amputees with myoelectric prostheses often use audio information from the motor of the prosthesis to help adjust the grip. One hypothesis is that if sensory feedback is added to a hand prosthesis, this should help to improve the motor performance.

Amputation of a hand

Amputation in the upper limb can either be acquired, as a result of a traumatic injury, or it can be a planned surgical intervention because of a malignant disease or an infection or vascular disease. Amputations can also be congenital, meaning that a person is born without a limb or part of a limb (congenital reduction deficiency / congenital limb deficiency). Experiences of an acquired amputation (as opposed to being born without a limb) vary. If acquired, something has been lost, but in the case of congenital reduction deficiency, this is the normal state of the individual. Even so, there can be functional limitations—or social considerations—in missing an arm, regardless of the cause (106). This thesis is mainly concerned with acquired amputations.

The main reason for acquired amputation in the upper limb is trauma, followed by cancer, infection, and vascular disease (79, 114, 155). Amputations in the lower limb are much more common than in upper limb, and of all amputations only 5% are estimated to be in the upper limb (9).

According to the National Board of Health and Welfare in Sweden (Socialstyrelsen), the prevalence of *traumatic* amputations in the upper limb in Sweden was 4.2 per 100,000 inhabitants in the years 2015–2017 (http://www.socialstyrelsen.se/statistik/statistikdatabas). The majority of traumatic amputations are at finger level, and complete loss of a hand affects less than 20 individuals per year (based on the period 1998–2006) (6). The population prevalence of acquired amputation of the hand or arm in Norway is 11.6 per 100,000 adults (114). In the USA in 2005, the estimated number of amputations in the upper limb was 541,000, 41,000 of which were major limb loss (through or proximal to the wrist) and 500,000 of which were minor limb loss (amputation of fingers or the whole hand). This is roughly equivalent to 13.6 major limb losses (hand or more) per 100,000 US citizens (155). In the International Statistical Classification of Diseases and Related Health Problems (ICD-10), amputations are classified either as traumatic and at different levels: ICD S48.0-48.9 (traumatic amputation at shoulder or upper arm level), S58.0-58.9 (traumatic amputation at forearm level), S68.0-68.9 (traumatic amputation of hand at wrist level), T11.6 (traumatic amputation in the upper limb, unspecified level); or as congenital: Q71.0-71.9 (congenital reduction deficiencies in the upper limb at different levels), Q73 (congenital reduction deficiency of unspecified extremity). The different anatomical levels of amputation in the upper extremity are shown in *Figure 3*.

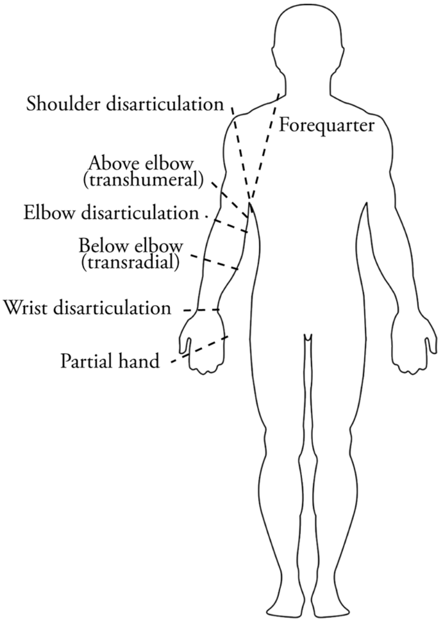


Figure 3. Amputation levels in the upper limb.
Illustration: Christian Antfolk.

Amputation of a limb can be one of the worst experiences imaginable. It is a catastrophic event that will have consequences for the rest of one's life. Emotions such as sadness and anger over losing a limb and the shock of the suddenly changed body image often follow an amputation. The body balance changes, and motor and sensory functions are lost—which affects the individual and changes his/her self-esteem (108).

The hand and the brain

Brain plasticity

The brain is not a static organ. It has a tremendous ability to change and adapt throughout one's whole lifetime, due for example to environmental demands, sensory inputs, learning, and injury—such as amputation. This dynamic ability to adapt is called brain plasticity (76).

Rapid plasticity can occur within minutes or hours after an injury. It is probably due to unmasking of pre-existing but inhibited synapses (16, 34, 119, 138). Plasticity can also be a slower process involving progressive changes over several months, and even years (34, 102). These slower changes include sprouting of axons and the formation of new synapses (142).

Many factors affect plasticity in the human brain, with age probably being the most important. The adult brain show less plasticity than the childhood brain, but the plastic capacity of the brain is never lost (101).

Brain plasticity is generally a positive adaptation, through compensation for new circumstances (119). However, brain plasticity can have negative consequences, i.e. it can be maladaptive, which is experienced by the patient as pain, e.g. phantom limb pain (PLP) after an amputation (44). Adaptive plasticity is a normal process whereby the brain adapts to practice and environmental demands. Plasticity is often driven by activity such as performing a sensory or a motor task repeatedly, which is called activity-dependent plasticity. This is the ability to improve certain skills through training (119), e.g. learning to play an instrument.

Injury-induced plasticity is another form of plasticity, based on changed afferent information that the brain receives. After an amputation, when sensory input is lost, the adjacent areas in S1 expand rapidly into the area that has lost contact with the peripheral body part. This means that neurons that used to respond to afferent information from the amputated part start processing afferent information from other areas of the skin, the arm, and the face (16, 34, 76, 128, 138, 147, 149). In addition, simulation of an amputation using local anaesthetic block of an individual finger in humans has been found to result in a rapid cortical expansion of the adjacent, unanaesthetized fingers. Along with these cerebral changes, tactile perception in the adjacent fingers improved (35).

Cerebral effects of an amputation

An amputation can be considered as the ultimate nerve injury. Within minutes or hours after amputation or nerve injury, the cortical area, formerly responding to signals from the amputated or injured nerve, is “taken over” by adjacent areas of the brain (102, 119, 121). Following amputation, changes also occur in both subcortical and thalamic areas (149). These plastic changes in the brain start very quickly after amputation, but changes also occur gradually over time—up to several years after the injury (102). In the early 1990s, Ramachandran et al. found that a sensation of the phantom hand could be evoked, directly after amputation, by touching the face (123)—which can be explained by the somatotopic representation of the body in the S1, where the face and the arm are adjacent to the hand. After the amputation, the neurons in S1 that previously received afferent information from the hand start to process afferent information from the face (121). Functional MRI (fMRI) has confirmed that neurons in the S1 that lose input from the hand start to respond to stimuli from the face and/or the residual limb (149). It has also been shown using fMRI on amputees that the cortical representation patterns are dependent on the amount of use of the residual arm. Those who used their intact hand more than the residual limb had increased representation of the intact hand (96), which is an illustrative example of activity-dependent plasticity.

Phantom phenomena

Phantom phenomena are defined as “the continuous awareness of a non-existent body part with specific form, weight, or range of motion” (125) and they are very common after a hand amputation (43, 69, 109). It has been reported that more than 80% of all upper limb amputees experience non-painful phantom sensations (62). The phantom limb can take a position as either relaxed, fixed, or distorted (67). Furthermore, phantom limb sensation is described as any sensation (except pain) originating from the lost hand (e.g. tingling, pressure, or itching) (52, 69, 109). The phantom limb awareness and/or phantom limb sensation can persist for several years after amputation (43, 69) and may even be experienced for decades (67). The phantom hand can be in any position, and is not dependent on the remaining hand and arm on the other side. Some amputees experience movement of the phantom hand, either voluntary movements or spontaneous ones as uncontrolled spasms (52, 126).

The mechanisms behind phantom phenomena are not completely understood, but phantom limbs occur in conditions with deafferentation, when parts of the PNS are disconnected from the CNS. It has been proposed that phantom phenomena originate from a combination of several mechanisms in peripheral nerves, from cortical reorganization of the somatotopical representation, and from pain memory (43, 109, 126). Neuronal activity at the level of the dorsal root ganglia could be another explanation. Moreover, peripheral phenomena such as regenerative sprouting of the injured nerve fibres and neuromas in the distal part of the residual arm, can influence the occurrence of phantom limb sensations (148).

There are several different types of phantom phenomena, such as telescoping, phantom limb pain, and referred sensation (43).

Telescoping

Telescoping of the phantom into the residual arm is a common phenomenon. It can be experienced as the phantom hand being attached directly to the residual arm, with part of the arm missing, or as the phantom hand having moved inside the residual arm (53, 60, 69, 126). The phenomenon often occurs early, within weeks, after the amputation, and it has been reported that 28–67% of amputees experience the phantom limb as being telescoped (52).

Phantom limb pain

Phantom limb pain (PLP)—“painful sensation referred to the absent limb” (110)—is common; it is assumed that between 50% and 80% of patients struggle with PLP after upper limb amputation (62, 69, 79, 109, 126). PLP is most often localized in the distal part of the limb: the fingers, the palm, and occasionally the wrist (67). Pain in the residual arm (stump pain) is also reported, and is described as a post-amputation pain that persists even after healing (69). Presence of stump pain is associated with increased levels of PLP (67), and when stump pain and PLP co-exist they can be difficult to differentiate (79, 109).

A positive correlation between PLP and cortical reorganization has been shown in an fMRI study; the degree of reorganization corresponded to the degree of PLP. Cortical reorganization was not seen to the same degree in those who did not experience PLP (44). Mirror therapy has been used to reduce the PLP, and hypothetically the reorganization. When observing the lost hand in a mirror, activity-dependent plasticity can be induced and the maladaptive cortical reorganization reduced (46). Even though there is some correlation between PLP and the degree of somatotopic reorganization, the causation is not clear (148) and the explanation with only maladaptive cortical plasticity as the origin for PLP has been discussed. Other explanations can be the absence of peripheral afferent information, as well as changed activity in the root ganglia (29). Also, the thalamus appears to play an important role in the experiencing of PLP (33). Tests with different types of anaesthesia (local, plexus, or epidural) to reduce PLP have not given clear results; this was successful in some amputees, but not in everyone (45). When local anaesthesia was administered in the area of the dorsal root ganglia, Vaso et al. (148) showed a positive effect on PLP. This highlights the complexity of phantom phenomena.

The phantom hand map

Another phantom phenomenon is the experience of referred sensation. This is described as a sensation from the phantom fingers when specific areas of skin are touched, most often on the residual arm or in the face; it is called the phantom hand map (PHM) (122). The theory behind the PHM is the cortical reorganization following an amputation; the cortical areas that used to respond to the amputated hand start to respond to skin areas adjacent to the amputation (*Figure 1*). This explains why the PHM most often occurs at these locations (122, 126). With fMRI, it has been possible to observe that stimulation of every experienced individual "finger" in the PHM on the forearm activates the cortical areas that usually correspond to the fingers (15).

Agency and body ownership

Agency

The feeling of initiating and performing a voluntary motor act, movement, or behaviour is referred to as the sense of agency (71, 144) and is defined as follows: "*The sense of agency is the feeling of making something happen. It is the experience of controlling one's own motor acts and, through them, the course of external events*" (61), and Haggard further states that "*the core of sense of agency, therefore, is the association between a voluntary action and an outcome*" (61). Self-recognition is to a large extent dependent on the experience of one's own actions and, along with body ownership, has been investigated in neuroscience and psychology for a long time—since they are core components of the conscious experience of self (48). In movement disorders, the sense of agency is disrupted and the loss can have major implications for quality of life (47). Sato et al. (2018) reported recently that agency as well as body ownership could be extended to an EMG-controlled robotic arm in amputees, suggesting that it is possible for amputees to alter the boundary of their body image to the tip of the prosthetic arm (131). The sense of agency has been demonstrated in experiments with a rubber hand. The position of the rubber hand was of importance. When in an anatomically correct position, the rubber hand was experienced as being part of the body and the feeling of agency was stronger compared to the situation where the rubber hand had an anatomically implausible position (75).

Body ownership

How we experience our own body is crucial for the conscious experience of ourselves (50, 71). The experience of the body being one's own is referred to as the feeling of body ownership (50, 75, 144). To achieve the experience of body ownership, the feeling of touch is crucial (17, 38-40). Collective tactile, proprioceptive, and visual information are put together to contribute a sensory image of one's own body (71). Botvinick and Cohen showed the importance of touch in their "rubber hand illusion" experiment. It is possible to experience a rubber hand as being one's own hand, when adding simultaneous stroking of the remaining hand that is covered (17). The "rubber hand illusion" has been tested on amputees with simultaneous stroking of the residual arm and a rubber hand, which also succeeded in evoking body ownership (39).

Body ownership and agency are often experienced simultaneously, but not necessarily. For an experience of body ownership, there is no need for self-generated movements, but instead it is enough with externally generated sensory inputs or passive movements (75, 144).

Consequences of a hand amputation

From a health perspective

The International Classification of Functioning, Disability, and Health (ICF) is the World Health Organization's framework describing health and health-related conditions (153). Health is defined by the World Health Organization as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (https://www.who.int/). The ICF has two parts, with two components each (*Figure 4*): (1) Functioning and disability, (a) body functions and body structures, (b) activity and participation; and (2) Contextual factors, (a) environmental factors, (b) personal factors. Every component can be expressed in both a positive and a negative way. "Body functions" are the physiological functions of body systems, while "body structures" are the anatomical parts of the body. "Activity" is the performance of a task or action and "participation" stands for involvement in a life situation. The "environmental factors" cover the physical, social, and attitude-based environment in which a person lives his/her life. The "personal factors" are the characteristics of the individual, such as gender, age, lifestyles, education etc. Health and health-related conditions can be seen as a dynamic interplay between all the components of the ICF (*Figure 4*) (153).

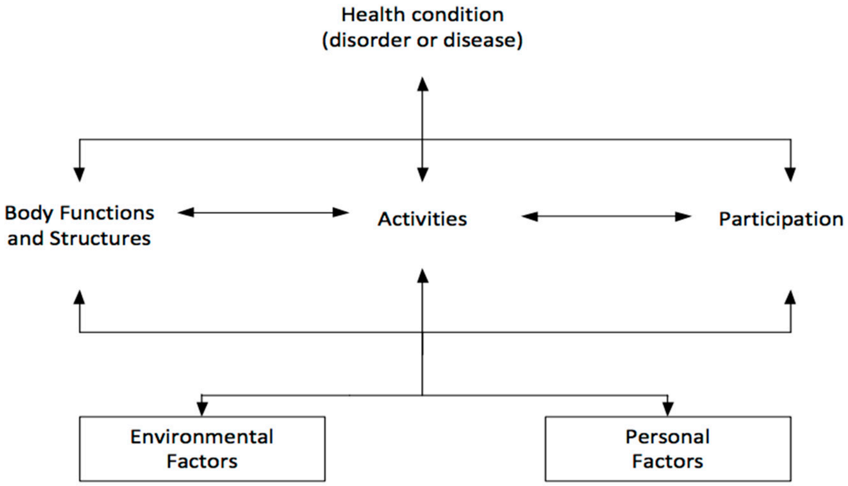


Figure 4. The ICF model: Interaction between ICF components (WHO, 2001).

Body functions and body structures

The lost weight of the amputated limb affects the body balance and body posture (70). The load on the existing hand increases and there is a risk of problems related to overuse, such as carpal tunnel syndrome, or pain in the shoulder, neck, or elbow (19, 74).

Psychological reactions following a hand amputation are natural. Changed self-esteem and the feeling of being incomplete affect the individual (90, 108). Long-term psychosocial problems often follow an acquired upper limb amputation (130). Psychological interventions and education, psychotherapy, and social support have been emphasized as key interventions in rehabilitation (108). The emotional reaction linked to the loss of a limb can be compared to a grieving process similar to that of losing a close relative, including an initial shock, denial, anxiety and depression, and finally adjustment (115).

Pain in the residual limb and phantom limb are common, as is pain as a secondary consequence of the amputation, such as pain in the back, neck, and the existing hand and arm. Regardless of the type or origin of pain, it is associated with disability (62).

Activity, participation, and quality of life

Our hands are essential for our definition of ourselves as individuals. Our independence in activities such as work, leisure, self-care, and social interaction is to a large extent dependent on well-functioning hands. Living with just one hand affects all activities that require two fully functional hands (63, 103).

Our hands are important—not only in activities, but also for body language, gestures, and communication. We use our hands in greetings, prayer, aggression, and intimacy (90). Our hands are also significant for body image and identity (63, 108). Regarding social participation, loss of the right hand means that the individual cannot shake hands, as is the cultural norm in western countries. The loss of the left hand would instead hinder the use of the wedding ring on the left hand (107). Individuals who suffer from arm amputation are often young and active, and have to live and work with the limb loss for a large part of their life (62). Important roles in life, such as being a worker, spouse, and caregiver, can be altered, which would affect the individual’s participation in society (108, 134).

Pain that often follows a limb loss leads to disability, and is associated with activity limitations, restrictions regarding participation, and an impaired quality of life (62).

Expectations regarding—and the need for—a hand prosthesis are highly individual, and the rehabilitation goals should be individualized from an activity point of view rather than by concentrating on physical functions (e.g. grip strength and range of motion) (106). Even though hand prostheses cannot compensate for the original human hand, they can have an important role regarding self-image, identity, social participation, and overall quality of life (80, 106).

From an occupational performance perspective

In addition to the ICF terminology regarding activity, occupational therapists often use the terms occupation and occupational performance. According to the Canadian Model of Occupational Performance and Engagement (CMOP-E), the term *occupation* is the core concept. Occupation involves activities that are composed of tasks, and actions, which in turn involve voluntary movements and/or mental processes (143). The ICF concept *activity* is similar but not as detailed, and is defined as “the execution of a task or action by an individual” (153). According to CMOP-E, occupational performance is a result of a dynamic interplay between occupation, person, and environment, and in turn occupational performance can be identified and grouped as self-care, productivity, or leisure. According to Townsend (143), when comparing the ICF concepts activity and participation, the term occupational performance in CMOP-E refers to the subjective experience of participation, and a sense of meaningfulness, and this dimension is not included in the ICF. The involvement or engagement in occupations affects health, gives structure to living, and gives meaning to life (143).

Hand prostheses

Hand prostheses have been used for centuries as a technical aid and for cosmetic purposes. Prosthetic hands with spring mechanisms that could be steered with the existing hand have been developed since the sixteenth century. One of the first hand prostheses that were written about was the one owned by a German knight called Götz von Berlichingen, who had lost his right hand in a battle. He made his own prosthetic hand of iron with movable joints, so that he could hold a sword and a lance and continue to participate in fights (92).

There are several types of prosthetic replacements, including hooks and hands—body-powered, electrically powered, or passive hands in different designs, from simple prefabricated cosmetic hands to individually made aesthetic hands.

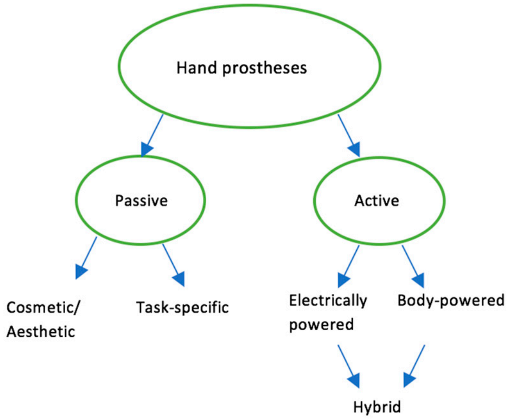


Figure 5. Classification of prosthetic hands.

The easiest way of describing prostheses is to divide them into a passive group and an active group (*Figure 5*). The passive hand prostheses are generally used for the sake of appearance and to re-establish the symmetry of the body. Passive prosthetic hands still have a functional role in activity, and are used as support for the existing hand in pushing, holding, and carrying.

Active prostheses can be divided into body-powered and electrically powered. In body-powered prostheses, a harness is used and with movements of other body parts (most often the shoulder or chest) it is possible—using cables—to control the prosthetic hand or hook. Electrically powered prostheses are usually controlled by using electromyographic (EMG) signals generated by the muscles in the residual arm. The widespread myoelectric hand prosthesis permits a single degree of freedom in movement when opening and closing the grip (41), and has looked almost the same since it was first presented decades ago (41). Two EMG electrodes in the socket of the prosthesis react to muscle contractions: the flexor muscles close the prosthetic hand and the extensor muscles open the hand. In the case of two components (e.g. hand and wrist) that are powered by the same EMG electrodes, it is possible to switch between the components using, for example, a double contraction or co-contraction of the muscles.

There also exist hybrid prostheses that are both body-powered and electrically powered, and they often consist of a body-powered elbow and a myoelectric hand/hook, for those with a higher level of amputation.

In recent years, prosthetic hands with multiple degrees of freedom have been presented. They have several motors and several grip patterns, with the possibility of performing some degree of movement of individual fingers. The simple EMG control of opening and closing is still the same. Even in later multi-articulated prosthetic hands (such as Bebionic® hand (OttoBock) and i-Limb® (Össur)) the control is the same, but different and individually programmed grip patterns to switch between has been added. Recently, systems for pattern regocnition has been presented on the market to make it possible to control the prosthesis in a more intuitive way. Several electrodes attached to the skin on the residual limb can recognize several different movement patterns of the muscles and can be individually adjusted and set (such as COAPT Gen2® by Coaptengineering and MyoPlus® by OttoBock).

The challenging problem in prosthetics is to replace the delicate human hand with advanced technology (7). The major goal in the development of hand prostheses is to mimic the human hand in all respects. The progress regarding multi-fingered dexterous prosthetic hands and pattern recognition for motor control is promising, but there is still a gap between the sophistication of research in the field and the capabilities of the hand prostheses that reach end-users (41).

Target muscle re-innervation (TMR) is a method whereby nerves are transferred surgically to separate segments of muscles for intuitive control of the prosthesis. For example, the ulnar, median, musculocutaneous, and distal radial nerves can be transferred to separate sections of the pectoral and serratus muscles in transhumeral amputees (83). The transferral of sensory nerves also makes it possible to create a pathway for cutaneous sensory feedback (83), and when the re-innervated skin is touched it is experienced as if the missing arm has been touched (82). Another method is to use an osseointegrated human-machine gateway (OHMG)—a bone-anchored interface that permits bidirectional communication between the person and the prosthetic hand (113). Despite these improvements, the hand prostheses that are available to the majority of users are the myoelectric prostheses with a single degree of freedom.

Sensory feedback in hand prostheses

If one is to mimic the delicate human hand using a prosthesis, only making use of motor functions will not suffice. The hand is a sensory instrument, and development of a hand prosthesis with conscious sensory feedback is challenging. The absence of sensory feedback may limit effective use of the prosthesis, and it has also been proposed as a reason for rejection of hand prostheses. The lack of sensory feedback and the importance of having it has been highlighted by several authors (4, 137, 139, 141).

Some sort of sensory information may be perceived via the socket, such as vibrations from the motors in the prosthetic hand or proprioceptive information from the muscles used for myoelectric control. This sensory feedback may be useful, but is not fully adequate (23, 41, 94). There should be a dynamic interplay between the object being acted upon by the motor output (control) and sensory input from sensors in the hand to achieve a closed-loop control between the prosthetic device and the user (23, 117). The big challenge is to implement sensory feedback for grasping, manipulation, and proprioception that is apprehended as real and authentic (41). In the training with myoelectric hand prostheses, and when learning to control the grasping force, other senses can be helpful, such as vision (18) and hearing (55). This requires a higher degree of mental effort (55), and when using an active prosthesis sensory feedback is presumed to reduce the cognitive load (23).

One way of thinking of sensory feedback systems is to divide them into *modality-matched*, *somatotopically matched*, and *substitution* feedback. Ideally, the feedback would be both modality- and somatotopically matched (137). When applying sensory feedback to hand prostheses the system should be modality-matched, meaning that pressure on the prosthesis fingers is perceived as pressure on the skin. Even if the modality is matched, the stimulation is not necessary matched regarding location. The user has to learn to interpret the location of stimulation, but a modality-matched system is still considered to be a method that requires less cognitive burden than systems that are not matched regarding modality (4, 137).

The sensory feedback should preferably also be somatotopically matched, meaning that the feedback should activate the neurons in the S1 that were originally (before amputation) activated by that sensory stimulation; i.e. sensory feedback from the prosthetic thumb should be processed by neurons in the original thumb area in the S1. If somatotopic matching is achieved, there will be no need for interpretation of the location of the stimulation received and therefore there will most likely be less cognitive burden for the amputee (137).

Sensory substitution is when other communication channels are used, e.g. vision or hearing. This is called cross-modal plasticity. It is neither somatotopically nor modality-matched. The user has to learn to interpret both the location and the stimulus, and learn to associate it with the prosthesis (137).

In the development of sensory feedback, it is of interest to investigate certain aspects such as activity and occupational performance, and dimensions such as subjective experiences, instead of evaluating simple grip force tasks.

There is one hand prosthesis with sensory feedback available on the market (VINCENTevolution 2; Vincent Systems GmbH, Germany), where feedback concerning the grasping force is accomplished through vibration in the socket. Several other solutions for sensory feedback are under development in research projects. For this purpose, different kinds of sensors for hand prostheses have been developed and evaluated experimentally (93). The tactile signals read by the sensors on the prosthesis can be converted and delivered to the user either invasively (through surgery) or non-invasively (*Table 1*).

Tabel 1. Overview of available sensory feedback methods

	Benefits	Limitations
Invasive sensory feedback		
TSR (Targeted sensory re-innervation)	• Promising for patients with shoulder disarticulation and transhumeral amputation	• Postoperative recovery time
Peripheral nerve stimulation	• Somatotopically matched • Possibility of percieving different textures	• Crude sensibility • Could possibly cause nerve damage • Possibly short life of implant
CNS stimulation	• Somatotopically matched	• Could possibly cause brain damage • Potentially short life of implant
Non-invasive sensory feedback	Somatotopically matching if applied to the PHM	
Mechanotactile	• Modality-matched • Close to ”real” touch	• Bulky • Power consuming
Vibrotactile	• Cheap • Small-sized • Low power	• Could be annoying with continuous vibration in everyday life
Electrotactile	• Quick respons • Small-sized • Low weight • Low power	• Can produce an unpleasant feeling • Possible interference with EMG sensors
Hybrid (multimodal)	• Possibly stonger feedback	• Overload of sensations, which can be confusing

(Modified from Svensson et al., 2017).

Invasive sensory feedback

Several solutions for solving sensory feedback invasively have been tested. Surgical procedures are always a risk, and a potential problem with peripheral nerve stimulation is possible interference with control of EMG electrodes (129).

Targeted re-innervation

Target re-innervation (TR) is a surgical method with nerve transfer, where nerves that previously innervated amputated sites are transferred to more proximal muscles. This makes it possible to move and increase the number of motor control sites. TR has mainly been used on transhumeral or shoulder disarticulation amputees, with the aim of improving motor control possibilities. When redirecting afferent nerves, the idea is to provide cutaneous sensation which is somatotopically matched. This method is called targeted sensory re-innervation (TSR) (65). The advantages of this method are the long-term stability, avoidance of foreign parts in the body, and a relatively natural sense of touch (129).

Peripheral nervous system stimulation

When electrodes are implanted on or in the peripheral nerves in the residual limb, the feedback can be made to be somatotopically matched. Different tactile sensations can be induced via electric currents, and are passed from the electrodes through the nerve. There are several different kinds of electrodes: cuffs that enclose the nerve, intraneural electrodes that are inserted into the nerve, and sieve electrodes where the nerve is split and has to grow into the electrode before it can be used (129, 141). One solution presented by Ortiz-Catalan et al. was to achieve bidirectional communication through an osseointegrated screw and implanted neuromuscular interface, for both motor control and sensory feedback (113).

Central nervous system stimulation

In animal studies brain-machine-brain-interface has been tested using a virtual arm. The performance with the virtual hand was improved when intracortical microstimulation was added (78, 112). A neural interface implanted in the motor cortex in a person with tetraplegia has also shown good performance with a prosthetic limb (27, 152). In another study, electrical stimulation of the primary sensory cortex showed that with simultaneous visual stimulation of a rubber hand, an experience of body ownership was evoked (28).

Non-invasive sensory feedback

Finding of an appropriate actuator that can provide immediate tactile feedback non-invasively, but still being small enough to fit inside a prosthetic socket, with low power consumption and weighing very little, is a challenge (141). Vibration actuators are often used because of their small size, ease of use, and low power consumption. However, the feedback in the form of vibrations can be distracting with day-to-day use (73). There have been several suggestions for pressure feedback, e.g. servomotors, but they are bulky and have a relatively high power consumption (141).

If the feedback is not somatotopically matched, each stimulus has to be interpreted and its representation has to be learned. One option to make the non-invasive sensory feedback somatotopically matched, regardless of modality, is to apply it to the PHM on the residual arm. In this way, the stimulation of the prosthetic fingers can be perceived in accordance with the corresponding positions of lost fingers (137).

Mechanotactile feedback

Mechanotactile feedback is modality-matched when force on the prosthetic fingers is transferred as force pushing on the skin. The feedback is easy to interpret and is easily associated with real touch of the hand (141).

Because of the matching in modality, mechanotactile feedback is preferred for elicitation of an experience of body ownership of the prosthesis (4) and has been investigated by applying stimuli on a rubber hand (39). The quality of inducing body ownership by using mechanotactile feedback makes it an appealing form of feedback, but the drawback is that the devices for mechanotactile feedback are big/bulky, generate a lot of noise, and may have a high power consumption (4). Sometimes mechanotactile feedback is applied to the upper arm for ease of use. Mechanotactile feedback has been investigated in several studies (8, 21, 54, 105).

A mechanotactile sensory feedback system presented by Antfolk et al. (3) was designed with silicon bulbs on the prosthetic fingertips, which picked up the pressure when gripping. The air-mediated pressure was transferred via plastic tubes to the actuators, silicon bulbs, that were attached inside the prosthetic socket, and placed individually according to the areas of the PHM (3). This is the concept that is used in this thesis.

Vibrotactile feedback

Vibrotactile feedback provides the user with vibration when the prosthetic fingers are touched/pressed. Thus, the feedback has mismatched modality. Advantages of vibrotactile devices are the small size, the low power consumption, and the ease of use. The vibrotactile feedback is mostly used to transfer information about grasp force (4). In combination with visual cues, vibrotactile feedback has been shown to evoke body ownership when the feedback was applied to the PHM, in a group of transradial amputees (31). Studies using a system termed discrete event-driven sensory feedback control (DESC), which generates vibrations during grasping and releasing, have shown improved grasping performance (24, 26). Vibrotactile feedback is the only system currently being used to provide sensory feedback in commercially available prostheses; in addition, it is a method that is often used in research (141).

Electrotactile feedback

Electrotactile feedback is another substitution of touch, and is produced by a small electric current being applied to the skin that stimulates the nerves. This modality has been used to elicit pressure and slip feedback in a virtual prosthetic hand and has been shown to improve grasping speed and stability (154).

Hybrid/multi-modality feedback

When several modalities are used simultaneously, providing different types of feedback, this is hybrid or multi-modality feedback. Electrotactile and vibrotactile stimulation is often used because of the small size of the actuators and the low power consumption. A combination of mechanotactile and vibrotactile stimulation applied to a myoelectric prosthesis has been used to provide simultaneous feedback regarding grip force (pressure) and object contact (vibrotactility) (25).

Auditory stimulation

Another alternative is to use the cross-modal plasticity; hearing can substitute for lost sensibility. A glove supplied with small microphones has been used, and by stroking surfaces, different sounds—depending on the friction—could be identified (95). Adding auditory feedback has been tested when controlling myoelectric prostheses, and it was concluded that the mental effort required to control the myoelectric prosthesis was reduced (i.e. there was an improvement) when auditory feedback was added to the visual feedback (55).

Use of hand prostheses

Hand prostheses have an important role in reducing the negative effects of an amputation (80, 106). However, according to clinical experience, expectations that are too high are not fulfilled, and limitations in the technical solutions often lead to rejection of the prosthesis (12, 13, 32, 140), with possible overuse of the existing hand as a consequence (19, 74).

A hand prosthesis can both facilitate and limit performance during activity (32). Acceptance of a hand prosthesis is driven by need, and if the prosthesis is not experienced as being useful, or if it is easier to perform activities without it, it will not be worn (11). Surveys have shown that the rate of rejection of the prosthesis in upper limb amputees is 19–39% (12-14, 32). There are several areas in which the users themselves express dissatisfaction—concerning appearance, overall function of grasping and grip strength, and control of the prosthesis due to the lack of sensory feedback (12, 32, 120, 140). When the prosthesis users prioritize their desires, sensory feedback gets high ranking (12, 120). It is supposed that sensory feedback is valuable for manipulating objects and controlling grip, to reduce the cognitive load and the amount of visual attention that is required (11). Improvements in controlling the grip force with the prosthetic hand—with both invasive and non-invasive sensory feedback—have been described in several case reports (26, 111, 118, 124, 136). The benefits of sensory feedback for performance have been discussed (42). Markovic et al. (98) concluded that sensory feedback (vibrotactile) did not have the expected effect on performance in easy tasks, but in complex tasks the performance improved when vibrotactile feedback was added. Regardless of the functional outcome, sensory feedback has an important role in the subjective experience of using a prosthetic hand (57, 98).

Sensory feedback may be important for the acceptance and embodiment of the prosthesis. Several solutions for sensory feedback, both invasive and non-invasive, are under development, but there remains a gap between what happens in the research laboratory and what is available to the end-users.

Aims

The overall aim of the thesis was to further investigate and implement a non-invasive concept for sensory feedback in hand prostheses.

Specific aims

- To explore forearm amputees’ views of prosthesis use and perception of sensory feedback in order to clarify prosthesis users’ own experiences, needs, and expectations regarding future research and prosthesis development (Paper I).
- To investigate and evaluate the sensory qualities of PHMs in amputees with unilateral forearm amputation (Paper II).
- To determine whether it is possible to learn to associate sensory stimuli on the forearm skin with specific fingers in healthy non-amputee volunteers (Paper III).
- To evaluate a non-invasive sensory feedback system for a prosthetic hand in the everyday lives of adult forearm amputees (Paper IV).

Material and methods

Participants

The participants in Papers I, II, and IV were mainly recruited by the regional amputation and prosthetic team at the Department of Hand Surgery, Skåne University Hospital, Malmö, Sweden. In addition, participants were also recruited by the regional amputation and prosthetic teams at Rehabcenter Sfären, Bräcke Diakoni, Stockholm, Sweden, and Aalborg University, Aalborg, Denmark. Several of the individuals participated in more than one study (*Table 2*). In Paper III, the participants were recruited from the Department of Hand Surgery, Skåne University Hospital, Malmö.

Paper II: Patients with acquired or congenital amputation who had had contact with the regional amputation and prosthetic centres at Skåne University Hospital, Malmö, and Bräcke Diakoni, Stockholm, and who met the inclusion criteria were asked to participate.

Papers II and IV: Patients from the regional amputation and prosthetic centres at Skåne University Hospital, Malmö, and Bräcke Diakoni, Stockholm, and one participant who had contact with a research group at Aalborg University, were included in the study.

Paper III: The participants were students recruited from the Faculty of Medicine, Lund University, Sweden, and staff of the Department of Hand Surgery, Skåne University Hospital, Malmö.

Tabel 2. Participants with amputation in the four studies.

Participant	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Paper I	x	x	x	x	x	x	x	x	x	x	x	x	x						
Paper II	x		x	x	x		x			x	x			x	x	x			
Paper III																			
Paper IV	x			x			x				x						x	x	x

The hand prosthesis with sensory feedback

The hand prostheses used in Paper IV had a simple non-invasive, non-electronic sensory feedback system described by Antfolk et al. (3). It was based on air-mediated pressure that is transferred from silicon bubbles in the prosthetic fingertips to bubbles integrated in the prosthetic socket and applied to the individual PHM on the residual arm. The stimulation was mechanotactile and the pressure was transferred from the silicon bulbs in the fingertips of the prosthesis via plastic tubes that reached actuators (silicon bulbs 13 mm in diameter) inside the prosthetic socket. The silicone glove with bulbs (35 mm in length) volar in every fingertip was applied on a MyoHand VariPlus Speed® (OttoBock). Thus, it was possible to use both modality-matched and somatotopically matched feedback (*Figures 6 and 7*).

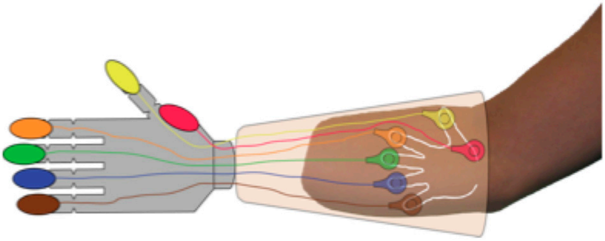


Figure 6. Illustration of the air-mediated sensory feedback system attached to the PHM with sensory acuators (silicon bulbs) inside the socket.

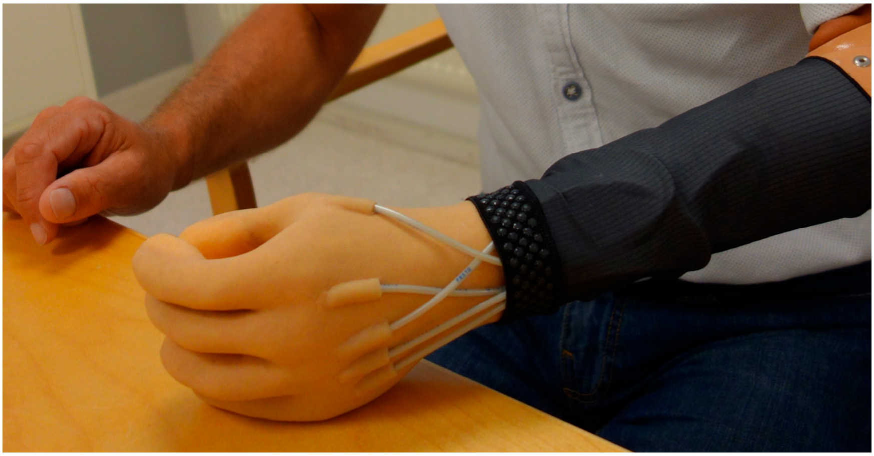


Figure 7. The air-mediated sensory feedback system integrated in a myoelectric prosthesis.

Outcome measures

In the ICF model, the outcome measures are sorted according to where their main focus is. However, some outcome measures cover more than one level of ICF (*Table 3*).

Table 3. Overview of the outcome measures in the ICF components

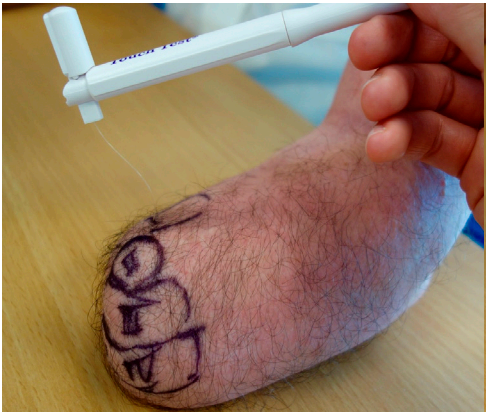
ICF component	Outcome measure	Paper #
Body function/ Body structure	ACMC	4
	2PD	2
	SWM	2
	Localization	3
	fMRI	2
	Performance questionnarie	4
	Qualitative interview	1, 4
Activity	ACMC	2
	Performance questionnaire	4
	Qualitative interview	1, 4
Participation	Qualitative interview	1, 4

Assessment of Capacity of Myoelectric Control (ACMC)

The Assessment of Capacity for Myoelectric Control (http://acmc.se/) is an observational measurement tool where the user's control of a myoelectric prosthesis is rated in terms of its capability. The skilfulness with the prosthetic hand is rated using an everyday bi-manual activity, with timing during grasping or movement of the prosthetic hand in different locations in relation to the body. The ACMC covers 22 items, with a 4-grade rating scale. The ACMC units are calculated on the ACMC website and reported in the range 0–100; the higher the score, the better the performance of the task (66, 85-87) (*Appendix 1*).

Semmes-Weinstein monofilaments (SWM)

Semmes-Weinstein monofilaments (North Coast Medical, Gilroy, CA, USA) are used for investigation of the touch thresholds. With the standardized nylon monofilaments, it is possible to determine the ability to detect stimuli from very light touch (0.008 grams) to hard pressure (300 grams) (5). The test was performed on the PHM area with the strongest phantom feeling and on the estimated corresponding area of the intact forearm. The assessment started with SWM #4.31 (equivalent to a pressure of 2 g, representing some protective sensibility) and thereafter in an ascending or descending order, depending on the answer to the filament first tested. Each filament was applied three times, in accordance with standard procedures (72) (*Figure 8*).



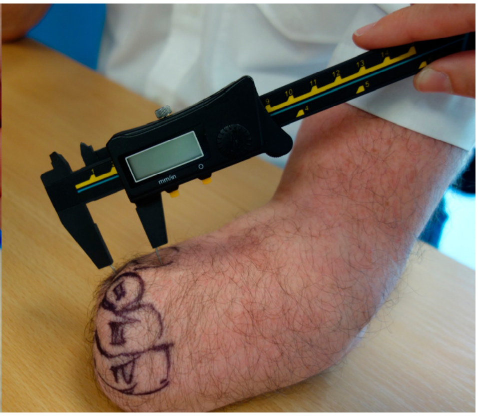


Figure 8. The monofilaments used in Papers II and IV. **Figure 9. The 2PD test used in Papers II and IV.**

Two-point discrimination test (2PD)

The two-point discrimination test (2PD) (5) measures the tactile gnosis/discriminative touch, which in this test is the ability to identify whether one or two touch points are applied to the skin (i.e., it is a passive test). In a standard situation the touch points are applied to the volar distal phalange, but here in the case of amputation, the tool was used on the forearm skin on one of the PHMs with the lowest touch threshold, and on corresponding areas of the contralateral, intact arm. The test was performed according to the Moberg method; the force that produced the first blanching around the prongs and the test instrument was applied perpendicular to the skin (104). The normal minimal distance for detection of two-point discrimination on the forearm is 40 mm (150) and the expected distances in our study were several cm. The test instrument used was a caliper modified with two blunt prongs one mm in diameter. Response alternatives for the participants were predefined as “one point” or “two points”. In random order, ten touches with equal numbers of one and two prongs were performed, and seven correct answers out of ten was accepted as being valid for a correct answer—to proceed to a smaller distance. Application was done in descending or ascending order, starting with 15 mm. The distance was decreased or increased by 5 mm each time it was changed. During repeated testing, a learning effect is always a risk, and to compensate for this we started testing at the control site (on the intact forearm) in every second test person (*Figure 9*).

Localization of touch

The participant's ability to localize touch between different areas of the PHM was assessed as described by Antfolk et al. (2012) (3). Areas of the PHM were randomly touched with a supra-threshold monofilament (SWM #6.65, equivalent to a pressure of 300 g). This was repeated six times for each skin area, resulting in a total of 30 stimulations for participants who had a map with five phantom fingers.

Questionnaire

In Paper IV, a questionnaire was developed regarding sensory feedback from the prosthesis, the feeling of agency and body ownership, performance in activity, and phantom limb pain. The questions were developed from the questionnaire used in the experiment with the "rubber hand illusion" by Botvinick and Cohen (17). The questionnaire had 21 questions that were rated on a 7-grade Likert scale, from "Strongly disagree" (---) to "Strongly agree" (+++). To capture possible suggestibility and compliance, six control statements were included in the questionnaire (*Appendix 2*).

Magnetic resonance imaging

Magnetic resonance imaging (MRI) (1.5T MRI scanner: Philips Achieva; Philips Healthcare, the Netherlands) was used in Paper II on two participants, to evaluate the occurrence of neuromas in relation to the PHM. Vitamin E markers that are visible in MR were applied to the skin on the forearm where the PHM was marked. The MR images were evaluated by an experienced musculoskeletal radiologist, concentrating on the visibility of the median, ulnar, and radial nerves and possible neuromas in relation to the PHM.

Interview

A qualitative descriptive method was used in Papers I and IV (58, 59, 68). In Paper I, it was the main approach and in Paper IV this method was used in combination with quantitative assessments. This qualitative approach was chosen to deepen our knowledge and to let the participants, in their own words, express their experiences and feelings about the subject. A semi-structured interview with open-ended questions was used in both studies, and the participants were asked to narrate their experiences. Follow-up questions were asked such as "How did you experience this?", "Can you describe this in more detail?", and "Can you give some examples of this?".

Statistics

Wilcoxon signed-rank test was used to compare two matched/paired samples when the data were not normally distributed. This method was used in Paper II where the touch threshold or discriminative touch in the PHM areas was compared to control areas on the contralateral arm in the same individuals. Wilcoxon signed-rank test was also used in Paper III when analyzing the learning progress and comparing training occasions during the period of learning.

In Paper III, unpaired two-tailed Mann-Whitney *U* test was used when comparing different groups regarding sex and age.

To analyze the agreement between stimuli given and the response, the linear weighted Cohen's kappa was used. A response close in location to the actual stimulation was calculated as being better agreement than a greater distance between stimulation and response.

In Paper II, the software SPSS (version 22; IBM Corp., Armonk, NY, USA) was used for calculation. The statistical analysis in Paper III was performed in Python, an open-source programming language. In the analysis, packages such as Pandas were used, to make the data easier to structure, analyze and visualize (https://pandas.pydata. org/). SciPy was used for Wilcoxon and Mann-Whitney *U* test (https://www.scipy.org/), and Scikit-learn was used for data mining and analysis of kappa (http://scikit-learn.org/stable).

In Paper IV, the results were presented descriptively (2).

Qualitative content analysis

Qualitative content analysis is an explorative research method aimed at deepening our knowledge of a certain topic. Originally this method was used to give an objective and quantitative view of the manifest content of a textually reported experience. It has been further developed to include the possibility of interpretation of latent content (58, 59). Conventional content analysis was used in Paper I to describe the phenomenon under study openly and to let new insights emerge. Directed content analysis was used in Paper IV, i.e. predefined categories were used in the analysis. These categories were developed from earlier research and the aim of the study (68).

Some core concepts regarding the *trustworthiness* of qualitative content analysis should be explained: *credibility*, *dependability*, *confirmability*, *transferability*. Credibility refers to how well the data and the analysis process address the intended focus of the research, and the participants and data must be accurately identified

(58, 59). Dependability describes how stable the data are under different conditions and over time (58, 59), and in our studies the co-authors read and interpreted the text independently, before coming together for in-depth discussions and analysis.

Confirmability describes how objective and accurate the data are (59). To ensure confirmability, the information given was clarified and confirmed throughout the interviews. Transferability refers to how the data can be generalized or transferred to other contexts or groups (59), so the characteristics of the group under study should be described well, to ensure transferability to other contexts.

The concept *saturation* of the data can be explained as reaching redundancy in the material. This refers to how many interviews would be needed until no new information comes up. To ensure comprehension and confirm the categories, the number of participants must be optimal (132). Saturation was considered to have been achieved in Paper I, but there were difficulties in reaching saturation in Paper IV, due to the limited number of participants.

Method triangulation was used in Paper IV, i.e. multiple methods were used (20, 116). Qualitative analysis of interviews—and also quantitative measures by use of a questionnaire and objective measurements—were used to gain a broad understanding of the research topic. In the analysis of the interviews in Papers I and IV, *investigator triangulation* was used (20, 116). The first author and one of the co-authors read and coded the interviews independently, and by in-depth analysis and discussion, interpreted the text together.

My contributions to the four studies are given in Table 4.

Table 4. The degree of my participation in each study

	Paper I	Paper II	Paper III	Paper IV
Planning	3	1	3	3
Ethics application	1	1	1	2
Data collection	3	2	3	3
Interpretation of results	3	2	3	3
Writing of the manuscript	3	3	3	3

1 = Did not participate; 2 = Partly participated; 3 = Participated to a great extent.

Ethics

All studies were conducted according to the Helsinki Declaration and were approved by the regional ethical review board in Lund. All the participants gave their written informed consent.

No harm or discomfort was reported during the studies.

Results

The following is a summary of the results. For more detailed information, the reader is referred to Papers I–IV.

Forearm amputees' views of prosthesis use and sensory feedback (Paper I)

Thirteen individuals participated in the study: seven with acquired amputation, and six with congenital reduction deficiency. All used a prosthesis on a daily basis, but different kinds (myoelectric or cosmetic/aesthetic), and in five the previously dominant hand was amputated. The results in this inductive interview study were analyzed with qualitative conventional content analysis and four main categories emerged (*Table 5*).

Table 5. Overview of the main categories and subcategories

Main category	Subcategory
Activity and participation	Prosthesis as a facilitating factor Prosthesis as a limiting factor
Perception of the "hand"	Sensibility through prosthesis Grip control Compensation with vision/hearing Phantom phenomena
Body image	Proprioception Balance Appearance and symmetry Social interaction Body ownership Identity
Future expectations	Mobility Sensibility Appearance

Hand prostheses can both facilitate and limit performance in activity. They are mostly experienced as a tool, and not a part of one's own body. The appearance was important, and in some cases the prime reason for wearing a prosthesis—to blend in, in social contexts. Expectations for future development were about improved mobility, appearance, and sensory feedback.

Sensory qualities of the phantom hand map in the residual forearm of amputees (Paper II)

Ten individuals participated in the study (five men and five women). Experiencing of a PHM was an inclusion criterion. Of the ten participants, six also experienced the phantom hand as being telescoped. The number of sites experienced with referred sensation varied from three to five among the different individuals (*Figure 10*).

Touch threshold in the PHM areas was within the normal range, and comparable to that in the control sites of the contralateral arm. The tactile discrimination was significantly better in the PHM areas than in the contralateral arm. Tactile discrimination is more complex than touch threshold, and requires both detection and interpretation of the stimuli (*Table 6*).

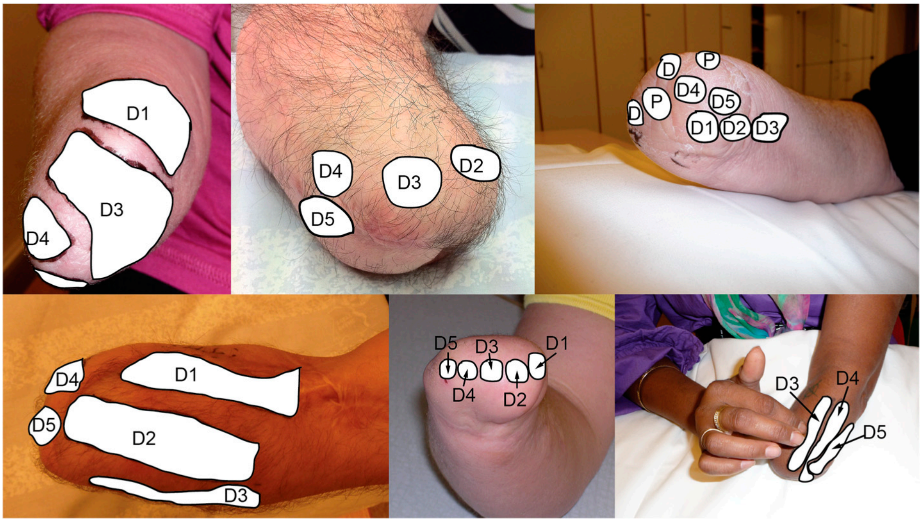


Figure 10. Phantom hand maps.
Examples of PHM. The areas with referred sensation are marked as corresponding digits (D).

Table 6. Touch thresholds, and discriminanative touch in PHM and control sites on the contralateral arm

	Touch thershold (SWM), g		Discriminanative touch (2PD), mm		Localization of touch in PHM	
Subject no.	**PHM area**	**Corr. contralat. arm**	**PHM area**	**Corr. contralat. arm**	**Correct answers, %**	**No. of sites**
1	0.008	0.008	25	50	97	5
2	1.4	0.6	25	50	71	4
3	0.16	0.008	25	45	100	3
4	0.008	0.008	25	45	27	5
5	0.008	0.008	40	60	100	3
6	0.008	0.008	15	30	83	3
7	0.04	0.008	20	40	94	5
8	0.008	0.008	30	50	90	5
9	0.008	0.008	25	15	100	4
10	0.008	0.02	10	12	80	4
Median	0.008	0.008	25	45	95	4

MRI was performed on two patients with PHM, to investigate whether there were any explanations for the PHM in the peripheral nerves. No neuromas were identified; nor were individual nerve branches and sprouts within the detection limits.

Touch on predefined areas on the forearm can be associated with specific fingers (Paper III)

A structured training protocol over 2 weeks was completed by 31 participants. Follow-ups were done one and two weeks after the training period, to examine the progress of learning and the retension of what was learned. The results showed that it is possible to learn to associate sensory stimuli on the forearm with specific fingers. The agreement was analyzed using Cohen’s kappa, which showed excellent agreement (> 0.8) between given stimuli and the response, as shown in *Figure 11*.

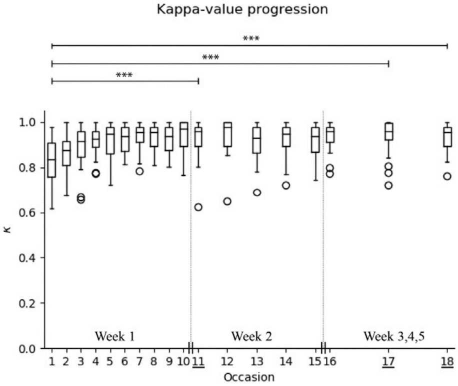


Figure 11. Kappa value progression
The box plot shows improvement (median kappa values, 95% CI) in learning during the training period, involving 18 occasions. The improvement was statistically significant between baseline and follow-ups on occasions 11, 17, and 18. ***p < 0.001.

It was easiest to distinguish the predefined area for the middle finger, where 95% of the responses were correct, followed by the index finger and the thumb, with 89% correct answers (*Figure 12*).

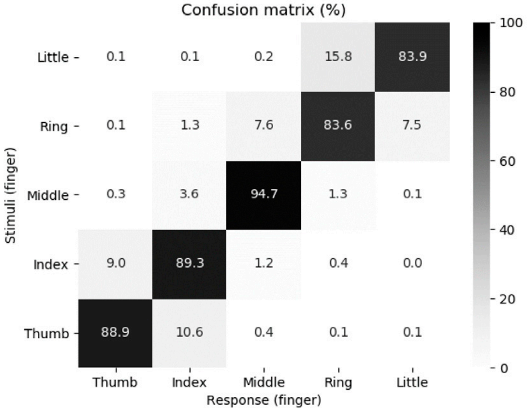


Figure 12. Confusion matrix of correct responses.
Correct answers are shown in %.

No statistically significant differences were seen when comparing sex and age.

Sensory feedback in hand prostheses: a prospective study of everyday use (Paper IV)

This was a longitudinal cohort study that included seven forearm amputees (three women and four men). Five had lost their dominant hand. All were experienced prosthesis users.

A mixed method was used, with both qualitative and quantitative measurements. A directed content analysis of the interviews was also used to analyze the material in the predefined categories: *sensory feedback from the prosthesis, agency, body ownership, performance in activity*, and *suggestions for improvement*.

This was the first time a non-invasive sensory feedback system for hand prostheses was implemented in home environment. The results from interviews showed that sensory feedback was experienced as a feeling of touch which contributed to an experience of completeness, linked to body ownership. However, the results from the questionnaire showed that the sense of agency and performance remained unchanged or deteriorated. A stronger and more distinct feedback was desirable. It was also difficult to feel and manipulate small objects due to the silicon bubbles in the prosthetic fingers. Phantom pain was alleviated in four out of five patients who suffered from it.

Discussion

Today, the most sophisticated hand prostheses allow the wearer to experience agency—an experience of controlling one's own motor acts—but our initial findings indicated that the lack of sensory feedback limits the achievement of body ownership of the prosthesis, i.e. how we experience our own body. The PHM on the stump is a phenomenon described by many amputees, and when it is touched it links the phantom feeling of the missing hand with the somatotopic representation of the hand in the brain. The PHM has better discriminative sensibility than the corresponding skin of the uninjured arm, and is probably not only a peripheral phenomenon but rather an effect of brain plasticity. Thus, use of the PHM in prostheses with a non-invasive sensory feedback concept might be a way to achieve increased body ownership of the prosthesis. After four weeks of use of the non-invasive sensory feedback system based on PHM in a prototype prosthesis, the users expressed that they experienced the sensory feedback as real and that it gave a strong feeling of completeness, to do with body ownership. However, this was not verified in the objective measurements, and the hand performance with the prosthesis was not improved. Considering that not all amputees have a PHM, it was interesting to find that it is possible to learn to associate stimuli on the skin of the forearm with specific fingers, i.e. it is possible to create a PHM.

Health and occupational performance

Regarding body function and body structure, with an amputation there is sensory loss and motor loss—and in addition, often intractable phantom limb pain. The loss of a hand limits all activities in which two hands are normally used. Occupational performance refers to the subjective experience of participation and meaningfulness and labled as self-care, productivity, and leisure (143). Restrictions to participation may appear in both productivity and leisure activities. The altered body image, changed identity, and impaired self-esteem can affect social situations—and one's whole quality of life (106, 108). The individual must cope with all these permanent problems that follow the amputation and must make behavioural, social, and emotional adjustments to the new circumstances (49). It is generally supposed that if the prosthesis is well integrated in the body image, it will support the individual in restoring a coherent own-body feeling, and that this will enhance the emotional adjustments to the amputation and in turn facilitate social integration (49, 57, 135).

In Paper I, it was found that a prosthesis could facilitate occupational performance, in self-care, at work, and in leisure activities. The prosthesis was described as being a useful tool that the individual could not be without. "*I feel disabled without my prosthesis when I want to do something.*" On the other hand, a prosthesis was also reported to be a limiting factor—that it was mostly worn outside the home, and was often taken off on arriving home. When intact tactile sensibility was deemed important, as in the care of infants, the participants preferred to use the residual limb only: "*When the children were small, when both were very young, then in the beginning I didn't have the prosthesis because I felt that I was afraid of pinching them and it happened, which was really tough because I didn't notice it until they screamed a lot.*"

Appearance is not often the most important factor when talking about hand prostheses, but it is still important. Sometimes appearance is the main reason for wearing a hand prosthesis, and it is often valued higher than functional properties (80, 127, 130). The appearance of the prosthesis was often mentioned as being of importance in order to blend into company (Paper I). A desire to feel complete regarding one's own body can be an important reason for wearing a hand prosthesis (107), and the prosthesis gives symmetry to the body (Paper I). In this way, the prosthesis can have significance for one's body image and identity (Paper I). This can be of importance in social contexts, when presenting oneself to others, and can be crucial for participation in social situations (80, 106). However, the appearance was not important to everyone, and some preferred function over aesthetics (Paper I) (107). The prosthesis prototype that was used in Paper IV has potential for improvement regarding aesthetics. Plastic tubes were visible on the dorsal side of the prosthetic hand, and the silicon bulbs, the sensors, on the fingertips were too large to be aesthetically appealing. The colour of the silicone glove was an attempt to emulate skin colour, but in most cases it was too light. Some of the participants did not want to show themselves among people, with the prosthesis prototype on. The symmetry of the body that is achieved with a prosthetic hand has importance for the appearance, the body balance, and even load (Paper I) (70).

In line with clinical experience, the lack of sensory feedback can partially be compensated for by alternative input—such as vision or hearing of motor sounds. These sources can be used for control of the prosthesis (23, 111), which was evident in the results of Paper I. Only relying on vision may confer a cognitive burden, and when several senses are added the mental effort required can increase (55).

From our results from the implementation of the sensory feedback system over a four-week period in home environment (Paper IV), no conclusions regarding improved function or performance in activity can be drawn. Just a few improvements were seen, with some unchanged and some worsened control/performance in activity. The worse performance that was experienced in some cases was probably due to changed socket fitting, the adjustment of the EMG electrodes, or bulky bulbs in the prosthetic fingertips. These changes may have altered the reliability of the prosthesis. In Paper IV, the participants were experienced prosthesis users and over several years had learned how to control their own prosthetic hand, probably relying on several sources of feedback such as vision, hearing, and proprioception. Markovic et al. (2018) showed that naive prosthesis users could learn to control an EMG electrode, just by learning how much muscle force was needed (99). This could be an explanation as to why it is difficult to prove the functional benefits of sensory feedback.

Others have had more positive results regarding the functional benefits of sensory feedback. Improvements in performance of activities and when manipulating fragile or soft objects were seen when electrocutaneous stimulus feedback was added (36). Clemente et al. (2015) also found a positive effect on controlling the grip force when vibrotactile sensory feedback was transferred from a DESC glove placed on the prosthetic fingers to an arm-cuff (26). Petrini et al. (2019) presented a case report in which they reported better grip adjustment when handling fragile objects when intraneural sensory feedback was added (118), and Graczyk et al. (2019) presented a qualitative case series in which the sensory feedback decreased the visual attention needed, which permitted better flow in the performance of activities (56). Whether or not the results described above are of importance for performance of activities is unclear. Markovic et al. (2018) did not find convincing results regarding functional advantages of using sensory feedback. They could only see the vibrotactile feedback that was used as being beneficial in more complex grip tasks, but they also saw improved motor control of the prosthesis irrespective of the feedback (98). The difficulties in drawing any firm conclusions about the functional benefits have been discussed by Dosen et al. (2015), who pointed out the necessity of understanding the meaning of sensory feedback from a more fundamental point of view—as a human control system that involves many other processes (e.g. learning, prediction, and feed-forward control) (37). Ninu et al. (2014) stated that if the feedback is not coherent with the motor control, the expected benefits of feedback—such as increased grasp precision, decreased time-to-complete, and making the movements more intuitive—will be altered. If the feedback cannot be improved with learning, it might be burdensome and frustrating, and may even increase the risk of prosthesis rejection (111). The importance of evaluation of sensory feedback in hand prostheses in a real-life environment has been highlighted by Graczyk et al. (2018), who emphasized that settings that are relevant to the individual are better for understanding of the impact of sensory feedback. In their study of two individuals with invasive neural connected sensory feedback, they saw extended use of the prosthesis (57).

When being critical to the idea of non-invasive sensory feedback, one can ask if there will be an overload of information for the individual to interpret. Could the feedback become less relevant in time? In my opinion, this should not be the case if the stimulation is intuitive, and preferably modality-matched—and in the best case also somatopically matched. This should give a value to the feedback that adds another dimension, instead of leading to an overload. An example of this is that in the evaluation of the prosthesis with sensory feedback (Paper IV), it was commented that the prosthesis was also worn in situations where it was not being used for practical purposes (e.g. when watching television), just because of the pleasure of experiencing touch through the prosthesis. This behaviour could possibly affect the performance in the long run. If the prosthesis is worn for long periods, it is presumably being used in all situations—which was also found in case studies when using invasive sensory feedback in hand prostheses (30, 56, 57).

The value of touch

Even though hand prostheses cannot replace the delicate human hand (92), prosthetic hands, both myoelectric and cosmetic/aesthetic, have a functional role in everyday life. According to the users' narratives in Paper I, a hand prosthesis facilitates performance of activities. Some activities are still challenging even with a hand prosthesis, especially heavy jobs such as shovelling snow, gardening, and sports activities. Activities where fine manipulation is required, such as playing an instrument, or cooking, can also be challenging with a prosthesis, as are social activities that involve a degree of intimacy (shaking hands, hugging, and sex) (12). We found in Paper I that the users preferred to be without their usual prosthesis in some situations, and it was most often when tactile sensibility was valued most highly. This applied especially to the care of others, or to skin-to-skin contact and closeness with small children (Paper I).

Several sensory feedback systems under development focus on active touching of external objects, and grip control (21, 24-26, 154). According to Beckerle et al. (2018), this is not sufficient, and more aspects of touch (social touch, affective touch, and self-touch) should be taken into account for creation of sensory feedback that is to be experienced as real touch (10), and this is in line what we found in Paper IV. The objective measurements did not show any changes, but in the narratives, some of the participants suggested that the sensory feedback had another value. They said that when they touched the prosthesis, they found it quite pleasant, like touching their own skin or like lightly scratching themselves, and they did not experience this with their usual prosthesis (Paper IV). The actuators in the prosthesis used in Paper IV were placed in the socket, and the feedback was given on the forearm skin. In contrast to the palm of the hand, the hairy forearm skin has a large number of afferent nerves that process affective touch, the C-tactile afferents (146). One possible reason for the touch being experienced as pleasant may be activation of C-tactile afferents.

The phantom hand map

The PHM has a key role in this thesis. The PHM can be considered to have a direct connection to the phantom hand in the somatotopic representation in the brain (15). In Paper II, the results indicated that the touch thresholds were similar in the PHM and on the forearm skin without referred sensation. The discriminative touch was, however, significantly better in the PHM. This can be interpreted as being due to the cortical reorganization, and that the former cortical hand area in S1 has been invaded. The former hand neurons serve the forearm skin instead. The results indicated that there is a high quantity of somatotopic information in the skin of the residual arm that could be used, and that the PHM can be considered as a direct connection to the brain. The PHM can therefore be considered as an optimal target for transference of non-invasive sensory feedback from a hand prosthesis (Paper II). The feedback given to the PHM is virtually somatotopically matched (15). This cortical connection can be illustrated with experiments using the "rubber hand illusion" in amputees, where synchronous stroking on the PHM and a rubber hand induced a feeling of ownership of the rubber hand (39).

A previous study showed that 12 out of 18 amputees experienced a PHM (39). Still, there are some people with acquired amputation who do not experience it; and nor do those with congenital reduction deficiency. In these cases, the direct connection to the phantom hand is lacking. This was the reason for Paper III, where we tried to determine whether it is possible to learn to associate touch on predefined areas of the forearm to specific fingers. The statistics showed excellent agreement after a short period of training, which strengthens the idea that it is possible to learn a sensory association with the fingers. The results also remained for at least one week without any training at all (Paper III). Similar results have been described by Chai et al. (2017) when using electrotactile feedback (22). The results cannot be seen as being somatotopically matched, but it would be interesting to investigate the brain activation with fMRI. The association can be learned, and the learning curve improved sharply. This can be seen as another example of the brain's tremendous ability to adapt and change.

Schofield et al. (2014) argued that the ideal sensory feedback system would combine benefits from modality and somatotopically matched systems in order to allow the user to feel the relevant stimulus in the right location (137). To use PHM in a sensory feedback system in prostheses allows somatotopic matching i.e. the touch of the thumb would feel like the touch of the thumb. Modality matching is also possible, and in our studies one single modality—pressure—was used. There are of course other modalities such as moving touch, stroking, that could add another dimension of affective and social touch, which would be interesting to consider in future development. The fact that the PHM is in an area where C-tactile (CT) afferents are present could be one of the explanations for the emotional benefits of this sensory feedback system. C-tactile fibres are afferent, unmyelinated skin receptors that usually respond to stimuli similar to a light, stroking touch (1) and they were first described in humans by Vallbo et al. in 1993 (145). CT afferents exhibit an apparent velocity-dependent firing frequency, which also coincides with subjective pleasantness ratings in healthy humans (1, 88). Some comments regarding the sensory feedback in Paper IV from the participants involved a feeling of pleasantness when touching the fingers of the prosthesis.

Phantom limb pain

Pain leads to impairment, disability, and consequences for certain activities (self-care, productivity, and leisure activities), social relationships, and participation. Treatment of pain and support for coping emotionally under circumstances where there is pain are therefore crucial (49). After amputation, phantom limb pain (PLP) is very common (126). In Paper IV, five out of seven subjects experienced PLP, and the results showed that there was a trend of decreased PLP after the 4-week period with the sensory feedback system. Dietrich et al. (2012) found a decrease in PLP when electrocutaneous feedback was added to a myoelectric prosthesis (36). However, the relationship between sensory feedback and decreased PLP is unclear. The effect of different modalities on PLP has not been investigated, and it is possible that some sort of feedback or stimulation could even exacerbate phantom limb pain. Other factors that are added at the same time as the feedback should also be considered. Increased attention to the hand, distraction from the PLP when concentrating on the prosthesis, or the positive attention to the individual that is experienced when participating in a research study might also influence the result (36).

The use of vision to reduce PLP has been addressed through the mirror neuron systems; with illusory phantom movement, via mirror visual feedback, virtual reality or with observing others performing an imagined movement (81, 84). Frequent use of a myoelectric prosthesis has also been shown to limit cortical reorganization and phantom limb pain (89). However, Giummarra et al. (2010) did not find that the experience of body ownership of the prosthesis correlated with type of prosthesis, level of amputation, limb amputated (upper vs. lower), or experiencing of PLP (52). As the origin of PLP is complex and not completely clear, it is difficult to explain what affects the pain and what can be done regarding treatment.

Agency

Agency, meaning having control of one's own movements, was not experienced by the participants to be strengthened when sensory feedback was added (Paper IV). It was the same prosthesis type as that the participants were used to (VariPlus Speed hand from OttoBock). The socket fit and the EMG electrodes were not adjusted to match their normal prosthesis, and this could even reduce the sense of agency. If the prosthetic hand was too sensitive and was experienced as reacting on its own, or if the opposite, more effort than normal was required to control the prosthetic grip.

The participants were all experienced prosthesis users and experts in controlling grasping with the prosthesis. Experienced users rely on vision, motor sound, and vibrations in the socket for interpretation of the grip force (23). In terms of touch, this would mean that response to touch with the prosthesis is not modality-matched to the actual touch. A fully functioning sensory feedback system would allow the prosthesis user to adjust the grasping and performance of activities based on the sensory input. As mentioned previously, a perception of touch as close as possible to physiologically natural perceived sensation is the goal. Some of the comments from the patients in Paper IV gave us hints that with the non-invasive sensory feedback based on PHM used in Paper IV, we were onto something useful.

The core of having a sense of agency is the relationship between a voluntary action and an outcome. To achieve a feeling of agency, the control of the movement should be smooth and fluent. If there is a mismatch between the intended action and the actual movement, the sense of agency is lost (61). With the sense of agency there is also the aspect of having an influence on the environment (61). It is possible to experience body ownership without having a feeling of agency. In non-voluntary movements, with afferent sensory feedback a sense of body ownership can be achieved—but no sense of agency. To achieve agency, there must be efferent motor commands that are associated with the movement (144).

Body ownership

In the narratives presented in Paper I, none of the patients had used a prosthesis with sensory feedback, and the existing prosthesis was mainly described as being a tool. It could be incorporated in the body image, such as having a perception of where the prosthesis ended, but it was rarely experienced as being a real part of the body. Why is it important to incorporate the prosthesis into the body image, leading to the possibility of it being an integrated part of the body and not only an external tool? It is possible that having the experience of body ownership of the prosthesis facilitates the acceptance of the prosthesis, and as a consequence leads to improved performance (10, 31, 56, 57, 70).

The experience of body ownership is thought to have an important role in the acceptance of the prosthesis, and the feeling of touch appears to be crucial in this process (10). It is said that cutaneous touch is closely linked to the identification of the bodily self (10, 17, 39). When visual, tactile, and proprioceptive information is matched as originating from the same body part, a feeling of body ownership arises (71, 97). Tsakiris et al. (2007) suggested that multisensory correlation alone is not sufficient to induce the feeling of body ownership in the “rubber hand illusion”. They also highlighted the importance of a visual correlation between the object and the body image. They suggested that body ownership originates from an interaction between processes of sensory integration and a process based on visual and functional representations of the body (144). When a hand prosthesis is worn there is visual input of a hand and of using it functionally (gripping) with motor commands, and when sensory feedback is added, several channels/senses are involved for achievement of the feeling of body ownership. This was expressed in Paper IV: “*I feel complete!*”.

Klackert and Ehrsson (2012) showed in experiments with the “rubber hand illusion” that agency and body ownership can be experienced separately. When there is an anatomical incongruence between the observed rubber hand and the position of the real hand, it is possible to experience agency but not body ownership. In the state of passive movements, but with tactile feedback, the feeling of body ownership is intact, but the experience of agency is lost. The states are not totally dissociated, and when body ownership is experienced the sense of agency gets stronger (75). In our results in Paper IV, we could see an increase in body ownership but not in the experience of agency, which is in line with the idea that the two states can be differentiated.

In the interviews in Paper IV, when the participants described the experience of sensory feedback in their own words, they explained it as a feeling of completeness, that the connection to the prosthesis became stronger. One individual reported that the prosthesis was worn for longer periods during the test period. The subjective experience of body ownership in the presence of sensory feedback has previously been reported to be achieved irrespective of functional improvements (56, 98). In the long run, acceptance and increased use of the prosthesis might improve the performance of activities. This is yet to be confirmed in long-term studies. The prostheses used in our experiments are still prototypes, and they still lack refined design regarding aesthetics and quality of grip. This could be one reason for the lack of improvement in performance.

If the prosthesis is perceived as being part of one’s own body, this cannot only be expected to facilitate its acceptance, but it will also influence the overall well-being of the individual in a positive way (10, 49), reduce the influence of hindrances in the surroundings (151), and have significance for social interaction and quality of life (57).

Methods

Participants

In Paper I, the group studied was heterogeneous. Individuals with either acquired amputation or congenital reduction deficiency participated, with the aim of having broad variation. There were considerable differences between the groups. Those with acquired amputation would always miss something that once belonged to them, in contrast to those with congenital reduction deficiency who generally had the experience of having a normal state with just one arm. The type of prosthesis used also varied (myoelectric, cosmetic, or aesthetic). For how long and how frequently the myoelectric prosthesis was used also varied, which may have affected the outcome measures in Paper IV. The interview in Paper I was carried out irrespective of the cause of amputation and the type of prosthesis, and one must bear in mind that the experiences may have differed due to the differences in cause of amputation and prosthesis type.

Time since amputation was another factor that varied in Papers I, II, and IV (from one year to 35 years) and it may have been of importance when considering, for example, body image and phantom pain.

Statistics

In Papers II and IV, the groups studied were small (seven to 13 participants), which may have limited the statistical power. However, in studies concerning amputees, it has been unusual to have large groups. Acquired arm amputation is uncommon, and when other inclusion criteria have been added (such as transradial amputation and experiencing of PHM), it is even more difficult to find appropriate participants.

We used mixed methods in Paper IV. Descriptive statistics were used for the objective outcome measures due to the small group size (seven participants) and to illustrate the varied results, with a low number of participants, which is the case in almost all reports about new approaches with hand prostheses. Here, the addition of a qualitative method can be considered as an initial validation of the quantitative results that (by definition) have low power due to the low number of participants. Qualitative methods were added to broaden the results, and to capture the participants' experiences in their own words; see "Qualitative method" below.

In Paper III, which was based on able-bodied participants, the number of participants was higher (n = 31) and the number of measurement points analyzed was more than 50,000 (every single stimulation compared with response). The results also showed very clearly that it is possible to learn to associate sensory stimuli on the forearm with specific fingers. Using Cohen's kappa, there was excellent agreement (> 0.8) between the stimuli given and the response.

Qualitative method

This research project was meant to be close to the patients and their use of the prosthesis. We allowed the participants, who were the end-users, to have their own points of view. It was high on the agenda when planning the studies that their views on the new functions that were being explored in their prosthesis should be investigated. This has also been the case when discussing future priorities.

In Papers I and IV, a qualitative method was used—a semi-structured interview for the data collection and a qualitative content analysis. For *dependability*, the first author (UW) and one co-author (IC) read and coded the interviews independently, and by in-depth analysis and discussion interpreted the text together (investigator triangulation) (20, 116). *Credibility* was achieved by including representative quotations from the participants, making the interpretation transparent for the reader. During the interviews, constant confirmation and clarifying of information ensured *confirmability*. We focused consistently on the text to reduce the risk of over-interpretation. *Transferability* was limited, but a thorough description of the participants and the study context was presented (64).

An inductive method was used in Paper I, meaning a search for patterns in the material. From the concrete data, generalizations could be made and abstracted. In Paper IV, we used a direct deductive method where we searched for explanations in existing predefined terms in the data. From an abstract level, movement to a more concrete and specific one was made (58).

The low number of participants was a limitation regarding the possibility of achieving saturation of the data. However, having a low number of participants is a frequent problem, due to the low number of cases with transradial amputation and to the specific inclusion criteria. The interviews were rich in detail.

All the interviews in Papers I and IV were carried out by the author of this thesis. Some of the participants had also met the interviewer at the clinic as patients, which may have influenced the interview situation, and affected the *dependability*. Previous contact between the interviewer and the person being interviewed may have affected the interplay between them, and also the answers given. It could have inhibited the respondents, but it might even have deepened the interview and the narratives being shared.

Technical issues

Performing research involving humans can be challenging enough, but when one adds techniques that the individual is supposed to use and integrate with at home (i.e. out of sight), this makes it even more difficult.

In Paper III a tactile display was used, which involved pressure from servo motors on the forearm. The practising with equipment using a laptop and a cuff with embedded servo motors on the forearm was performed at home by the 31 participants. So, there were possible technical problems as well as problems of adherence. However, the computer methods used checked that all training sessions had been done. The servo motors made a weak sound, and this was because the speed of rotation of the servo motor was set to be the same. When applying pressure, the five servo motors had the same sound. However, more observant participants could have noticed slight differences in sound, which may have affected their learning and progress.

Other technical issue in Paper III was the automatic saving of data online. This was not a problem when the participants remembered to connect to a network, which was done in almost every case. In a few cases, the servo motors or the tactile display malfunctioned. This was most often due to a lack of connection between the program and the tactile display. It could easily be fixed by restarting the program or the computer.

In Paper IV, a myoelectric prosthesis with a non-invasive sensory feedback system was tested and evaluated. The solution must be seen as a prototype (*Figure 7*) with huge potential for improvement. The aesthetics needed to be improved, so that it could be used without embarrassment in social contexts. In this prototype, the silicon bulbs (sensors) on the fingertips were quite large, which made them bulky in fine manipulation. In some situations it was also experienced as too soft, which made it difficult to hold small objects or to get a distinct grip. The silicon bulbs in the socket (actuators) could probably also be improved. The participants wished for a stronger or more distinct pressure, which should be considered in further development of the actuators.

Minor discrepancies in the adjustment of the sensitivity of the EMG electrodes in the new prosthesis—compared to the one normally used—could also affect the degree of skilfulness.

Measurements

In Paper II, we used the contralateral arm as a control when comparing touch threshold with SWM and tactile gnosis with 2PD. A control group would have been ideal, but due to the limited number of forearm amputees we needed to include all of them in the test group. Another alternative to using the corresponding arm as a control would have been to use the skin of the residual arm. But the heterogeneity of the stumps—both in terms of length and skin quality—would have made that very complicated.

Our implementation study (Paper IV) differed from many other studies, since it was performed and evaluated in the participant's home environment, and concentrated on performance of activities and also the experience of sensory feedback. This approach was quite unique, and most research in the field of sensory feedback is made in a laboratory environment. Usually, in trying to standardize the tests and evaluations, most evaluations end up as simple grip tests (26, 100, 133). Instead, we wanted to evaluate the performance and value of sensory feedback in an environment that was relevant and meaningful to every single participant, i.e. at home. Due to the prototype appearance of the prosthesis with cables on the outside, some participants choose to use it only at home. But a few of the seven used it all the time, including at work, in sports activities, and at home. It was not possible to have full control over the timing of using the prosthesis, or over what the participants did when wearing the prosthesis. Perhaps a wearing time of two hours a day, which was suggested as a minimum over a four-week period, is not enough to change the behaviour and capacity of experienced users.

While the objective measurements did not show any clear change in either direction, and the results varied from case to case, it is difficult to draw any conclusions. Perhaps the assessment tools were not sensitive enough, or maybe there were no changes. The aim was to evaluate how forearm amputees experienced the use of a non-invasive sensory feedback system in daily life over a four-week period, and we chose assessment tools to achieve this aim. It would have been possible to widen the measurements and include further assessment tools and questionnaires. However, this is something that one has to consider as a researcher—in order not to overload the participants in a research study.

Future priorities

To achieve a closed loop between human and machine, a dynamic interaction between motor output and sensory input is needed (137).

Previous survey studies have shown that the light weight of the prosthesis, improved aesthetics, and sensory feedback (e.g. grasping force) are desirable (12, 120), and also speed in grasping (120), increased dexterity, glove durability, dirt resistance (12), and wrist control (7, 12). Reliability of the prosthesis, such as robustness, is another consideration that must be taken into account. If a prosthetic hand often breaks, or needs extensive service time, it may be considered to be too much bother and end in rejection (107). Our results regarding future expectations included improved aesthetics, mobility, and sensory feedback (Paper I). These initial findings were the starting point for subsequent studies, including implementation and evaluation of adding a non-invasive sensory feedback system to a hand prosthesis. In the development, the end-users must be consulted, and their viewpoints should be investigated and considered.

The optimal sensory feedback system should achieve a matching in modality and also be somatotopically matched, for the experience of real and direct touch at the correct location (137). It is possible to elicit conscious sensory feedback from hand prostheses in a relatively simple, non-invasive way (3). That it is a conscious sensory feedback that goes beyond the prosthesis components must be understood. Sensory feedback can elicit the feeling of body ownership, which could add a new dimension to the prosthesis, the experiencing of it, the use of it, and the total well-being of the individual.

The long-term goal is that this concept will be applicable to several types of hand prosthesis, at various levels of amputation. It might also be hypothetically possible to apply the findings to amputations of the lower extremities.

Conclusions

- Today’s hand prostheses can be both facilitatory and limiting regarding performance in activity, and they are often experienced as a tool rather than as part of the body. Users experience agency of their hand prosthesis, but the lack of sensory feedback may be a factor that blocks the feeling of body ownership of the prosthesis.
- The ability to detect and localize stimuli in the PHM is very good, and the superior discriminative touch in the PHM (compared to the control) suggests that the PHM is an optimal target for transference of sensory stimuli from a prosthetic hand to the user.
- In cases where there is a lack of PHM, it is possible to learn to associate touch on predefined areas of the skin of the forearm with specific fingers, which widens the potential for non-invasive sensory feedback systems in hand prostheses.
- A non-invasive somatotopically matched sensory feedback system implemented in a myoelectric prosthesis has positive qualities regarding the feeling of body ownership and sensory feedback experienced with the prosthesis. Objective measurements did not show any improvement regarding performance in activity, but the participants described their positive experience concerning the sensory feedback and a feeling of completeness while wearing the prosthesis.

Sammanfattning på svenska

Det övergripande syftet med min avhandling var att vidareutveckla och implementera ett icke-invasivt system (utan kirurgi) för känselåterkoppling i handproteser. En amputation av en arm kan ge förödande konsekvenser och förändra livet. Det som normalt kräver två händer för att utföras måste nu klaras med bara en. Kroppsbalansen och hållningen ändras och ofta följer överbelastningsproblem som smärta i ryggen, nacken och den kvarvarande handen och armen. Även psykologiska faktorer påverkar personens identitet, sociala liv och delaktighet i samhället. Handproteser kan till viss del överbrygga problemen men dessvärre blir den första handprotesen ofta en besvikelse, då den aldrig kan ersätta den förlorade handen fullt ut. Även den mest avancerade protesen kan hamna byrålådan eftersom livet fungerar lättare utan protes. Tack vare känseln i den kvarvarande armens hud är det ibland lättare att använda armen utan protes.

Studie 1 var en intervjustudie och resultaten visade att dagens myoelektriska handproteser ger en upplevelse av *agency,* det vill säga en känsla av att kontrollera protesen, men det verkar som att avsaknaden av känsel kan vara en orsak till att protesen inte upplevs som en del av den egna kroppen (*body ownership*).

Ett centralt begrepp i avhandlingen är *phantom hand map* (PHM). Det är en slags ”känselkarta” och beröring på underarmshuden (eller i ansiktet) väcker en fantomkänsla av beröring på den förlorade handen. Det finns en punkt för tummen, en för pekfingret, och så vidare, och är ett relativt vanligt fenomen hos amputerade. Sannolikt beror detta fenomen på både förändringar i nerverna i armen och plastiska förändringar i hjärnan efter en amputation. Tidigare forskning har visat att PHM har en direkt koppling till den amputerade handens representation i hjärnan. Studie 2 syftade till att undersöka och utvärdera känseln i PHM hos amputerade. Resultaten visade att förmågan att identifiera beröring är bättre i PHM på underarmsstumpen jämfört med motsvarande punkter på andra armen. Alla amputerade har inte en PHM och därför var syftet i Studie 3 att utreda om det är möjligt att lära sig att associera sensoriska stimuli på underarmen till specifika fingrar. Efter ett träningsprogram på två veckor med en ”taktil display” kopplad till en dator för beröring i form av tryck, visades det möjligt att icke-amputerade kan lära sig att associera beröring på förutbestämda punkter på underarmen med specifika fingrar. Associationsförmågan var fortfarande mycket god två veckor efter avslutat träningsprogram. Slutligen ville jag utvärdera ett icke-invasivt känselåterkopplingssystemet i en handprotes på underarmsamputerade i deras hemmiljö under fyra veckors tid (Studie 4). De objektiva bedömningarna visade inte någon förbättrad funktion eller aktivitetsutförande med protesen, däremot uttryckte flera av deltagarna att känselåterkopplingen gav dem en känsla av helhet, närmare upplevelsen att protesen är kroppsegen.

Sammanfattningsvis kan slutsatsen dras att PHM har egenskaper som gör att den lämpar sig väl för icke-invasiva system för känselåterkoppling för armamputerade. Tack vare att det dessutom är möjligt att lära sig att associera känselstimuli på underarmen till specifika fingrar, det vill säga att man kan skapa en slags PHM, öppnas möjligheterna upp för utveckling av det känselåterkopplingssystem som använts här samt liknande system. Efter en fyra-veckors period med en protes med känselåterkoppling blev inte motoriken med protesen bättre. Däremot uttryckte flera av deltagarna att de upplevde att protesen mer kroppsegen och att de kände sig mer hela när protesen med känselåterkoppling användes jämfört med vad de gjorde med sin vanliga protes. Det finns potential i icke-invasiva känselåterkopplingssystem och det är därför motiverat att fortsätta denna utveckling i nära samarbete med protesanvändare.

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Appendix

Appendix 3: ACMC Scoring Sheet

Client (name, DOB): Male Female

Congenital Acquired Side, level: Use time:

Task: Assessment date:

Gripping		**Holding**	
With support		With support	
Power grip, without support		Without support	
Precision grip, without support		In motion	
Appropriate grip force		Without visual feedback	
In different positions		In motion, without visual feedback	
Timing		**Releasing**	
Coordinating both hands		With support	
Without visual feedback		Without support	
Appropriate grip force, without visual feedback		In different positions	
Re-adjusting the grip		Timing	
Repetitive grip & release		Coordinating both hands	
Repetitive grip & release without visual feedback		Without visual feedback	

Namn:
Datum:
PRE TEST / FOLLOW UP

PROTESFRÅGOR

Gör en markering på linjen hur du förhåller dig till varje påstående.
Längst till vänster (---) betyder ”håller inte med alls” och längst till höger (+++) betyder ”håller fullständigt med”. 0 betyder ”osäker”, jag kan varken hålla med eller inte hålla med.

I min vardag när jag använder protesen upplever jag ofta:

1. Jag kan använda protesen utan att samtidigt titta

0 + ++ +++

2. Det känns som om protesen är min hand

--- -- - 0 + ++ +++

3. Jag kan ställa ifrån mig en plastmugg med vatten utan att titta på den

--- 0 + ++ +++

4. Det känns som om protesen kontrollerar mina rörelser

--- -- - 0 + ++ +++

5. Hela armen känns gummiaktig när jag använder protesen

0 + ++ +++

6. Jag kan kontrollera greppet i protesen

--- -- - 0 + ++ +++

7. Det känns som om det är jag som styr protesens rörelser

0 + ++ +++

Namn:
Datum:
PRE TEST / FOLLOW UP

8. Jag kan tänka mig att ta i ett litet barn med protesen

			0	+	++	+++

9. Jag känner att jag kan kontrollera hur hårt jag håller i något

---			0	+	++	+++

10. Det känns som om protesen har en egen vilja

				+	++	+++

11. Jag har fantomsmärtor när jag använder protesen

			0	+	++	+++

12. Jag har fantomsmärtor när jag <u>inte</u> använder protesen

			0	+	++	+++

13. När jag tar i något med protesen känns det som jag tar i något med mina riktiga fingrar

---			0	+	++	+++

14. Det känns som om proteshanden är en del av min kropp

---	--	-	0	+	++	+++

15. Hela armen känns robotaktig när jag använder protesen

			0	+	++	+++

Namn:
Datum:
PRE TEST / FOLLOW UP

16. I bland förnimmer jag beröringskänsla i tomma luften någonstans utanför protesen

--- 0 + ++ +++

17. Det känns som om fantomhanden är i protesen

0 + ++ +++

18. Protesen känns som ett verktyg

--- -- - 0 + ++ +++

19. Protesen rör sig som jag vill att den skall röra på sig, som om jag kontrollerar dess rörelser med min vilja

--- 0 + ++ +++

20. När jag greppar föremål så känner jag beröringskänsla i protesens fingrar

--- 0 + ++ +++

21. När jag greppar föremål känns det som om beröringskänslan på stumpen projiceras upp mot överarmen och/eller bröstet

--- 0 + ++ +++

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