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The Short-Term Repeatability of Subdermal Electrical Stimulation for Sensory Feedback

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ABSTRACT Modern hand prostheses are used to restore the motor functions lost due to an amputation. However, the lack of sensory feedback remains a major challenge. Subdermal stimulation is a promising technique to restore tactile sensations when using prostheses, since it may overcome the disadvantages of surface electrodes without resorting to surgery that is required for a direct nerve interface. The present study evaluated the short-term repeatability of the perceptual properties of subdermal electrical stimulation over eight hours in healthy subjects and compared them to those of surface stimulation. Specifically, the detection threshold, pain threshold, dynamic range, just noticeable difference, resolution and quality of evoked sensations were tested and used for short-term repeatability evaluation. The results demonstrated that the detection threshold was more stable under subdermal stimulation, whereas the short-term repeatability of the pain threshold and just noticeable difference was better under surface stimulation. On the other hand, several psychometric parameters (dynamic range, resolution, sensation quality, intensity, and comfort) were equally stable and did not change significantly across sessions in either surface or subdermal stimulation. The subdermal stimulation was better localized and elicited fewer unwanted sensation modalities ($p < 0.05$), whereas surface stimulation was characterized by a higher resolution ($p < 0.05$). The results suggest that subdermal stimulation could be a viable alternative for the implementation of electro-tactile feedback as it generates sensations that are equally stable as in surface stimulation, and yet it has some important advantages for the practical applications (e.g., compact interface, permanent placement).

INDEX TERMS Prostheses, sensory feedback, surface electrical stimulation, subdermal electrical stimulation.

I. INTRODUCTION

It was reported in 2005 that approximately 1.6 million persons in the USA were living with the loss of an upper or lower limb [1]. The incidence of limb loss was estimated to reach 3.6 million in 2050 [1]. The quality of life concerning physical, psychological and vocational aspects can be extremely impaired after the loss of a limb. Artificial limbs, such as hand prostheses, have been employed for several decades to improve the quality of life of amputees. After years of extensive research and development, the fitting of prostheses has become highly individualized. Furthermore, prostheses have become more anthropomorphic in the past decade, and the most advanced systems feature individually controllable fingers and thereby many grasp types, approaching the dexterity of the human hand [2]. These devices are controlled by translating muscle electrical activity into prostheses commands, which is an intuitive control interface. Nevertheless, myoelectric prostheses are still not widely accepted among amputees. As reported in a recent review of user needs, the amputees were not content with the comfort and functionality of the myoelectric prostheses [3]. The rejection rates reported in user surveys [4] range between 17% and 80%. The addition of sensory feedback was proposed as a possible way to improve the functionality of myoelectric prostheses (thereby potentially lowering the rejection rate) [5] and it was

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often cited as a desired feature in the list of consumer design priorities [6]. Apart from a few recent examples with a limited clinical application [7], [8], none of the commonly used commercial prostheses provide somatosensory feedback to the user. Indeed, sensory feedback in able-bodied humans plays an important role in motor control, haptic exploration, and social communication. Therefore, the integration of sensory feedback could potentially enhance prostheses' performance and utility by closing the control loop through the user [9].

Different methods, such as mechanical stimulation using vibration motors, electrical stimulation of remaining peripheral nerves through implanted interfaces and surface electrical stimulation of the skin, could be used to restore sensory feedback in a prosthesis [9]–[11]. If delivered to peripheral nerves or to a phantom map that exists on the residual limb in some amputees, the stimulation can elicit somatotopic sensations in the phantom hand [12], or fingers [13], [14]. Electrocutaneous stimulation is a non-invasive technique that has been studied extensively in the past [15], [16]. In this approach, low-amplitude electrical pulses are delivered to the skin of the residual limb to activate cutaneous afferents and elicit tactile sensations. The feedback information is transmitted to the user by modulating stimulation parameters. For example, the prostheses grasping force can be communicated through the intensity of stimulation, i.e., the higher the force, the stronger the stimulation delivered to the subject. Typically, the detection and discomfort thresholds are first measured to obtain the range within which the stimulation amplitude can be modulated.

Some advantages of electrocutaneous stimulation over mechanical vibration are the absence of moving parts, steady contact with the skin, and efficiency concerning power consumption. Furthermore, the control of electrocutaneous stimulation parameters (frequency and intensity) is more flexible compared to vibration motors, where these parameters are often mechanically coupled (e.g., through a resonance behavior) [17].

Despite these advantages, electrocutaneous stimulation suffers from drawbacks, such as the need to reposition surface electrodes each day, poor consistency of evoked sensations, occasionally evoking unpleasant sensations and the difficulty of maintaining skin hydration. Placing electrodes under the skin may overcome some of these disadvantages, as the electrodes are placed permanently, bypassing the skin impedance. This can be achieved by using implanted interfaces to directly stimulate peripheral nerves via circumferential electrodes [18], [19] or intraneural electrodes [20]–[24], or through the application of cortical surface stimulation [25], [26] and intracortical microstimulation [27], [28]. These methods have led to promising results [9], [29], [30]; however, a surgical procedure is required which may not be accepted by all amputees.

Subdermal stimulation is a minimally invasive approach that does not require surgery, as the wire electrodes are applied subcutaneously using a hypodermic needle [31], [32]. While the psychometric properties of the peripheral nerve stimulation [18] as well as surface stimulation [10], [24], have been characterized, this has not been done for the subdermal stimulation. Importantly, the utility of artificial stimulation for sensory feedback relies on its ability to elicit consistent and repeatable sensations during hours of prosthesis use [33]. However, the short-term repeatability and usability of electrotactile sensations generated using subdermal stimulation have not yet been systematically investigated [31].

This study aimed to assess the short-term repeatability of the tactile sensations that are elicited using subdermal electrodes over eight hours and compare it to that of conventional surface electro-tactile stimulation. We evaluated the changes in the detection threshold (DT), pain threshold (PT), dynamic range (DR), just noticeable difference (JND), resolution and quality of evoked sensations. The short-term repeatability of these perceptual properties was compared to that of surface stimulation.

II. METHODS

A. SUBJECTS

Fourteen able-bodied subjects (9 males and 5 females, 26 ± 5 years) were recruited from Aalborg University, Denmark. All subjects provided written informed consent in accordance with the Declaration of Helsinki and all of them joined both surface and subdermal stimulation experiments. The study protocol was approved by The North Denmark Region Committee on Health Research Ethics (N-20160021). The subjects had no visible broken skin or infections in the application area.

B. EXPERIMENTAL PROCEDURE

During the experiment, the subjects were seated in a chair in a comfortable posture. An area of approximately 2 cm $\times$ 3 cm in the middle of the non-dominant dorsal forearm was gently shaved when needed and locally disinfected with a 70% alcohol swab. Then, the subdermal and surface electrodes were placed as explained in the next section.

A charge-balanced, biphasic, rectangular, and symmetric waveform with a pulse width of 200 µs produced by a USB-powered constant current stimulator (Inomed, ISIS Neurostimulator, Emmendingen, Germany) was used for both surface and subdermal stimulation. The pulse width (200 µs) was constant in all the tests, whereas the stimulation amplitude and frequency were modulated as described below. A custom-made LabVIEW program controlled the stimulator.

A sterilized fine wire electrode made of Teflon-coated stainless steel (A-M Systems, Carlsborg, WA, diameter 50 µm) was placed under the skin guided by a 25-gauge hypodermic needle. The tip of the wire was uninsulated by 5 mm [34]. A self-adhesive pre-gelled electrode (Ambu Neuroline 700, 20 mm $\times$ 15 mm) was used for surface stimulation. The two stimulation electrodes were placed in the middle of the dorsal side of the non-dominant forearm, as the more reliable sensation was observed dorsally in a previous study [35]. A self-adhesive pre-gelled electrode

(PALS Platinum, 40 mm × 64 mm, oval) was used as a common ground electrode and placed over the wrist on the dorsal side of the non-dominant forearm. The subdermal electrode was first inserted into the skin by a well-trained experimenter and fixed to the skin using 2 cm × 2 cm medical tape (Fixomull®stretch). Thereafter, the surface electrode was positioned 5 mm proximal to the insertion site. The electrodes placement and stimulation setup were similar as in our previous study [32], except that only the dorsal side of the forearm was tested in the present experiment.

Three evaluation sessions were implemented immediately (0 hour (0 hr)), 4 hours (4 hr) and 8 hours (8 hr) after placing the electrodes. All three sessions were performed on the same day and each session lasted approximately one hour. After each evaluation session, the electrodes were disconnected from the stimulator. The reusable common ground electrode was removed from the skin. The surface and subdermal electrodes were covered with an elastic bandage to avoid any unexpected displacement, as there was no limit to the daily activities of the subjects between the sessions. When the subject returned for a new measurement, the common ground electrode was reapplied, the bandage was removed, and the surface and subdermal electrodes were reconnected to the stimulator.

C. PSYCHOPHYSICAL MEASUREMENTS

1) DETECTION, PAIN THRESHOLD AND DYNAMIC RANGE

The DT is the lowest level of electrical stimulus that can be detected by the subject. The staircase procedure [36] was employed to measure DT. First, an approximate DT was determined by delivering single pulses of increasing amplitude at a starting amplitude of 3 mA for surface and 0.3 mA for subdermal stimulation. Then the pulses were delivered every 2 s, and the amplitude was increased in steps of 0.5 mA for surface and 0.3 mA for subdermal stimulation [32]. The approximate DT was identified when the subject felt the stimulation for the first time. This value was then used as the starting amplitude for the staircase procedure. If the subject did not feel the stimulation, the amplitude of the following stimulus was increased in steps of 0.05 mA for surface and 0.03 mA for subdermal stimulation; otherwise, the amplitude was decreased in the same steps. If the subject reported no detection after a trial of successful detection, or vice versa, this was defined as a 'reversal'. The procedure was stopped when 10 'reversals' were recorded or if the number of stimuli reached 30. Finally, the DT was calculated as the mean of all intensities at the 'reversals' with the first three excluded.

The PT is defined as the stimulation intensity at which the subject starts feeling pain. The method of limits [37] was used to measure the PT. Single pulses were delivered every 2 s with the amplitude increasing in steps of 0.3 mA for surface and 0.1 mA for subdermal stimulation until a pain sensation was reported by the subject. This measurement was repeated three times and three values were obtained. Finally, the PT was calculated as the mean of the three measurements.

The DR was computed as the ratio between PT and DT (PT/DT); the higher the DR, the wider the parameter span that can be used to encode the feedback information (e.g., prosthesis grasping force).

2) JUST NOTICEABLE DIFFERENCE AND FEEDBACK RESOLUTION

The JND is defined as the smallest change in stimulus amplitude that can be perceived by the subject. The JND was measured with respect to a specific baseline amplitude.

In the present experiment, the baseline amplitude was three times DT (3×DT) for both surface and subdermal stimulation. When the amplitude of 3×DT was above the PT, either 2× or 1×DT was used instead (highest amplitude that was still below the PT). To determine the JND, the baseline stimulus (single pulse) was first delivered, and after 1 s, the comparison stimulus (single pulse) was applied. If the subject reported that he/she could not feel a difference in the intensity of the two pulses, the amplitude of the comparison stimulus was increased by 0.03 mA for surface and 0.01 mA for subdermal stimulation. The iterations stopped when the subject could feel a difference. The difference between the amplitude of baseline and comparison stimulus was then adopted as the JND. The test was repeated three times, and the mean value of the three JNDs was used for data analysis. The baseline stimulation amplitude for JND measurements was not constant among the three sessions, as the DTs were different between sessions. Therefore, the Weber fraction (WF) was used to evaluate the short-term repeatability of the JND. According to Weber's law, the ratio between the JND and the baseline stimuli is constant [38]. The WF was calculated by the following equation (1):

$$k = \Delta I / I \tag{1}$$

in which ΔI represents the JND and I is the baseline stimulus intensity.

The obtained WF was then used to determine the potential resolution of the respective electro-tactile feedback. The resolution was defined as the number of intensity levels that the subject can discriminate between DT and PT. The resolution was calculated by the following recursive equation (2):

$$I_n = I_{n-1} + I_{n-1} \times k \tag{2}$$

where I_0 = DT, k is WF and the recursion stops once $I_N >$ PT. The number N is thereby the feedback resolution. Higher-resolution represents better ability of the subject to discriminate stimulation levels.

3) EVALUATION OF SENSATION QUALITY

The quality of sensations elicited by surface or subdermal stimulation was evaluated using trains of pulses at 20 Hz and 100 Hz. One-second pulse trains at the amplitude of 3×DT were delivered five times to the subject. For this assessment, trains of pulses were used to elicit sensations that are clear and long enough to allow the subjects to perceive the quality

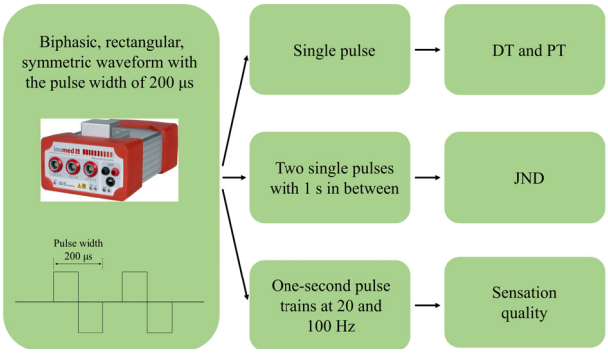

FIGURE 1. The stimulation parameters used in different psychometric tests. DT represents the detection threshold; PT represents the pain threshold and JND represents just noticeable difference.

and intensity. The frequencies of 20 Hz and 100 Hz were selected based on our previous study [32] since they were within the range that is typically used for sensory feedback. If the intensity of 3×DT was above the PT, either 2× or 1×DT was used. Three one-second pulse trains with the amplitude of 3×DT and frequency of 50 Hz and 80 Hz, respectively, were used as oddballs. Therefore, a total of 16 stimuli were randomly presented to the subject for the surface and subdermal stimulation, respectively. The stimulation pulse parameters used in this study to assess DT, PT, JND and sensation quality are summarized in Fig. 1.

The elicited sensation was evaluated by a questionnaire (Table 1) addressing the quality, intensity, comfort, and location. Multiple choices of 12 pre-defined words were offered to describe the perceived sensation quality. A numerical rating scale (NRS) from 0 to 10 was used to assess the sensation intensity, where 0 represented no sensation and 10 represented the upper limit of sensation. A Likert-type scale ranging from 1 to 7 was used to assess comfort, where

TABLE 1. Questionnaire for sensation evaluation.

	Questions			
Modality	Q1: Please choose the words that best describe the sensation.			
	□ Pressure	□ Tap	□ Vibration	□ Tingling
	□ Pinprick	□ Itch	□ Pinch	□ Pain
	□ Muscle twitch[c]	□ Movement	□ Warm	□ Cold
Intensity[a]	Q2: Please rate the intensity of the stimulation.			
	0 1 2 3 4 5 6 7 8 9 10			
Comfort[b]	Q3: Please rate the comfort of the stimulation.			
	1 2 3 4 5 6 7			
Location	Q4: Where did you feel the stimulation?			
	□ Local	□ Radiation	□ Referred	

Intensity[a], the numbers from 0 to 10 represent the stimulus intensity, in which 0 represents no intensity and 10 represents the intensity at PT. Comfort[b], the numbers from 1 to 7 represent 'Very comfortable', 'Comfortable', 'Slightly comfortable', 'Neutral', 'Slightly uncomfortable', 'Uncomfortable' and 'Very uncomfortable', respectively. Muscle twitch represents the sensation of muscle response perceived by the subject. This is not a quality of sensation per se, but it was included in the questionnaire for completeness, because muscle activation should be avoided when providing feedback.

1 represented 'very comfortable', 4 represented 'neutral' and 7 represented 'very uncomfortable'. The words 'Local', 'Radiation' and 'Referred' were used to describe the perceived location of the stimulus. 'Local' defined a perception located under or around the electrodes. 'Radiation' defined a perception spreading out away from the electrodes. 'Referred' defined a perception that appeared further away from the place where the electrode was positioned (e.g., paresthesia in the hand while stimulating the forearm skin). Answers to all the questions were recorded and saved on the computer for later analysis.

D. DATA ANALYSIS

To evaluate the short-term repeatability of surface and subdermal stimulation (within-modality comparison), the psychometric measures across sessions were assessed by using one-way repeated measures ANOVA, if the data were normally distributed (Shapiro-Wilk test); otherwise, the Friedman test was used. The Greenhouse-Geisser correction was applied when the data violated the assumption of sphericity (Mauchly's test). This was followed by post hoc tests if a significant difference was detected. The paired t-test was used for normally distributed data, and the Wilcoxon signed-rank test was used otherwise, with Bonferroni correction. To compare the psychometric parameters between the two stimulation modalities, paired t-test was used to assess the difference between surface and subdermal stimulation in each session (i.e., 0 hr, 4 hr, and 8 hr) if the data were normally distributed; otherwise, the Wilcoxon signed-rank test was used.

Regarding the analysis of sensations, the subject's data were excluded if the stimulus amplitude was not consistent (different multiple of DT) across the three sessions. Overall, the amplitudes were less consistent in subdermal stimulation, and in total, the data from 12 (surface stimulation) and 8 (subdermal stimulation) subjects were used for the analysis. In each session, the subjects provided five answers (one-second pulse trains at the amplitude of 3×DT were delivered five times to the subject) for each stimulation frequency (20 and 100 Hz) to evaluate the sensation quality and location. The answer 'yes' was recorded as a '1', and the answer 'no' was recorded as a '0'. Then, the ratio of 'yes' answers (selection ratio) was used to evaluate the short-term repeatability. The heat map figures were used to show the selection ratio in which blue represents smaller rates (near 0) and red represents higher rates (near 1). Since the number of subjects was not matched between the modalities (n=8 for subdermal and n=12 for surface), the data were compared using unpaired t-test or Mann-Whitney test.

The statistical analysis was performed using the IBM SPSS version 25, and the significance threshold was set to $p < 0.05$. The results are reported in the text using the median and interquartile range (IQR) in the format of median (Q1-Q3).

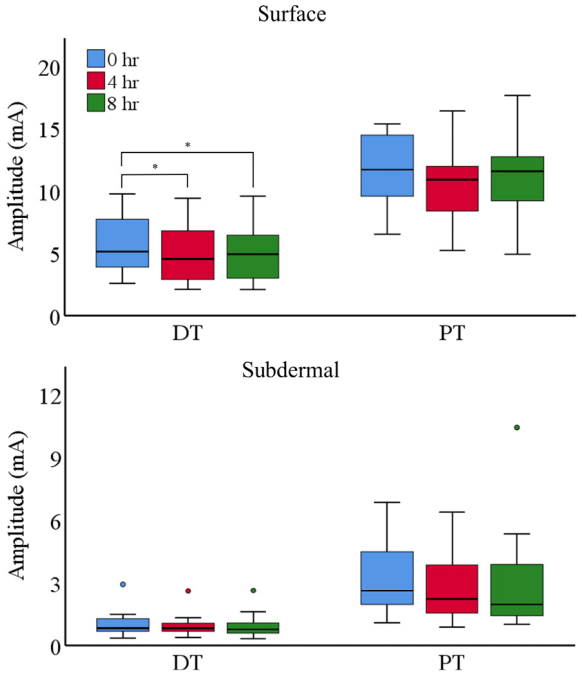

FIGURE 2. The boxplots of DT and PT for surface and subdermal stimulation across the three sessions, $*$ $p < 0.05$. 0 hr, 4 hr, and 8 hr represent the three evaluations immediately, 4 hours and 8 hours after placing the electrodes, respectively. DT represents the detection threshold and PT represents the pain threshold.

III. RESULTS

A. DETECTION, PAIN THRESHOLD AND DYNAMIC RANGE

The summary of the results for DT and PT is presented in Fig. 2. The medians (IQR) in three sessions for DT were 5.15 (3.74-7.85) mA, 4.53 (2.80-6.79) mA and 4.94 (2.81-6.57) mA for surface stimulation and 0.84 (0.66-1.32) mA, 0.84 (0.63-1.13) mA and 0.77 (0.58-1.19) mA for subdermal stimulation. One-way repeated-measures ANOVA with a Greenhouse-Geisser correction showed that the mean DT for surface stimulation changed significantly across sessions ($p < 0.01$), whereas the Friedman test revealed that there was no significant change in the DT for subdermal stimulation across sessions. The post hoc pairwise comparisons (paired t-test) revealed that the mean DT of surface stimulation significantly decreased at 4 hr ($p < 0.001$) and 8 hr ($p < 0.01$) with respect to the initial test (0 hr). In each session, the DT for the surface stimulation was significantly higher (all $p < 0.001$ for three sessions, Wilcoxon signed-rank test) than those for the subdermal stimulation.

The medians (IQR) in three sessions for PT were 11.72 (9.45-14.48) mA, 10.87 (8.25-12.26) mA and 11.58 (8.87-12.90) mA for surface stimulation and 2.62 (1.77-4.53) mA, 2.22 (1.42-4.26) mA and 1.96 (1.41-4.19) mA for subdermal stimulation. One-way repeated measures ANOVA showed that the mean PT for surface stimulation did not exhibit differences across sessions. For subdermal stimulation, Friedman's test revealed that there was a significant difference ($p < 0.05$) in the PT across the three sessions; however, the post hoc comparisons did not indicate significant pairwise differences. In each session, the PT for the surface stimulation was significantly higher (all $p < 0.001$ for three sessions, Wilcoxon signed-rank test) than those for the subdermal stimulation.

The medians (IQR) for DR were 2.22 (1.83-2.76), 2.27 (1.74-2.70) and 2.39 (1.80-3.25) for surface stimulation, and 3.41 (1.77-4.04), 2.47 (1.73-4.23) and 2.75 (2.22-3.36) for subdermal stimulation. Friedman test indicated no significant difference across the sessions for DR of surface and subdermal stimulation, suggesting that DR was equally stable for both stimulation modalities. Furthermore, there was no significant difference (Wilcoxon signed-rank test) in DR between the surface and subdermal stimulation in any of the sessions.

B. WEBER FRACTION AND STIMULATION RESOLUTION

The summary of the results for WF is presented in Fig. 3. The medians (IQR) of WF for surface stimulation were 0.02 (0.01-0.03), 0.02 (0.01-0.03), 0.01 (0.01-0.05) and subdermal stimulation were 0.09 (0.04-0.20), 0.05 (0.02-0.11), 0.05 (0.02-0.08) across the three sessions. The Friedman test revealed that the WF for subdermal stimulation changed significantly across sessions ($p < 0.05$), and the post hoc pairwise comparisons indicated that the WF decreased substantially from 0 hr to 8 hr ($p < 0.05$, Wilcoxon signed-rank test). However, there was no significant difference (Friedman test) across sessions in the WF for the surface stimulation. The WF for the surface stimulation was significantly smaller ($p < 0.01$ at 0 hr, $p < 0.01$ at 4 hr, and $p < 0.05$ at 8 hr, Wilcoxon signed-rank test) compared to that for subdermal stimulation in each session.

The Friedman test indicated that in both stimulation modalities, the medians (IQR) of the resolution were 54.00 (35.00-86.25), 51.50 (21.25-119.50), 66.00 (21.50-126.25) for surface stimulation, and 10.50 (6.75-24.25), 15.50 (8.75-52.00), 21.50 (11.75-42.00) for subdermal stimulation, and they did not change significantly across sessions.

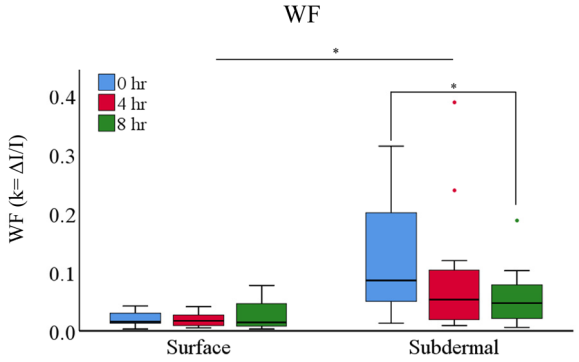

FIGURE 3. The boxplots of WF for surface and subdermal stimulation across the three sessions, $*$ $p < 0.05$. 0 hr, 4 hr, and 8 hr represent the three evaluations immediately, 4 hours and 8 hours after placing the electrodes respectively. WF represents Weber fraction.

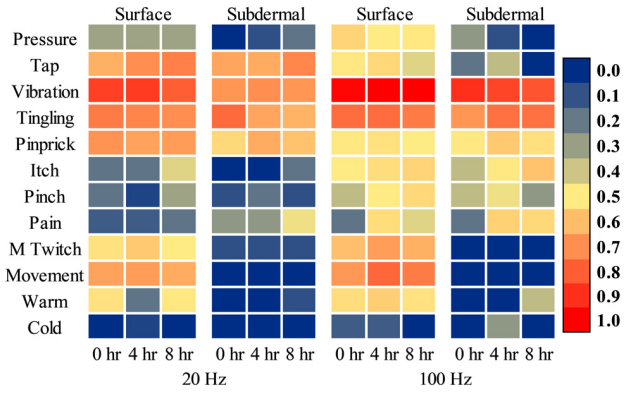

FIGURE 4. The heat map of selected sensation modalities across the three sessions for surface and subdermal stimulation at 20 Hz and 100 Hz. The selection ratio for muscle twitch at 100 Hz and the sensation of movement at both 20 Hz and 100 Hz were significantly higher in each session for surface stimulation than subdermal stimulation ($p < 0.05$). 0 hr, 4 hr, and 8 hr represent the three evaluations immediately, 4 hours and 8 hours after placing the electrodes respectively.

The resolution of the surface stimulation was significantly higher ($p < 0.001$ at 0 hr, $p < 0.05$ at 4 hr, and $p < 0.05$ at 8 hr, Wilcoxon signed-rank test) compared to that of subdermal stimulation in all the three sessions.

C. EVOKED SENSATIONS

The heat map (Fig. 4) shows the ratio for reporting a specific sensation quality during surface and subdermal stimulation. In general, fewer sensation modalities were elicited by subdermal stimulation with respect to surface stimulation (e.g., less blue color (near 0) in the map for surface stimulation). The Friedman test indicated that there were no significant differences in the ratios in any of the selected sensation modalities across sessions, implying that the quality of sensation was equally stable for surface and subdermal stimulation. Mann-Whitney U test showed that there were no significant differences between surface and subdermal stimulation in selection ratios for most of the modalities. The only exceptions are the selection ratio for muscle twitch at 100 Hz (all $p < 0.05$, for three sessions) and sensation of movement at both 20 Hz (all $p < 0.05$, for three sessions) and 100 Hz (all $p < 0.05$, for three sessions), which were significantly higher in each session for surface stimulation than for subdermal stimulation.

Fig. 5 (upper plot) presents the summary results for the perceived intensity of stimulation. The intensity at 100 Hz was significantly higher in every session compared to the intensity at 20 Hz, ($p < 0.05$ at 0 hr, $p < 0.01$ at 4 hr and $p < 0.05$ at 8 hr for surface stimulation, paired t-test) and (all $p < 0.05$ for three sessions of subdermal stimulation, Wilcoxon signed-rank test). However, the intensity of surface stimulation was not different from that of subdermal stimulation in either of the sessions, at both 20 Hz and 100 Hz. This means that similar intensity was perceived in surface and subdermal stimulation (despite the difference in stimulation parameters). The one-way repeated measures ANOVA (20 Hz for surface, 100 Hz both for surface and subdermal) and Friedman test (20 Hz for subdermal) revealed that the perceived intensity was not significantly different across sessions.

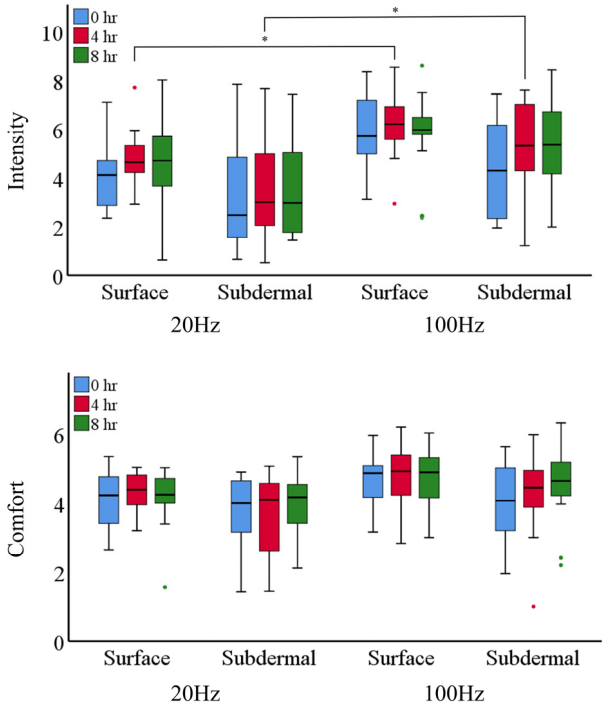

FIGURE 5. The amplitude for intensity and comfort of the three sessions. $* p < 0.05$. 0 hr, 4 hr, and 8 hr represent the three evaluations immediately, 4 hours and 8 hours after placing the electrodes respectively.

Fig. 5 (lower plot) depicts the summary of the perceived comfort of stimulation. The comfort at 20 Hz was not different ($p > 0.05$) compared to the comfort at 100 Hz for both surface and subdermal stimulation in either of the sessions. The comfort of surface stimulation was not different in either of the sessions compared to subdermal stimulation. The one-way repeated measures ANOVA demonstrated that the comfort for both surface and subdermal stimulation at 20 Hz, as well as both surface and subdermal stimulation at 100 Hz, did not change significantly across sessions.

The heat map of the perceived location was presented in Fig. 6. Mann-Whitney U test showed that there was no significant difference in selection ratios in most of the modalities between the surface and subdermal stimulation, except that less referred sensations ($p < 0.05$) were elicited by subdermal stimulation compared with surface stimulation at 100 Hz in 8 hr session. The likelihood of reporting referred sensation increased over time in surface stimulation at 100 Hz (Friedman test, $p < 0.05$), and the post hoc pairwise comparisons indicated that selection ratios increased at 4 hr and 8 hr (all $p < 0.05$, Wilcoxon signed-rank test) compared to 0 hr.

IV. DISCUSSION

The present study explored the short-term repeatability of several psychometric properties in subdermal and surface stimulation. Specifically, the short-term repeatability of DT,

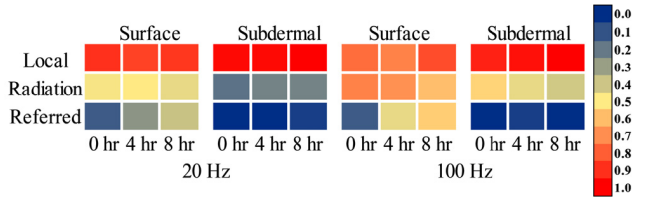

FIGURE 6. The heat map of the selected location of sensation across the three sessions, for surface and subdermal stimulation at 20 Hz and 100 Hz. Less referred sensations were elicited by subdermal stimulation compared to surface stimulation at 100 Hz in an 8 hr session ($p < 0.05$). The likelihood of reporting referred sensations increased over time in surface stimulation at 100 Hz ($p < 0.05$), and the post hoc pairwise comparisons indicated that selection ratios increased at 4 hr and 8 hr ($p < 0.05$) compared to 0 hr. 0 hr, 4 hr, and 8 hr represent the three evaluations immediately, 4 hours and 8 hours after placing the electrodes respectively.

PT, DR, JND, resolution and sensation quality were assessed in three sessions 4 hours apart.

The study demonstrated that subdermal stimulation might be an attractive option for providing sensory feedback. Most psychometric parameters (DR, resolution, sensation quality, perceived intensity, and comfort) remained similar across time in both stimulation modalities. However, DT changed significantly in surface stimulation, and PT (weakly) and WF in subdermal stimulation. Therefore, none of the stimulation modalities was superior in terms of short-term repeatability over time. However, subdermal stimulation is advantageous when considering the aspects of practical application in prostheses such as the need to mount and remove surface electrodes each day [10]. The sensations elicited by subdermal stimulation will not be necessarily somatotopic compared to, for example, direct stimulation of peripheral nerves. Nevertheless, the application is much simpler (no surgery) and therefore it could still be an attractive solution for prosthesis users who are reluctant to undergo additional surgery.

With subdermal stimulation, the DT was more stable, whereas the DT of surface stimulation decreased over time. This was likely because the impedance of the electrode-skin interface changed during the eight hours of placement (gel impregnation and sweating) [39], thereby decreasing the minimal current required to activate the afferents. However, there was no significant change in DT in subdermal stimulation, despite possible acute inflammation [40] and swelling around the subdermal electrode hours after placement, which could influence the impedance of the electrode [41]. With sensory feedback, unpleasant sensory modalities should be avoided, such as 'tingling', 'pinprick', 'itch' 'muscle twitch', 'pinch' and 'pain'. This study revealed that muscle twitch was elicited more frequently by surface stimulation at a higher stimulation frequency (100 Hz). Whereas, muscle twitch and movement were rarely elicited by subdermal stimulation at both lower (20 Hz) and higher (100 Hz) stimulation frequency. This was consistent with the results reported in a previous study [32]. Furthermore, surface stimulation requires higher current amplitude to activate afferent fibers, which contributes to a higher chance of eliciting unwanted motor responses, such as muscle twitch and movement. In this regard, subdermal stimulation may be more acceptable than surface stimulation for providing sensory feedback.

The WF decreased significantly over time in subdermal stimulation. This was a potentially useful result for the application of electro-tactile feedback because this means that the subjects' ability to discriminate the stimulus amplitudes increased over time. Interestingly, the WF was higher for subdermal stimulation than for surface stimulation, which contradicts our previous work [32]. This may be because the JND was obtained on the dorsal forearm in the present work, whereas in the previous study, the tests were performed over the ventral forearm. This could be since the ventral and dorsal forearm sides belong to separate dermatomes [42] and they have different sensitivity to electro-tactile stimulation [43]. However, it could be also due to potential small differences in the application of the intramuscular electrode in the two studies (e.g., the depth of insertion). This finding implies that a comparison of the two stimulation modalities may depend on the exact location of the application. In any case, the surface stimulation was characterized by a higher resolution compared to subdermal stimulation, despite decreasing WF in the latter. However, as demonstrated in several studies, the high resolution was not necessary to implement effective feedback. The feedback was often "discretized" into several levels and/or communicated spatially [44], [45] to ease the discrimination for the subject. In spatial coding, for example, the feedback variable was communicated not by modulating the amplitude of stimulation, but by activating different stimulation channels (e.g., electrode 1, 2 and 3 indicate low, medium and high grasping force).

With surface stimulation, the PT was stable across the three sessions [33], whereas the PT changed for subdermal stimulation. Practically, this means that both stimulation modalities might be used sub-optimally over time if we assume that the electro-tactile feedback system was calibrated only once at the beginning (0 hr). More specifically, after some time, the subjects might be able to detect smaller or tolerate lower amplitudes in surface and subdermal stimulation, respectively, than what was determined through initial calibration. To address this, fast re-calibration could be conducted during prostheses use.

Different current amplitudes were used for surface and subdermal stimulation, as the DT and PT of surface stimulation were significantly higher ($p < 0.001$) than that of subdermal stimulation. The current amplitude of three times the DT ($3\times$DT) [32] was used for the assessment of the JND and sensation quality (sensation quality, intensity, comfort, and sensation location). The current amplitude for these tests was referenced to DT in order to produce a clear and painless sensation with both stimulation modalities. A single pulse was used to test DT, PT and JND, whereas a one-second pulse train was applied when assessing the sensation quality. A single pulse was a brief stimulus that elicits a short sensation (single tap), which was therefore not enough to appreciate the

difference in quality. However, the trains of pulses produced clear and longer sensations that could be compared in quality.

The drawbacks of surface stimulation are the need to reposition surface electrodes each day, poor consistency of evoked sensations, occasionally evoking unpleasant sensations and the difficulty of maintaining skin hydration [31]. Subdermal stimulation, on the other side, has a minimal risk of infection due to the use of the needle and the electrode wire penetrating the skin (percutaneous application). A superficial infection rate of only 3.1% over a 12-week period was reported in previous studies, and the infections can be treated with topical sterilization and oral antibiotics; no removal was needed afterward [46]. The infection rate of only 0.4% was reported by Memberg *et al.* within 710 implanted electrodes for months to years, and they could be treated by a local antibiotic, even though removal of the electrode was needed sometimes [47]. In the present study, there was no sign of visible swelling or irritation during eight hours and none of the subjects reported infection afterward.

The approach of subdermal stimulation is minimally invasive, and this could be more accepted by amputees that can be hesitant to undergo an additional surgical procedure. However, in this case, there is a challenge in interfacing the implanted subdermal electrodes to the outside of the body. Nevertheless, the electrodes are close to the surface, just below the skin, and this can be beneficial in establishing the radio link. Furthermore, an interface has been presented recently [48] where a subdermal electrode, envisioned for chronic applications in prosthetics, has been placed in the skin with a percutaneous connection point (''button'').

The electrical stimulation for providing sensory feedback would affect the electromyographic (EMG) signals that are used for the myoelectric prosthesis control [49]. The subdermal electrode produces a smaller electrical field, and it might, therefore, generates less interference; however, this is still to be tested.

The psychometric procedures in the present study were selected based on time constraints since many tests were performed in a single session. More robust results could have been obtained by using more advanced methods (e.g., a staircase procedure with the two-alternative forced-choice task [50] to determine DT, PT and JND). Nevertheless, the same methods were used for both stimulation modalities (surface and subdermal) and their comparison was indeed the most important aim of the present study.

The evaluation period in this study lasted only eight hours; however, for its ultimate use in prostheses, the long-term repeatability of subdermal stimulation remains to be further evaluated in future studies. The present study aimed to investigate potential differences in the quality and/or quantity of elicited sensations during this time in response to changes in the electrode-skin interface or in subjective experience due to prolonged electrode application. The interval of eight hours has been selected since this is the duration of a typical working day. We assume that an amputee will don the prosthesis in the morning and then wear it throughout the working hours. The surface electrodes will remain in constant contact with the skin during this time. Therefore, we have selected eight hours as a functionally relevant interval to compare surface and subdermal stimulation in the same conditions (electrodes on/in the skin). A long-term (7 days) study evaluating the variability of psychophysical measurements with subdermal stimulation in amputees has been planned. Also, the sensory adaptation to electro-tactile stimulation [51] is an important phenomenon when considering the clinical application and it should be therefore investigated if there is any difference in habituation between surface versus subdermal stimulation. This is an important goal for future work.

As demonstrated recently [12]–[14], [52], surface stimulation can be used to provide somatotopic feedback by eliciting referred sensations 'located' in phantom hand/fingers. In the present study, subdermal stimulation also evoked referred sensations, but they occurred less frequently, which means that it could be more difficult to provide somatotopic feedback using this approach. Nevertheless, this likely depends on multiple factors (e.g., depth of insertion, size of the uninsulated tip, stimulation amplitude, etc.) and these should be investigated systematically in future work. In the present study, the stimulation was delivered to the forearm. Nevertheless, we expect that the elicited sensations and general conclusions would be similar if the stimulation is delivered to the skin of the upper arm. Therefore, subdermal stimulation could be applicable both to trans-radial and trans-humeral amputations.

Finally, it is important to emphasize that direct comparison between the surface and subdermal stimulation may not be on the same grounds as the surface electrode is bigger than the subdermal electrode and they are placed on/in different layers of the skin. Nevertheless, this was not the goal of the present study. Instead, the aim was to compare the short-term repeatability of the psychometric parameters overtime when the two stimulation modalities were delivered using setups that are representative of the future clinical applications.

V. CONCLUSION

The present study found that subdermal stimulation might be a promising method to provide stable electro-tactile feedback. The comparison with surface stimulation suggests that the two stimulation modalities were equally stable in most measures (DR, resolution, sensation modalities, and intensity). The application of subdermal stimulation needs to be tested in the amputee population using a sensate prosthesis to accomplish functional tasks. We expect that the general conclusions related to the difference between subdermal and surface stimulation would remain valid; nevertheless, the absolute values characterizing the tactile sensitivity (e.g., DT and PT) might change between healthy subjects and amputees due to stump conditions (e.g., scar tissue, phantom limb). In addition, subdermal electrodes could be inserted in the regions of the skin, activating the phantom map, which would provide somatotopic feedback [53] and might decrease the phantom limb pain [54].

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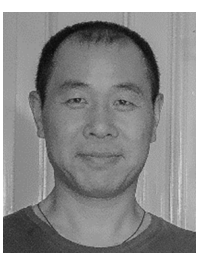

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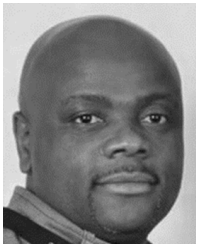

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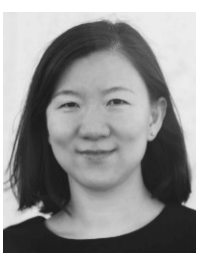

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