

## BIOENGINEERING

# Restoration of natural thermal sensation in upper-limb amputees

Francesco Iberite<sup>1</sup>, Jonathan Muheim<sup>2</sup>, Outman Akouissi<sup>2,3</sup>, Simon Gallo<sup>4,5</sup>, Giulio Rognini<sup>4,5</sup>, Federico Morosato<sup>6</sup>, André Clerc<sup>2</sup>, Magnus Kalff<sup>2</sup>, Emanuele Gruppioni<sup>6</sup>, Silvestro Micera<sup>1,2\*,†</sup>, Solaiman Shokur<sup>1,2\*,†</sup>

The use of hands for gathering rich sensory information is essential for proper interaction with the environment; therefore, the restoration of sensation is critical for reestablishing the sense of embodiment in hand amputees. Here, we show that a noninvasive wearable device can be used to provide thermal sensations on amputees' phantom hands. The device delivers thermal stimuli to specific regions of skin on their residual limb. These sensations were phenomenologically similar to those on the intact limbs and were stable over time. Using the device, the subjects could successfully exploit the thermal phantom hand maps to detect and discriminate different thermal stimuli. The use of a wearable device that provides thermal sensation can increase the sense of embodiment and improve life quality in hand amputees.

**T**he human hand provides rich sensory information crucial for effective and safe manipulation (1, 2). For prosthesis users, the ultimate goal is to restore sensation by creating a link with artificial sensors (3). Tactile sensations on users' phantom hands can be achieved by means of direct neural stimulation (4, 5). A similar effect can also be noninvasively obtained by exploiting tactile phantom hand maps—regions of the residual limb able to elicit tactile projected sensations (6).

Although these approaches have been successfully used to restore haptic information, such as texture (7), shape (8), and stiffness (9), to the best of our knowledge, thermal feedback has not yet been restored. The very small size of thermal fibers does not allow reliable targeted direct electrical stimulation with state-of-the-art implantable neural interfaces (10). Here, we show that a noninvasive wearable device can be used to generate thermal sensations, similar to those experienced in an intact arm, in upper-limb amputees. To achieve this, we stimulated specific spots on the amputees' residuum and investigated whether the stimulation could elicit a thermal phantom hand map.

Twenty-seven adult (24 to 65 years old; four female) upper-limb amputee participants were included in the study (table S1). Twenty-two

of the participants had transradial amputation, four of the participants had wrist disarticulations, and one participant had partial hand amputation. In all cases, amputations occurred at least 1 year prior. All but five participants used robotic prosthetic hands (two participants used body-powered prostheses, and three used cosmetic hands), and they all reported mild to no phantom limb pain on a visual analog scale (VAS < 3).

First, we investigated the presence of tactile phantom hand maps in all participants. Using the round side of a pen to stimulate different parts of the residual arm (Fig. 1A), we found evidence of projected sensation in 26 of the 27 participants (table S2).

## Presence of thermal phantom hand maps in upper-limb amputees

Next, we performed a thermal investigation on the residuum using a custom thermal device named MetaTouch (Metaphysiks, Lausanne) (Fig. 1B and supplementary materials). We found evidence of thermal phantom hand maps in 17 out of 27 participants. The sensation manifested in several points (up to four in some participants) with distinct somatotopic projection on the phantom hand and thermal description; for example, one participant reported "I feel you are cooling down my left index finger." For each spot on the residual arm, we tested three thermal stimuli, at 25°, 32°, and 37°C, and asked the participants to rate their thermal perception on a visual analog scale ranging from very cold to very hot (Fig. 1C).

The thermal perception was not uniform on all the tested spots; in some cases, the participants only perceived the hot stimuli, and in other cases, they only perceived the cold stimuli (fig. S1). We focused mainly on spots where the participants could perceive the cold, neutral, and warm stimuli (spots of coherent thermal perception) and where the projected

sensations overlapped for the three stimuli (coherent locations). We considered these thermal phantom spots that could be used for neuroprosthetics (Fig. 1D). We found evidence of thermal phantom spots in 15 of the 27 participants (table S2 and fig. S3), suggesting that in 56% (15/27) of the subjects, thermal phantom hand maps might be exploited for prosthetic use (Fig. 1E).

We also discovered that in some participants, the thermal phantom hand maps were present even in the absence of tactile stimulation. We used a chemical cooling agent (menthol cream) on one of the thermal phantom spots (1I) of five participants. Among the participants, two reported thermal projected sensations (table S3). The cooling sensations were projected on similar regions of the phantom hand when we used the cooling agent and the MetaTouch (Fig. 1F).

## Thermal phantom sensations are phenomenologically similar to those of the intact hand

To further investigate the phenomenological experience of the thermal projected sensations, we compared the sensation elicited by the MetaTouch on a thermal phantom spot with the physical stimulation on the mirrored intact body part with four amputee participants. Before the tests with the amputee participants, and to validate that the MetaTouch could deliver sensations similar to those produced by contact with real objects, we ran a control experiment with eight nonamputee subjects where the MetaTouch and the physical objects were placed on mirrored body parts. We chose the lower abdomen as the stimulation region; in a previous study (12), we reported that this is a region with particularly good sensitivity (better than that of the hand) to material detection. The MetaTouch produced the signature thermal drop of the skin in contact with one of the following three materials: copper, glass, and plastic (Fig. 2A). On the contralateral side, we used slabs constructed of the same three materials and of the same size as the MetaTouch thermode (3 cm by 4 cm). The participants had to report whether the two stimuli matched in terms of both location and thermal sensation. On average, the nonamputee participants reported that the physical and MetaTouch-mediated stimuli matched at 76.4%, with the highest rates of matching for plastic (86.8%), followed by glass (72.9%) and copper (68.75%) (Fig. 2B). In all cases, when we used nonmatching parameters (for example, physical copper on one side and MetaTouch-mediated plastic stimuli on the other), the probability of participants reporting that two stimuli matched was significantly lower (30.1%,  $P = 0.004$ , on average; 15%,  $P = 0.004$ , for plastic; 41.1%,  $P = 0.008$ , for glass; and 34.1%,  $P = 0.039$ , for copper; Friedman test).

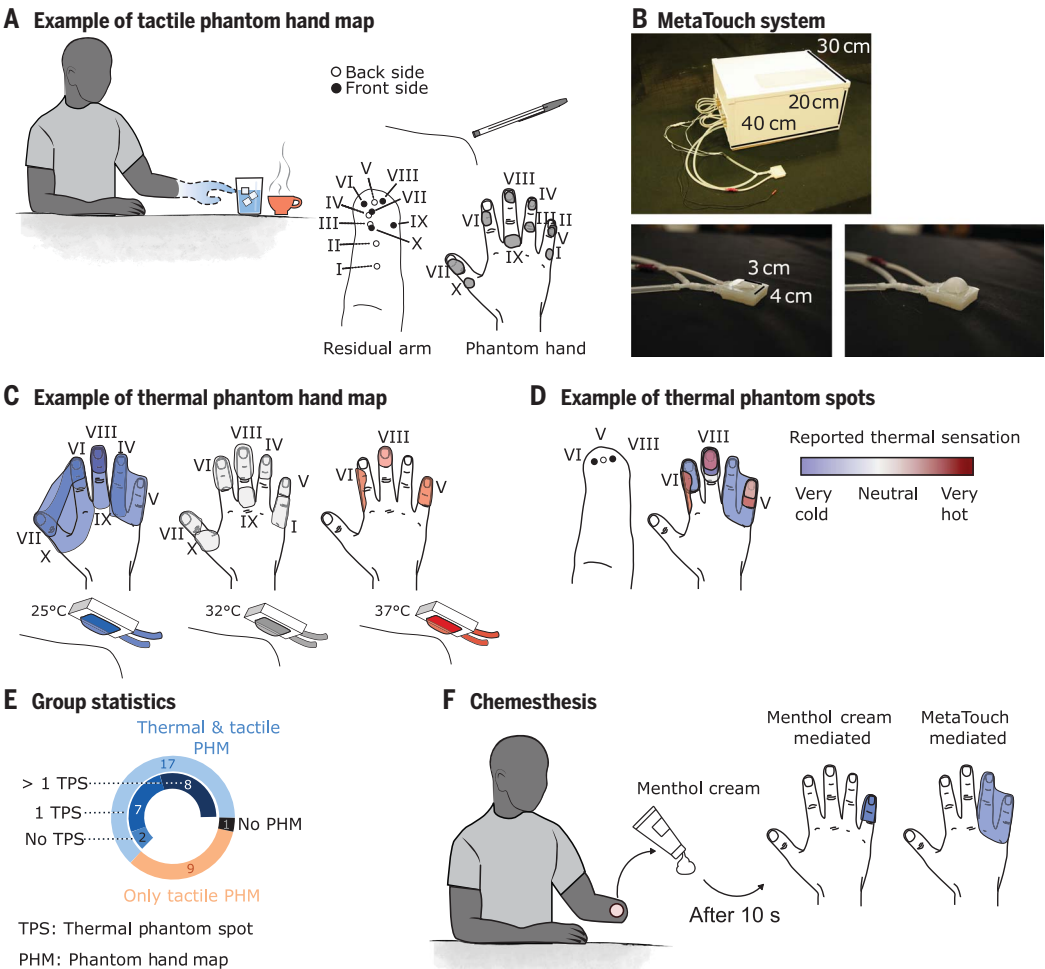
<sup>1</sup>The BioRobotics Institute, Health Interdisciplinary Center, and Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, 56127 Pisa, Italy. <sup>2</sup>Bertarelli Foundation Chair in Translational Neural Engineering, Neuro-X Institute, École Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland. <sup>3</sup>Bertarelli Foundation Chair in Neuroprosthetic Technology, Neuro-X Institute, École Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland. <sup>4</sup>Bertarelli Foundation Chair in Cognitive Neuroprosthetics, Neuro-X Institute, École Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland. <sup>5</sup>Metaphysiks Engineering SA, 1260 Nyon, Switzerland. <sup>6</sup>Centro Protesi INAIL, 40054 Vigorso di Budrio, Italy.

\*Corresponding author. Email: silvestro.micera@epfl.ch (S.M.); solaiman.shokur@epfl.ch (S.S.)

†These authors contributed equally to this work.

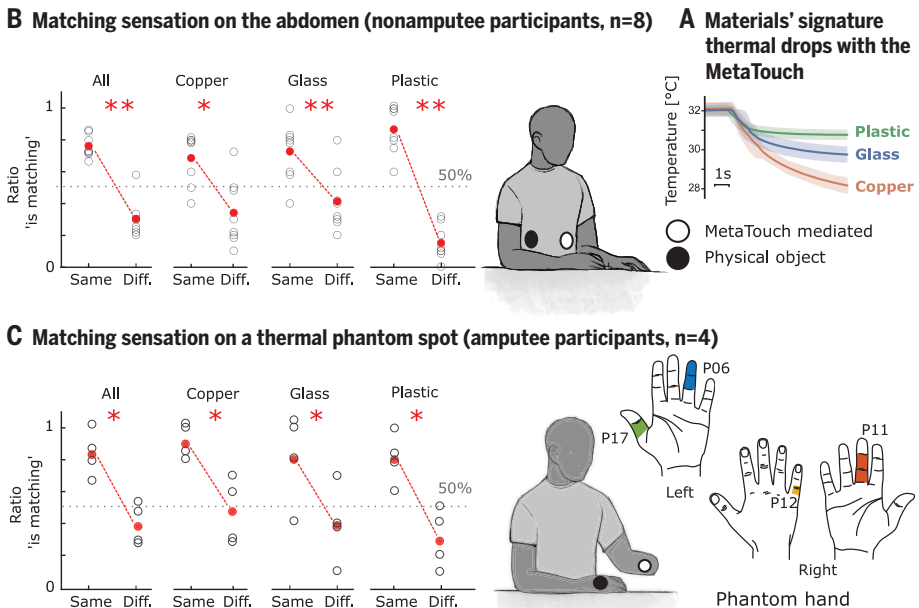


**Fig. 1. Tactile and thermal phantom hand maps.** (A) Tactile stimulation was performed on the residual arm using the round part of a pen. (Left) Top view of the residual arm, with spots on the front (black circles) and back (hashed circles) of the arm labeled, and (right) the corresponding tactile projection onto the phantom hand. (B) The MetaTouch system (Metaphysiks, Lausanne): a custom-made, hydraulic, thermal device that allows precise thermal display on a 3 cm by 4 cm inflatable silicone cell. (C) Reported projection on the phantom hand for stimulations performed on the residual arm [same points as in (A)] with the thermode set at 25°, 32°, or 37°C. The color corresponds to the participants' response, using a thermal visual analog scale, that ranges from very cold (dark blue) to very hot (dark red). (D) Example of three thermal phantom spots. (E) Group statistics for the 27 participants. (F) Comparison between a MetaTouch-mediated thermal sensation in the phantom hand and the sensation mediated by applying menthol cream. All examples in this figure are derived from participant P12.



**Fig. 2. Phenomenological experience.**

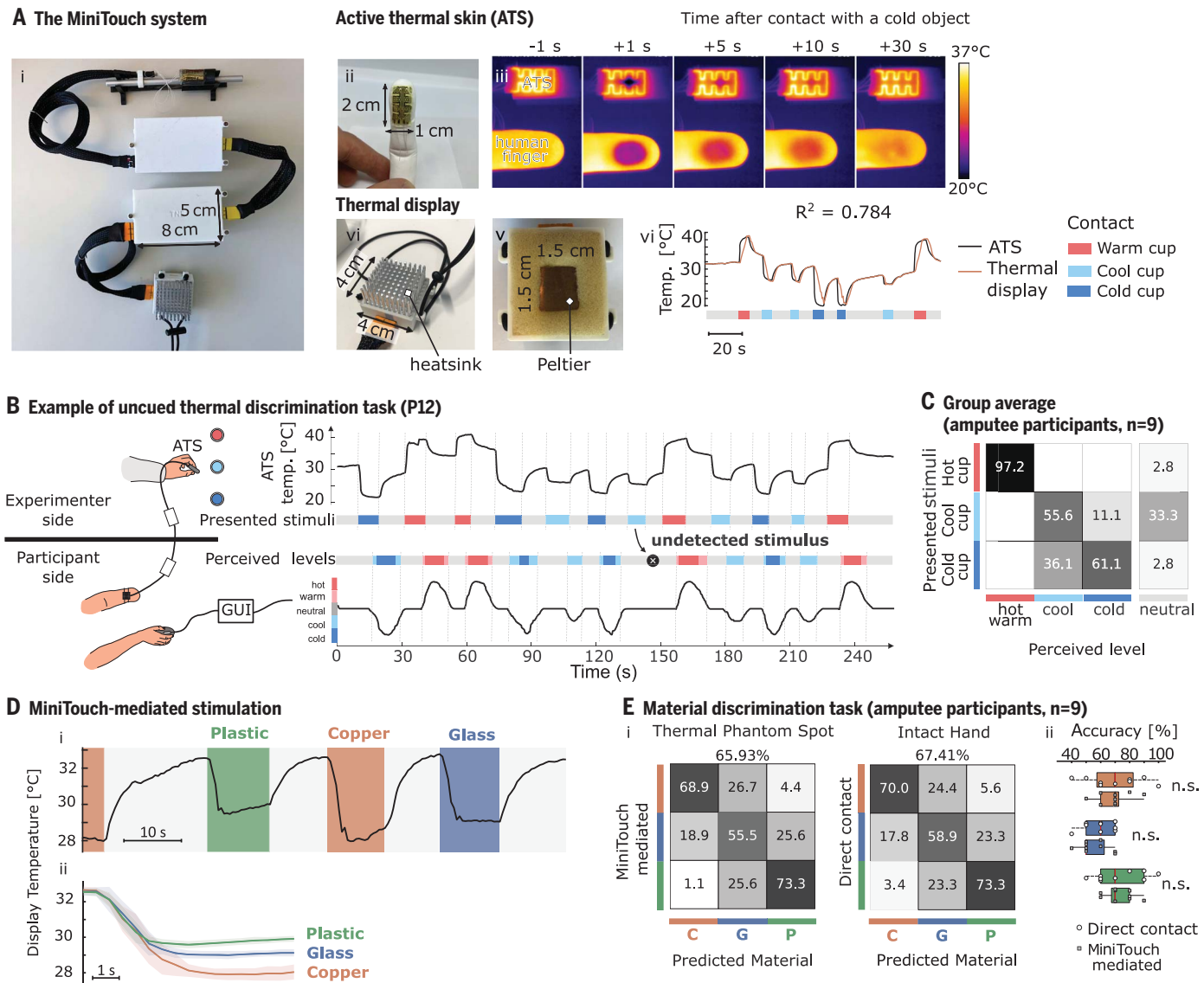
(A) MetaTouch-mediated thermal curves. (B) Healthy participants ( $n = 8$ ) reported whether stimuli with a physical slab constructed of copper, glass, or plastic placed on their abdomen matched or did not match (in terms of the position and thermal properties) the MetaTouch-mediated stimuli on the mirrored side. (C) The test with amputee participants ( $n = 4$ ) was performed with the MetaTouch placed on a thermal phantom spot on the residuum and physical objects placed on the mirrored intact body part. The set of physical and MetaTouch-mediated stimuli were not described to the participants. A gray dot represents, for each participant, the percentage of trials where they perceived the stimuli as matching, considering the trials where the stimuli were the same ("Same") and those that were different ("Diff."). The red dots denote averages.  $*P < 0.05$ ,  $**P < 0.01$ ; Friedman test.



Next, we ran the matching task with four amputees, all of whom had at least one thermal phantom spot (Fig. 2C). On average, the amputee participants reported that the phys-

ical and MetaTouch-mediated stimuli matched at 83.3%, a rate similar to what we had observed in nonamputee participants (76.4%). The highest rates in this case were found for copper

(90%), followed by plastic and glass (both at 80%) (Fig. 2B). When we presented non-matching parameters, the probability of participants reporting that two stimuli matched



**Fig. 3. Thermal feedback in sensory perception tasks.** (A) Composition of the MiniTouch: (i) The controller (white boxes), sensor, and Peltier elements that stay in contact with the skin. (ii) The active thermal skin (ATS) sensor mimics temperature dynamics of the (iii) skin temperature. The heatsink element (iv) mounted on the Peltier elements (v) allows heat dissipation. (vi) The Peltier elements follow the temperature given by the ATS sensor. Red, light-blue, and dark-blue regions correspond to contact periods with hot, cool, and cold objects, respectively. Between contacts (gray regions), the ATS recovers to the skin baseline temperature (32°C). (B) The experimenter randomly placed the ATS in

contact with objects at 15°, 24°, or 40°C, and participants were asked to report their sensation on a visual analog scale changing from cold to hot on a graphical user interface (GUI). (C) Confusion matrix. (D) (i) Temperature at the surface of the Peltier elements at the contact onset and offset with plastic, glass, and copper. (ii) Mean ± SD for all three materials (10 trials per material). (E) (i) Confusion matrix for three-class forced-choice material identification for MiniTouch-mediated materials and physical objects (mean score over nine participants) and (ii) their comparison per material type. n.s., nonsignificant; Wilcoxon rank sum test.

was again significantly lower (39.17%,  $P = 0.04$ , on average; 47.5%,  $P = 0.04$ , for copper; 30.0%,  $P = 0.04$ , for plastic; and 40.0%,  $P = 0.04$ , for glass; Friedman test). Our results show that thermal phantom sensations are phenomenologically similar to those of the intact hand.

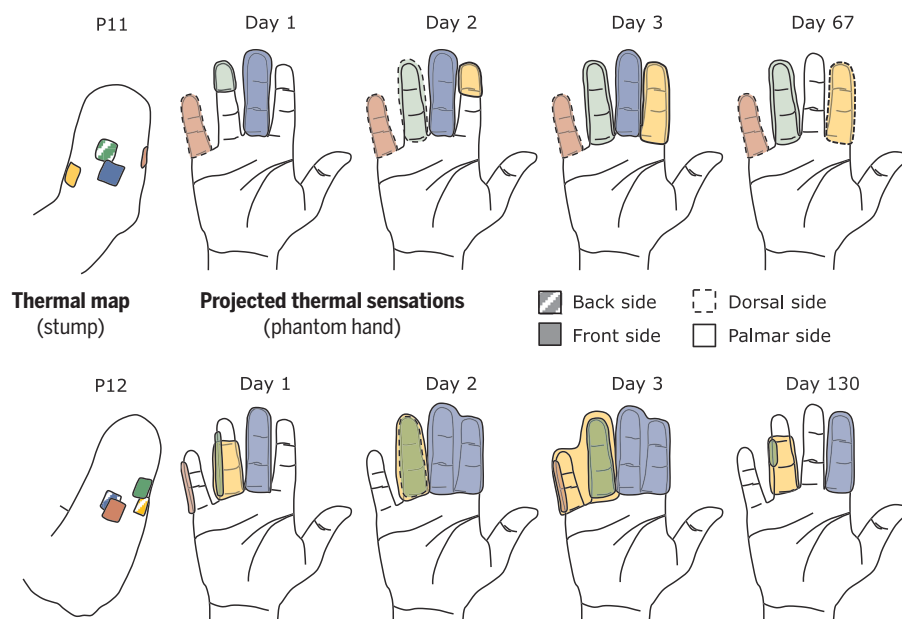
**Delivering thermal phantom sensations through a wearable device**

We then investigated whether our approach could be used to deliver stable sensations over

time. We designed a custom-made wearable device, the MiniTouch system (Fig. 3A and supplementary materials). The MiniTouch uses two Peltier elements to cover a 15 mm by 15 mm stimulation area. An important feature of the MiniTouch is the active thermal skin (ATS) sensor, which is a flexible thin-film (200-μm) device with heating and sensing properties designed to be mounted on existing prostheses. The ATS sensor keeps the temperature at sensor's surface at 32°C under a constant power

supply, mimicking the thermal response of the skin.

We tested the MiniTouch in nine amputees for whom we had previously identified the presence of thermal phantom spots; two different thermal discrimination tasks were used. In the first test, we placed the MiniTouch on one of the thermal phantom spots and asked the participants to continuously report their thermal sensation using a slider on a graphical user interface (movie S1). The experimenter



**Fig. 4. Stability test.** Examples of spots on the residual arm with stable projection over 3 days and after 67 and 130 days for P11 and P12, respectively. The temperature of the thermode (MiniTouch) was set to 25°C. On the residual arm, dashed regions correspond to the back side; on the phantom hand, solid lines represent projections on the palmar side (dashed lines indicate projections on the dorsal side).

randomly placed the ATS sensor in contact with one of three glasses of water at different temperatures (15°, 24°, or 40°C). Overall, 24 uncued events were presented for each participant (four repetitions for each glass and their recovery to baseline) (Fig. 3B).

On average, the participants detected 97.2% of the warm/hot (40°C) and cold (15°C) stimuli; for the cold stimuli, 61.1% were reported as cold and 36.1% as cool. For the cool stimuli (24°C), 66.7% were detected (55.6% were reported as cool and 11.1% as cold) (Fig. 3C). Considering a conservative estimate of four possible classes (cold, cool, neutral, and warm/hot) and chance level with  $P < 0.01$  at 35.2% (13), we found that the participants were significantly above chance in discriminating between the stimuli (group mean accuracy: 71.3%). Participants detected, on average, 83.3% of the recovery-to-baseline events. Individual score analysis (fig. S4) shows that, in some cases, participants' perception was attenuated [for example, one participant (P19) rated three out of four times the cool stimuli as neutral and the cold stimuli as cool], suggesting that a simple gain factor between the ATS and thermode might have resulted in even better scores.

In the second test, the experimenter randomly placed the ATS sensor on slabs of copper, glass, or plastic and asked the subjects to identify the material (Fig. 3D and movie S2). Considering that the chance level for a three-label classification, with statistical significance of the identification with  $P < 0.01$ , was

40.0% (13), we again found that participants' detection rates were, on average, significantly above chance (65.93%, Fig. 3E, and see fig. S5 for individual scores). In addition, detection accuracy using the MiniTouch was similar to accuracy measured in the same participant touching physical objects with the intact hand (67.41%), and no significant difference could be found between (i) detection with MiniTouch on the phantom hand and (ii) physical objects on the intact hand for any of the materials: copper [mean score for (i): 68.9%; mean score for (ii): 70%;  $P = 0.92$ , Wilcoxon rank sum test], glass (55.6% versus 58.9%,  $P = 0.50$ ), and plastic (73.3% versus 73.3%,  $P = 0.92$ ).

### Thermal phantom sensations are partially stable over months

As the last step, we tested the MiniTouch over a 3-day experiment in two participants, P11 and P12, for whom we had found thermal phantom spots. We placed a two-dimensional grid on the residual arm using a temporary tattoo (fig. S2). We used the grid to perform a systematic investigation of the tactile and thermal phantom hand maps. The phantom hand maps showed an indication of partial stability over consecutive days. For participant P11, we considered 37 locations on the residual arm, of which 11 were stable (their projection onto the phantom hand overlapped); for P12, across 12 locations, three remained stable. The probability that the stable points were given by chance was  $7.7 \times 10^{-7}$  for P11 and 0.003 for P12 (bootstrap method, sup-

plementary materials). Representative examples of these spots for both subjects are given in Fig. 4. A follow-up test after 2 months for P11 and after 4 months for P12 confirmed evidence of partial stability. The stability of the projected points on the residual arm was also confirmed by a simplified yes/no questionnaire (supplementary materials).

### Outlook

Altogether, our results show that thermal phantom hand maps can be applied in a partially stable and reliable way to restore thermal sensation in upper-limb amputees. We developed a relatively easy-to-implement solution for thermal restoration through a noninvasive approach that provided intuitive and phenomenologically close-to-natural sensation. Our approach might ultimately improve prosthetic users' experience, creating a foundation for affective touch (14, 15), perception of wetness (16), and increased embodiment (17). Our approach could also improve sensation naturalness when integrated with existing solutions for tactile restoration by means of nerve stimulation (4, 5, 8) and provide a multimodal and more effective sensory experience to the users.

### REFERENCES AND NOTES

1. A. R. Sobinov, S. J. Bensmaia, *Nat. Rev. Neurosci.* **22**, 741–757 (2021).
2. R. S. Johansson, J. R. Flanagan, *Nat. Rev. Neurosci.* **10**, 345–359 (2009).
3. S. J. Bensmaia, D. J. Tyler, S. Micera, *Nat. Biomed. Eng.* **2020**, 1–13 (2020).
4. M. Ortiz-Catalan, E. Mastinu, P. Sassu, O. Aszmann, R. Brånemark, *N. Engl. J. Med.* **382**, 1732–1738 (2020).
5. G. Valle et al., *Neuron* **100**, 37–45.e7 (2018).
6. B. Stephens-Fripp, G. Alici, R. Mutlu, *IEEE Access* **6**, 6878–6899 (2018).
7. C. M. Oddo et al., *eLife* **5**, e09148 (2016).
8. S. Raspopovic et al., *Sci. Transl. Med.* **6**, 222ra19 (2014).
9. D. W. Tan et al., *Sci. Transl. Med.* **6**, 257ra138 (2014).
10. S. Raspopovic, G. Valle, F. M. Petrini, *Nat. Mater.* **20**, 925–939 (2021).
11. D. M. Bautista et al., *Nature* **448**, 204–208 (2007).
12. M. N. Kalf, S. Shokur, E. F. Lavado, S. Micera, "Material surface detection on various body parts: A preliminary study for temperature substitution for upper arm amputees," International IEEE/EMBS Conference on Neural Engineering (NER), 4 to 6 May 2021, pp. 195–198.
13. E. Combrisson, K. Jerbi, *J. Neurosci. Methods* **250**, 126–136 (2015).
14. R. Ackerley et al., *J. Neurosci.* **34**, 2879–2883 (2014).
15. L. S. Löken, J. Wessberg, I. Morrison, F. McGlone, H. Olsson, *Nat. Neurosci.* **12**, 547–548 (2009).
16. D. Filingieri, D. Fournet, S. Hodder, G. Havenith, *J. Neurophysiol.* **112**, 1457–1469 (2014).
17. M. P. M. Kammers, K. Rose, P. Haggard, *Neuropsychologia* **49**, 1316–1321 (2011).

### ACKNOWLEDGMENTS

We thank A. d'Alicandro, I. Furfaro, A. Sorriento, and E. Cigna for their valuable help, and we thank the subjects who freely donated their time to the study. We thank M. Herbelin for help with the illustrations. **Funding:** This work was supported by the Bertarelli Foundation (including the Catalyst programme); the Swiss National Science Foundation through the National Centre of Competence in Research (NCCR) Robotics and the CHRONOS project; and the European Union's Horizon 2020 research and innovation program under Marie Skłodowska-Curie grant

754354. This work was also supported by the Horizon Europe Research & Innovation Programme under grant 101092612 (Social and hUman ceNtered XR - SUN project) the #NEXTGENERATIONEU (NGEU) and partially funded by the Ministry of University and Research (MUR), National Recovery and Resilience Plan (NRRP) with two projects: MNESYS (PE0000006)–A Multiscale integrated approach to the study of the nervous system in health and disease (DN. 1553 11.10.2022) and THE (IECS00000017)–Tuscany Health Ecosystem (DN. 1553 11.10.2022). **Author contributions:** Conceptualization: F.I., J.M., E.G., S.M., and S.S. Data collection: F.I., J.M., F.M., M.K., and S.S. Data analysis: F.I., J.M., S.M., and S.S. Development of MetaTouch: S.G. and G.R. Characterization of MetaTouch: F.I. and M.K. Development of MiniTouch: J.M., O.A., A.C., and S.S.

Supervision: S.M. and S.S. Writing – original draft: F.I., J.M., S.M., and S.S. Writing – review & editing: All authors. **Competing interests:** S.M. holds shares in SensArs, which aims to develop bionic limbs for amputees. G.R. and S.G. hold shares in Metaphysiks, which builds thermal devices. F.I., J.M., O.A., A.C., S.M., and S.S. are coinventors of a thermal sensing device and sensory feedback system and method using said thermal sensing device (application number EP22207038.5). **Data and materials availability:** All data are available in the main text or the supplementary materials. **License information:** Copyright © 2023 the authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original US government works. <https://www.science.org/about/science-licenses-journal-article-reuse>

SUPPLEMENTARY MATERIALS

[science.org/doi/10.1126/science.adf6121](https://doi.org/10.1126/science.adf6121)  
Materials and Methods  
Figs. S1 to S6  
Tables S1 to S3  
References  
MDAR Reproducibility Checklist  
Movies S1 and S2

[View/request a protocol for this paper from Bio-protocol.](#)

Submitted 2 November 2022; resubmitted 22 February 2023  
Accepted 5 April 2023  
[10.1126/science.adf6121](https://doi.org/10.1126/science.adf6121)