

The MyoKinetic prosthetic hand: Implanted magnets restore grasping in humans with upper limb amputation

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Abstract

The loss of a hand disrupts the sophisticated neural pathways between the brain and the hand, severely affecting the level of autonomy of the patient and the ability to perform daily, work and social activities. Recent years have witnessed a rapid evolution of surgical techniques and technologies aimed at restoring dexterous motor functions akin to those of the human hand through bionic solutions. These approaches mainly rely on probing electrical signals from the residual nerves and muscles for achieving control. Here we report on the first clinical implementation of a novel interface aimed at achieving this goal by exploiting muscle deformation, sensed through passive magnetic implants: the *myokinetic interface*. One participant with a transradial amputation received the implantation of six permanent magnets in three muscles of the residual limb. For the first time, a truly self-contained myokinetic prosthetic arm which embedded all hardware components and the battery within the prosthetic socket, was developed. By retrieving muscle deformation caused by voluntary contraction through magnet localization, we were able to control in real-time a dexterous robotic hand following both a direct control strategy and a pattern recognition approach. In just six weeks, the participant successfully completed full batches of functional tests, achieving scores similar to standard of care solutions with comparable physical and mental workload. We are aware that this first experience raised conceptual and technical limits of the interface, which nevertheless pave the way for further investigations in a partially unexplored field. It also undoubtedly demonstrates a new viable possibility for interfacing humans with robotic technologies in an intuitive way.

Main Text

People affected by hand amputation suffer severe consequences in terms of physical and psychological well-being, resulting from significant functional impairments and major changes in social life. To help them regain the lost functionality, bioengineers are searching for a human-machine-interface (HMI) which allows real-time, parallel, direct and simultaneous control over multiple degrees of freedom (DoFs) of an artificial limb in a physiologically appropriate manner, and a bi-directional flow of information. Machine learning algorithms applied to surface electromyography (EMG) signals, developed by academic research for more than 50 years, are currently the most technologically advanced control solution clinically available^{1,2}. However, while clinically available technologies lack the restoration of highly dexterous motor skills equivalent to those of the human hand, a new spectrum of opportunities aimed at filling this gap is being explored by researchers. Advanced surgical techniques to uncover concealed control sources and develop mechanically stable attachments of the prosthesis, combined with highly selective probing technologies and advanced control algorithms, are paving the way for the so called *bionic reconstruction* of amputated limbs^{3,4}.

Most of the control and sensory feedback strategies available or proposed so far rely on the transduction/encoding of efferent/afferent electrical signals from/to the brain, exploiting the peripheral physiological structures (nerves and muscles). Fitting into this panorama yet abandoning such paradigm,

we proposed an alternative HMI that takes advantage of the physical displacement undergone by skeletal muscles during contraction, to decode the user's intention.

Borrowing from the Greek roots, we named it the *myokinetic interface*^{5,6}. Core of the interface is a multitude of permanent magnets implanted through a minimally invasive procedure into the residual muscles. Magnet displacement induced by muscle contraction, and retrieved through a Transcutaneous Magnet Localizer (TML), is translated in a driving signal for the prosthesis (the *myokinetic control interface*). The myokinetic interface is based on implantable technologies but remarkably, the implanted devices do not require wireless powering nor percutaneous wires. Although applicable to all kind of limb amputations, the myokinetic interface finds its greatest clinical and scientific motivation in the treatment of transradial amputations, as magnets implanted in the several extrinsic muscles of the forearm could potentially restore the stunning dexterity of hand movements. In the past eight years we extensively investigated the theoretical feasibility⁶⁻¹⁰ and developed the enabling technologies for the myokinetic control^{11,12}.

Here we present the first-in-man demonstration of the *myokinetic control interface* controlling a self-contained prosthetic arm, in a transradial amputee, through a temporary implant of six weeks. The participant was amputated to the distal third of the left forearm (non-dominant side) following a traumatic event which had occurred five months before the enrolment, and started using a myoelectric prosthesis one month prior to the implant. The outcomes from this pilot study proved highly promising given the short duration of the trial: the participant was indeed able to complete full batches of functional tests, achieving performance comparable to standard of care solutions. Nevertheless, this first experience also invites further studies on the biomechanics of muscle contraction and tissue deformation, on the conceptual and technical limits of the proposed HMI, and on the solutions to overcome them.

Clinical implementation

Preliminary clinical assessments (ultrasound imaging and needle EMG) ensured the absence of moderate to severe degrees of muscle fibrosis and allowed to identify the optimal set of muscles to receive the implants, based on the observed displacement. The participant could activate the digits of the phantom hand, as confirmed by corresponding activations in the extrinsic muscles observed with ultrasound.

Six cylindrical (2mm radius and height), axially magnetized, neodymium magnets coated with medical grade parylene C were implanted in three target muscles (two magnets per muscle), namely the Flexor Carpi Ulnaris (FCU), the Extensor Digitorum (ED), and the Flexor Pollicis Longus (FPL) (Fig. 1). Before surgery, target muscle sites were marked with a skin pen under ultrasound guidance, asking the participant to activate each muscle. The surgical procedure was performed under local anesthesia and deep sedation in the operating theater. The magnets were inserted in pairs per muscle belly, respectively in the proximal (FCU_p, ED_p, FPL_p) and distal (FCU_d, ED_d, FPL_d) portion of the muscle, and were separated by a minimum distance of 3cm to prevent migration due to magnetic attraction/repulsion. Small

incisions less than 2cm were performed over the target sites. Non-magnetic tweezers were used to manipulate the magnets, which were implanted in the target site enclosed in a cube of Spongostan™ to minimize the surrounding tissue reaction and mobilization. The implantation site in the target muscle was verified under ultrasound sterile guidance. Fibrin sealant was injected at the implant site and intradermal suture with absorbable threads was performed on the skin incision. Wounds were covered with standard bandaid and were desutured on the 10th postoperative day. The entire surgical procedure (from incision to sutures) lasted for 1.5h.

Periodic ultrasound imaging throughout the implantation period, revealed a stable average displacement of 0.5mm and 1mm, in FPL_p and FPL_d respectively, induced by thumb flexion, in both the longitudinal and transverse muscle plane (Fig. 1a,b). An average displacement of 1mm was induced by ulnar deviation on FCU_p (longitudinally and transversely) and FCU_d (longitudinally), while an average displacement of 0.5mm was measured for FCU_d in the transverse plane. The extension of the four digits led to a marginal increase in displacement in ED_p and ED_d in the weeks following implantation, ultimately reaching an average value > 1mm.

Note, as these measures were restricted to the 2D space, a complete description of the magnet displacement could only be derived from the localization output (Extended Data Fig. 1). The latter showed a maximum displacement above 6mm achieved by FPL_d during wrist supination. During the six weeks, the pain associated with the phantom limb (R score) increased from ~ 8 before surgery to ~ 10 after surgery, but gradually decreased to a value of ~ 5 at completion of the clinical trial, according to the McGill pain questionnaire¹³. The participant described the pattern of pain as “continuous” and their phantom hand as “telescoping”.

After six weeks the magnets were explanted in the theatre under local anaesthesia and deep sedation. Surgical accesses were even smaller than those performed for the implantation procedure as the magnets did not migrate from the implantation site. Magnets were removed under ultrasound intraoperative guidance. Intradermal sutures with absorbable threads were performed. The duration of the explant lasted for 1.5h.

The magnets did not give any type of reaction in the surrounding tissues with the exception of one who had not kept the Spongostan™ wrap around it. Intraoperative biopsy of a small piece of reactive tissue was performed and the anatomical-pathological result confirmed a low-grade granulomatous inflammation. The remaining tissues were healthy.

Signal characterization

Candidate control inputs for the myokinetic controller were the variations of the poses (position and orientation) relative to each pair of magnets, from the relaxed to the contracted state in the muscles (in the following, contraction-shift). These control inputs were retrieved by sampling the magnetic field

produced by the magnets, using a grid of 140 sensors distributed over the implantation sites within a prosthetic socket, and solving the inverse problem of magnetostatics⁶.

A real-time tracking task aimed to assess the dynamic performance of the HMI and quantify the effective independence of the implanted muscles proved, however, an imperfect separability of the three myokinetic channels (Fig. 1c). When the participant was instructed to perform non-fatiguing movements corresponding to a prevalent activation of each of the three implanted muscles (FCU, FPL, ED), only the contraction-shifts associated to FCU ($\sim 1\text{mm}$ median) and FPL ($\sim 2.6\text{mm}$) proved independent, with elbow extended. However, such pattern could not be observed when the elbow was flexed. The flexion/extension of the elbow also affected the absolute pose of the magnets and the distance between all pairs of magnets in the relaxed state of the muscles (Fig. 1d). For example, when going from 0° to 70° of elbow flexion, the rest distance between FPL_p and FPL_d decreased by $\sim 2\text{mm}$, while for ED it decreased by a maximum amount of $\sim 12\text{mm}$ (Fig. 1d).

On the contrary, wrist pronation and supination movements, as captured using the poses from FPL_d and FCU_p , demonstrated a high degree of controllability (the participant could finely modulate the signal, when matching sinusoidal waveforms on a PC screen, Fig. 1e), signal to noise ratio (the contraction-shifts associated to voluntary contractions proved considerably larger than those observed in other magnet pairs, Fig. 1c,e), and robustness against elbow angle (similar contraction-shifts at different elbow angles, Fig. 1e). For example, when the participant supinated the wrist at $\sim 50\%$ maximum voluntary contraction, a maximum contraction-shift of 3mm was measured with the elbow extended, whereas a maximum of 4.5mm was reached with the elbow flexed at 80° .

These patterns proved stable throughout the six weeks period, in agreement with the outcomes of the periodic ultrasound measures (Extended Data Fig. 1).

Self-contained prosthetic hand

We developed a self-contained prosthetic hand which integrated all the functional components including a Transcutaneous Magnet Localizer (TML), battery, robotic hand and a self-suspending socket (Fig. 2). As anticipated, the TML retrieved the poses of the implanted magnets, via numerical solving methods fed with the magnetic field sampled by a grid of 140 sensors distributed over the implantation sites, within the socket. The poses of the magnets were thus used as inputs to a control system (either a speed direct controller or a pattern recognition controller¹⁴), also implemented in the TML, that decoded the user's intention by sending the appropriate commands to the hand.

For comparison with standard of care solutions, the week prior to the surgery we fitted the participant with a two-state amplitude modulated myoelectric controller and administered the same functional tests used to evaluate the prosthesis under myokinetic control. As for the hand, we used the MIA research hand (by Prensilia Srl, Italy), i.e. an instrumented, human-sized, multi-articulated, versatile robotic hand that enabled palmar, precision, and lateral grasps.

Direct control

The characterization of the signals helped modelling an optimized direct control strategy, finely tuned to the observed contraction-shifts and artifacts caused by elbow flexion. According to this model, the TML mapped the contraction-shift induced between FPL_d and FCU_p during supination and pronation of the wrist, to the opening and closing of the robotic hand, respectively (Fig. 3a). As FPL_d and FCU_p got closer during supination and moved away during pronation, a positive and a negative threshold were set to detect the participant's intention to open and close the hand, respectively. The control input granularly captured the degree of muscle contraction (Fig. 1a), thus proportional control could be implemented by linear mapping to the corresponding speed of hand opening/closing. Once the target position was reached, it was maintained with no need to keep muscle contraction. When the opening command (i.e. wrist supination) was maintained for more than 1s, the hand switched to the next grasp type.

To avoid unwanted hand activations due to elbow artifacts, we implemented an enable/disable switch by setting a threshold on the slope of the rest distance between ED_p and ED_d , viz. no drive signal could be sent to the hand if this threshold was exceeded (Fig. 3b). New control inputs were re-enabled after the slope remained below threshold for at least 400ms.

Pattern recognition

The TML run a 3-classes pattern recognition controller using linear Support Vector Machines (SVM) with a one versus all approach and a majority voting post-processor (three out of five classifications). Such pattern recognition algorithm proved a viable alternative to direct control as different voluntary contraction patterns (wrist pronation, supination and rest) resulted into linearly separable clusters in terms of distances and relative orientations between magnet pairs. However, while this separation proved stable within a single fitting/donning of the prosthesis (intra-cluster radii $< 0.5\text{mm}$, inter-cluster distances $> 1\text{mm}$), it did not across multiple donnings (Fig. 3c). As such it was necessary to retrain the model following each new donning of the prosthesis.

The SVM trained with three classes (radial deviation, supination and rest) and assessed in real-time via a virtual test (similar to a Motion Test¹⁵), while wearing the prosthesis: (i) with the arm in a fixed position, or (ii) with the arm reaching six different target positions (Extended Data Fig. 2), yielded to completion rates of 100% and maximum completion times of 1.25s and 3s, respectively (blue and green curves in Fig. 3d). Retrained with two sets of five classes and assessed while reaching six target positions, the SVM yielded to completion rates of 77% or 98% and maximum completion times of 4.05s or 6.35s (red and yellow curves in Fig. 3d). Notably, as such maximum completion times included the time to reach the target position, and (by definition) the 1s hold period, these outcomes suggest that the patient in most of the cases ($\sim 70\%$), executed the trial and reacted to eventual misclassifications very quickly (less than 300ms of overhead time).

The pattern recognition approach proved also capable of discriminating up to 16 classes offline (including grasps, independent digit flexion and wrist movements), with the arm in a single position, with accuracies greater than 94% for all movements and equal to 77.5% for the rest class (Fig. 3e). Classification errors mainly stemmed from the misclassification of independent digit flexion movements as the rest and vice-versa.

Functional outcomes

The participant was able to complete functional tests commonly employed to assess the dexterity of upper limb prostheses using both direct and pattern recognition controllers (in the following DC and PR) (Fig. 4a and Extended Data Table 1). The myoelectric hand fitted before the surgery was also used to complete the functional tests, for comparison (in the following EMG). In the Southampton Hand Assessment Procedure (SHAP), the participant achieved an Index of Function (IoF) of 38 with DC (Supplementary Video 1), and of 52 with both PR and the EMG controller. The Minnesota Manual Dexterity Test (MMDT, placing only, three repetitions) yielded to completion times of 807s for DC, 747s for PR, and 531s for the EMG controller. The Clothespin Relocation Task (CRT) was completed in 52.84s with DC, 48.65s with PR, and 40.46s with the EMG controller, considering a cumulative completion time for upward and downward trials (Supplementary Video 2). The Bimanual Activity Test (BAT), administered by a physiotherapist, showed that the limb fitted with the prosthesis under PR and EMG control were equally integrated into bimanual activities (Fig. 4b). The Pick and Lift Test (PLT) revealed an improved motor coordination when using PR compared to EMG, and comparable temporal delays across all controllers (Fig. 4c). According to the NASA Task Load Index (NASA TLX) questionnaire, the three controllers demanded similar (and generally low) physical and mental workload (Fig. 4d).

Finally, and anecdotally, the participant proved able to perform a broad range of activities of daily living requiring fine movements with both DC and PR, like manipulating fragile objects (an egg, a plastic glass) while moving the limb in space, extracting pills from a blister pack, or tying the shoes (Supplementary Video 3 and 4).

Discussion

This is the first clinical implementation of a self-contained myokinetic hand prosthesis controlled in real-time in a trans-radial amputee. Implanted magnets and a transcutaneous magnetic localizer embedded in the prosthetic socket allowed for a wireless, safe and stable monitoring of muscle contractions over a six-weeks implant, clinically demonstrating the viability of this new approach for the control of bionic hands. The closest study is that by Moradi and colleagues¹⁶ who recently reported on the implantation of single magnets in three flexor forearm muscles of a trans-radial amputee. The authors could demonstrate the clinical viability of the approach, albeit presenting only bench tests, and mostly offline outcomes. Taylor and colleagues¹⁷ also contributed to this idea by implanting pairs of magnets in a turkey animal model and demonstrating that multi-magnet localization is more precise in close proximity to magnetic field sensors, even more than fluoromicrometry.

While the minimal invasiveness of the implantation procedure led to short surgery and recovery time, it also determined a suboptimal placement of the magnets. Ultrasound examination showed that the implants were located just below the muscle fascia and not in the muscle belly. Thus, even if a displacement of more than 5mm was observed preoperatively in all target muscles, only FPL_d had enough independence and a signal-to-noise ratio for implementing direct control (Extended Data Fig. 1). Nevertheless, as it proved possible to decode the motor intentions from the displacement of the magnets using also direct control, we demonstrated that the myokinetic control can indeed be modelled, with no need of resorting to non-explainable solutions. Given this, it stands to reason to believe that the availability of multiple independent control channels could allow parallel control over multiple movements, albeit this possibility could not be investigated in the present study. To complement that, the successful performance of functional tests with results not dissimilar to the standard of care suggests that the system is readily learnable, i.e., biomimetic, supporting the assumptions made in conceiving the myokinetic interface – the achievement of physiological control⁶.

The technicalities associated to the mechanical disturbances did not result from the displacement of the socket relative to the skin, as expected⁹, but from the movement of the elbow. Although not explicitly anticipated, the observed tissue displacements, in the order of a few millimetres, did not appear surprising in retrospect, considering the elastic properties of muscle tissues (Fig. 1d). However, since this displacement proved of the same order of magnitude as that caused by voluntary contraction, it posed a problem for direct control that was solved through the enable/disable switch based on the elbow speed. The ED muscle, especially in its proximal segment, proved severely affected by the physical folding of the socket during elbow flexion, which amplified the mechanical disturbance on the implanted magnets. The six weeks available for the trial, combined with the number of planned tests, did not allow us to manufacture a better socket, hence we had to drop ED_p and ED_d as potential control signals. This inconvenience suggested that in future trials, the implant sites should be identified also by considering socket constraints.

We hypothesize the need of re-training the pattern recognition model to be partly caused by a variable/unpredictable deformation induced by the socket on the soft tissues in multiple donnings, affecting the input feature space. In addition to that, different donnings, as well as different day-long arm swelling, likely caused millimetric changes in sensor placement relative to the implanted magnets, which possibly determined a different convergence point of the localization algorithm. Further investigation of these factors should lead to strategies to improve the robustness and generalization of the control algorithms.

Results obtained with the PLT, especially with the pattern recognition controller, suggested a good integration of the prosthesis in the sensorimotor control loop of the participant, although the control on the grasping force was poor. In this context, conveying relevant sensory feedback through physiological channels would potentially refine dexterity and support the integration of the artificial limb in performing functional tasks. Notably, by triggering remote vibrations in the magnets using an external stimulator we could potentially activate proprioceptive muscle receptors or mechanoreceptors in the muscles or skin,

thus eliciting natural kinaesthetic and vibro-tactile sensations. If these strategies proved effective, the myokinetic interface would be able to provide the user with a bi-directional direct communication with the prosthesis, like the natural hand.

This first clinical implementation provided important guidelines for future trials, including a better understanding of the actual pros and cons brought by this new approach. First, there are key aspects to consider in the recruitment process: optimal candidates have a recent amputation, trained and healthy (non-atrophied) muscles, free of fibrosis or denervated areas, and a relatively long stump. These are all factors that allow for larger displacement of residual muscles, and thus contribute to increase the signal-to-noise ratio for control. Although they appear as restrictive inclusion criteria, it is important to note that many new surgical techniques are becoming available for residual limb treatment that may improve muscle mobility and access to independent muscle patterns. Among these, we cite Targeted Muscle Reinnervation (TMR), which creates novel control sources by grafting severed nerves from the stump into surrogate muscles¹⁸. We already suggested the opportunity of merging TMR with the myokinetic interface¹⁹, as such reinnervated muscles exhibit a large displacement during contraction and well-distinguishable activation patterns following different movements. Note, the combination with different surgeries readily translates into the combination with other amputations levels, e.g. glenohumeral amputations with TMR, or transtibial ones treated with the agonist-antagonist myoneural interface²⁰. Furthermore, a proper re-design of the hardware of the TML, such as a reduced dimension of the sensor boards, would allow to reduce the system footprint, that could be housed in a less bulky and more flexible enclosure around the stump. If combined with advanced suspension systems like osseointegration^{21,22}, this solution would significantly improve user comfort, thus addressing a major factor contributing to prosthetic abandonment²³.

Synthesising all these factors, and assuming an improved placement of the magnets inside the muscles, the myokinetic interface holds the potential to reveal unique signals related to specific phantom limb movements, allowing to achieve natural and sophisticated control strategies. For example, single muscle movements could be used to control the speed of corresponding movements in the robotic hand, e.g. the displacement measured in the thumb flexor could proportionally drive the flexion of the robotic thumb. Complementing this, the delivery of feedback through remote vibration would allow to provide relevant sensory feedback which, albeit non-somatotopically matched nor entirely natural, would allow to build an internal model of the motor task, and because of this to grasp in a predictive feedforward fashion.

To conclude, the important results achieved in such a short period of time clearly demonstrated the potential of the myokinetic interface to restore the long-sought natural motor control in people who have lost their limbs.

Declarations

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Author contributions: M.G., V.I., F.M., F.P., D.D., E.L.F., and K.D performed experiments and analysed data. N.F., L.M., S.D., and C.A.C. conducted the neurophysiological tests and supervised the administration of the BAT test. E.I., O.M., and L.A. carried out the implantation and explanation surgical procedures. M.N. managed anaesthesia during surgical interventions. M.G. wrote the paper with V.I. and C.H.C., and all the authors contributed to its editing. C.H.C. conceived and supervised the whole study.

Competing interests: Christian Cipriani holds shares in Prensilia S.r.l.

Data and materials availability: All data are available in the main text or the supplementary materials.

References

1. Scheme, E. & Englehart, K. Electromyogram pattern recognition for control of powered upper-limb prostheses: State of the art and challenges for clinical use. *J. Rehabil. Res. Dev.* (2011).
2. Roche, A. D., Rehbaum, H., Farina, D. & Aszmann, O. C. Prosthetic Myoelectric Control Strategies: A Clinical Perspective. *Curr. Surg. Reports* **2**, (2014).
3. Farina, D. *et al.* Toward higher-performance bionic limbs for wider clinical use. *Nat. Biomed. Eng.* **2021** 1–13 (2021).
4. Roche, A. D. *et al.* Upper limb prostheses: bridging the sensory gap. *J. Hand Surg. Eur. Vol.* **48**, 182–190 (2023).
5. MYKI ERC project. <http://www.mykierc.eu/>.
6. Tarantino, S., Clemente, F., Barone, D., Controzzi, M. & Cipriani, C. The myokinetic control interface: Tracking implanted magnets as a means for prosthetic control. *Sci. Rep.* **7**, 1–11 (2017).
7. Gherardini, M., Clemente, F., Milici, S. & Cipriani, C. Localization Accuracy of Multiple Magnets in a Myokinetic Control Interface. *Sci. Rep.* **11**, 1–10 (2021).
8. Masiero, F., Sinibaldi, E., Clemente, F. & Cipriani, C. Effects of Sensor Resolution and Localization Rate on the Performance of a Myokinetic Control Interface. *IEEE Sens. J.* **21**, 22603–22611 (2021).
9. Paggetti, F., Gherardini, M., Lucantonio, A. & Cipriani, C. To what extent implanting single vs pairs of magnets per muscle affect the localization accuracy of the myokinetic control interface? Evidence from a simulated environment. *IEEE Trans. Biomed. Eng.* 1–8 (2023).
10. Milici, S. *et al.* The myokinetic control interface: How many magnets can be implanted in an amputated forearm? Evidence from a simulated environment. *IEEE Trans. Neural Syst. Rehabil. Eng.* **28.11**, 2451–2458 (2020).
11. Clemente, F., Ianniciello, V., Gherardini, M. & Cipriani, C. Development of an embedded myokinetic prosthetic hand controller. *Sensors* **19**, 1–10 (2019).

12. Ianniciello, V., Gherardini, M. & Cipriani, C. Transcutaneous Magnet Localizer for a Self-Contained Myokinetic Prosthetic Hand. *subm. to IEEE Trans. Biom. Eng.*
13. Melzack, R., Of, S. R.-T. J. of the A. S. & 2005, U. The McGill pain questionnaire: from description to measurement. *pubs.asahq.org* **103(1)**, 199–202 (2005).
14. Hargrove, L. J., Miller, L. A., Turner, K. & Kuiken, T. A. Myoelectric Pattern Recognition Outperforms Direct Control for Transhumeral Amputees with Targeted Muscle Reinnervation: A Randomized Clinical Trial. *Sci. Reports* 2017 71 **7**, 1–9 (2017).
15. Kuiken, T. *et al.* Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. *jamanetwork.com* (2009).
16. Moradi, A. *et al.* Clinical implementation of a bionic hand controlled with kineticomyographic signals. *Sci. Rep.* **12**, 1–13 (2022).
17. Taylor, C. R. *et al.* Magnetomicrometry. *Sci. Robot.* **0656**, 1–10 (2021).
18. Kuiken, T. A. *et al.* Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. *Lancet* **369**, 371–380 (2007).
19. Gherardini, M. *et al.* Feasibility Study on Disentangling Muscle Movements in TMR Patients Through a Myokinetic Control Interface for the Control of Artificial Hands. *IEEE Robot. Autom. Lett.* **7**, 7240–7246 (2022).
20. Srinivasan, S. S. *et al.* Agonist-antagonist myoneural interface amputation preserves proprioceptive sensorimotor neurophysiology in lower limbs. *Sci. Transl. Med.* **12**, eabc5926 (2020).
21. Ortiz-Catalan, M., Bo Håkansson & Brånemark, R. An osseointegrated human-machine gateway for long-term sensory feedback and motor control of artificial limbs. *Sci. Transl. Med.* **6**, (2014).
22. Ortiz-Catalan, Max, *et al.* A highly integrated bionic hand with neural control and feedback for use in daily life. *subm. to Sci. Robot.*
23. Salminger, S. *et al.* Current rates of prosthetic usage in upper-limb amputees—have innovations had an impact on device acceptance? *Disabil. Rehabil.* **44**, 3708–3713 (2022).
24. SHAP. <http://www.shap.ecs.soton.ac.uk/index.php>.
25. Desrosiers, J., Rochette, A., Hébert, R. & Bravo, G. The Minnesota Manual Dexterity Test: Reliability, validity and reference values studies with healthy elderly people. *Can. J. Occup. Ther.* **64**, 270–276 (1997).
26. Kuiken, T. A., Dumanian, G. A., Lipschutz, R. D., Miller, L. A. & Stubblefield, K. A. The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee. *Prosthet. Orthot. Int.* **28**, 245–253 (2004).
27. Lee, J. H., Hong, I., Park, J. H. & Shin, J. H. Validation of Yonsei-Bilateral Activity Test (Y-BAT)-Bilateral Upper Extremity Inventory Using Rasch Analysis. *OTJR Occup. Particip. Heal.* **40**, 277–286 (2020).
28. Johansson, R. S. & Westling, G. Coordinated isometric muscle commands adequately and erroneously programmed for the weight during lifting task with precision grip. *Exp. Brain Res.* **71**, 59–71 (1988).

29. Hart, S. G. NASA Task Load Index (TLX). (1986).
30. Ortiz-Catalan, M., Håkansson, B. & Brånemark, R. Real-time and simultaneous control of artificial limbs based on pattern recognition algorithms. *IEEE Trans. Neural Syst. Rehabil. Eng.* **22**, 756–764 (2014).

Methods

Study design

All experiments were carried out as part of the ongoing clinical study MYKI ('Interventional pilot study on the evaluation of the functionality, the safety, and the reliability of an implantable bi-directional MYoKinetic Interface for the natural control of artificial limbs'), which investigates the feasibility and safety of a novel bi-directional interface for hand prostheses. All surgical and experimental procedures were carried out at AOUP hospital (Azienda Ospedaliero Universitaria Pisana). The study was approved by the Ethical Committee of AOUP and the Italian Ministry of Health (Eudamed CIV-IT-22-03-039173).

Before signing of the informed consent, we verified that the participant met the inclusion criteria of the study. The participant then underwent pre-operative clinical evaluations to assess the functionality of the residual muscles in terms of contraction capabilities and eventual presence of fibrotic tissue or muscle atrophy. For comparison with standard of care solutions, the week before the implantation we fitted the participant with a two-state amplitude modulated myoelectric controller. To this aim a custom resin self-suspending socket was fabricated. It included stainless steel electrodes (Ottobock, Inc.) placed above the flexor and extensor muscles of the wrist, respectively providing the closing and opening of the hand. The participant was administered with state of the art tests commonly used to assess the functionality of upper limb prostheses, namely: the Southampton Hand Assessment Procedure (SHAP), in which the participant grasps a variety of objects²⁴; the Minnesota Manual Dexterity Test (MMDT), in which the participant places a series of cylinders in matched holes²⁵; the Clothespin Relocation Task (CRT), where the participant moves three clothespins from a horizontal to a vertical pole²⁶; the Bimanual Activity Test (BAT), administered by a physiotherapist, which assesses the degree of integration of the impaired limb in bimanual tasks²⁷. In addition, the participant performed the Pick and Lift Test (PLT), a well-established procedure in motor control studies²⁸, used to assess the integration of sensorimotor control paradigms. The NASA TLX was administered at completion of the functional tests to evaluate the physical and mental workload²⁹. The McGill Pain Questionnaire was also administered to provide a quantitative measure of pain related to the phantom limb prior to surgery¹³. Furthermore, we recorded videos of the participant performing ADLs, including: unscrewing a jar/bottle cap, manipulating a fragile object (plastic glass), extracting pills from a blister pack, slicing a soft object with a knife, holding a rubber ball or an egg while moving the arm in space, and tying the shoes. These videos allowed to qualitatively assess (i) the robustness of the controller against the limb movements in space, and (ii) the ability of the participant to finely control the prosthesis.

The participant subsequently underwent the implantation surgery, followed by a one-week rest period that allowed the surgical wounds to heal. During the following five-weeks, experimental sessions to implement and assess the myokinetic control interface were carried out at AOUP three days a week. Ultrasound imaging was used to monitor magnet position and displacement caused by muscle contraction throughout the whole implantation period. Specifically, an ultrasound scanner (MyLab Omega, Esaote s.p.a.) was used to acquire videos of the FCU, ED, and FPL muscles, both in the longitudinal and the transverse muscle planes, while the participant was performing non-fatiguing movements corresponding to a prevalent activation of each of the three implanted muscles, i.e. ulnar deviation, four-digit extension and thumb flexion, respectively. These videos were analysed offline to retrieve the displacement undergone by each magnet with respect to its rest (i.e. relaxed muscle state) position. Regarding the implementation of the control strategy, the first two weeks were dedicated to prosthetic fitting and to the characterization of the candidate control inputs and potential sources of disturbance. Based on the outcomes of this characterization, the last three weeks were dedicated to the implementation of two different myokinetic controllers (direct and pattern recognition based, see below). The evolution of the pain associated with the phantom limb throughout the implantation period was monitored by administering the McGill Pain Questionnaire on a weekly basis.

Transcutaneous Magnet Localizer

The TML employed in the study and its performance in terms of computation time, power consumption, and localization precision/accuracy were comprehensively described in our recent work¹². Briefly, the system included seven Acquisition Units (AUs) each hosting 20 magnetic field sensors, one geomagnetic field compensation sensor and a microprocessor-based computation unit (CU), based on the i.MX RT1060 Real Time Processor running on an Arm Cortex-M7 core at 600 MHz. The AUs were arranged above the implanted muscles in locations empirically selected to ensure accurate and stable localizations. The AUs sampled synchronously, meaning that readings from the 140 sensors occurred all at the same time instant, thus ensuring consistent measurements. After sampling, they sequentially transferred the acquisitions to the CU which retrieved the poses of the magnets by feeding them to the localization algorithm, operating in pipeline (concurrently) with the AU sampling and AUs-CU data transferring. The AU-CU rate, defined as the interval of time at which complete data packages were transmitted to the CU, proved equal to $\sim 23.6\text{ms}$, which coincided with the output rate of the whole system, unless the localization algorithm took more time.

Akin to our previous works, the CU derived the poses of the six magnets by modelling the field at the j^{th} sensor as a linear superposition of that produced by six magnetic dipoles and reversing these equations through numerical approximation methods. Specifically, the CU run the Levenberg-Marquardt algorithm (LMA) for each new data package received from the AUs, and considered the results acceptable only if the magnets were localized within a user defined workspace. Such workspace was set following each donning of the prosthesis through a calibration procedure, in which the participant was asked to contract the implanted muscles while moving the limb in space, e.g. bending the elbow and shoulder. After obtaining a comprehensive set of localizations, the final volumes were determined by adding a 2cm

safety bias to the minimum and maximum x, y, and z coordinates at which each magnet was localized. During normal use, in case a magnet was retrieved outside of its volume, the localization was marked as incorrect and the event was notified to the user, while the LMA was re-run until a correct localization was achieved.

Prosthetic fitting

Following the rest week after surgery, the participant was fitted with a custom-made temporary self-suspending resin socket that allowed free placement of a variable number of AUs on its external surface. As mentioned above, we empirically searched for an AU number and placement which ensured a stable localization of the six implanted magnets, and found optimal localization precision (repeatability) using seven AUs placed above the implantation sites. The AU selection was achieved by exploiting a custom graphical interface coded through the Processing graphical library which displayed in real-time the current poses of the magnets and the AUs, and allowed to save localization and acquisition data for further offline analysis. The socket could not be connected to the prosthesis, thus it was employed during the first two experimental weeks to characterize the available control signals (see below) while the final socket was being manufactured by a prosthetist. The latter was a custom-made carbon fibre self-suspending socket which integrated all TML components in dedicated slots. Specifically, it included slots to host the seven AUs in the optimal selected locations, and two additional pockets on the outer layer and accessible from the outside that hosted the CU and the battery used to power both the TML and the robotic hand.

Signal characterization

Different datasets were acquired to investigate the candidate signals for control as well as the type and extent of potential disturbances. For this purpose, we had developed a custom Graphical User Interface (GUI) using C# in Visual Studio (Microsoft Corporation) to instruct the participant to perform specific movements while acquiring synchronized localization data from the TML.

To evaluate the independency of the three myokinetic channels at different limb positions, the GUI showed sequences of steps that the participant had to match by contracting the implanted muscles while performing different movements. Specifically, the participant was asked to perform three movements expected to induce a prevalent activation in ED, FCU and FPL with both extended and flexed elbow. These movements were respectively four-digit extensions for ED, ulnar deviation for FCU, and radial deviation for FPL (after excluding thumb flexion because the induced contraction-shift was poor). To avoid muscle fatiguing, contractions were divided into steps of 3s, separated by relaxation intervals of 8s. The acquisitions were repeated multiple times during the implantation period, in order to assess the stability of the contractions over the weeks as well as the intra- and inter-day variability due to multiple donnings of the prosthesis or arm swelling (Extended Data Fig. 1). The same acquisition protocol was also employed to assess muscle activation induced by common grasps (palmar, precision, lateral, wrist pronation/supination, wrist flexion/extension), flexion/extension of the individual fingers, and ab-adduction of the thumb. The GUI temporized the activation and rest intervals and provided a real-time

feedback by displaying the contraction-shift of three user-defined magnet pairs over the step sequences. At the end of each acquisition, localization data were saved in a text file for offline analysis.

To investigate the effect of limb movements on the rest distance between magnet pairs and disentangle it from voluntary muscle activation, we asked the participant to move the elbow and shoulder following sinusoidal waves with different periods (8s, 6s, 4s, 3s, and 2s) displayed on the GUI, while keeping the implanted muscles relaxed. In particular, the participant performed elbow medial/lateral rotation and elbow and shoulder flexion/extension, and the mapping between joint angle and localization data was obtained by concurrently tracking optical markers arranged on the wrist, elbow and shoulder of the impaired limb through a three-camera 6DoF optical tracking system (V120:Trio, OptiTrack, US) (Extended Data Fig. 3). Moreover, in order to evaluate the feasibility of modulating muscle activation and capturing such modulation through localization, we asked the participant to mirror the same sinusoidal waves by gradually contracting the implanted muscles. This exercise was performed only for those movements that had demonstrated sufficient signal-to-noise ratio and robustness against limb movements in the sequence of steps.

This signal characterization procedure led to the identification of the optimal strategy and signals to implement the direct controller. In addition, the same GUI was also employed to acquire the data for training the pattern recognition controller, as described below.

Direct control

After signal characterization, the contraction-shift between FPLd and FCUd induced by wrist pronation and supination was identified as the optimal signal to control the closing and opening of the robotic hand, respectively. In addition, the speed of the contraction-shift between the magnets in ED was used to counteract the artifacts caused by limb movements, particularly by elbow flexion/extension. According to this, the controller was implemented as a four-state machine in which the robotic hand could be in the following states: (i) disabled state, i.e. no control input could be sent to the hand when the slope related to the magnets in ED overcame a set threshold $th3$; (ii) opening state, when the contraction-shift caused by supination overcame a set threshold $th2$; (iii) closing state, when the contraction-shift caused by pronation overcame a set threshold $th1$; (iv) rest state, when none of the previous thresholds was overcome. In case (iv), the value of the rest distance between FPLd and FCUd was updated to take into account slow variations caused by different factors over time (e.g. slow limb movements). Practically, two moving average filters with a 90ms and a 1s window were applied at discrete steps of 50ms, in accordance with the robotic hand control frequency, to update the current and rest magnet distance, respectively. The difference between these two measures, i.e. the contraction-shift between FPLd and FCUd, was subsequently compared against the set thresholds $th2$ and $th3$. In addition, proportional speed control was implemented by linearly mapping the retrieved contraction-shift to the opening and closing speed of the hand. The GUI was used to tune the value of $th1$, $th2$, and $th3$ and to transmit the updated values to the CU, which implemented the control algorithm and sent the appropriate command to the

hand, i.e. the degree of opening/closing in the current grasp type (palmar, precision, or lateral). If the opening signal was maintained for more than 1 s, the hand switched to the next grasp type.

The direct controller was assessed quantitatively by administering the same functional test used to evaluate the EMG controller (except the BAT test), and qualitatively by repeating the same ADLs. Accordingly, the NASA TLX was employed to evaluate the physical and mental workload required to complete each functional test.

Pattern recognition

We employed a SVM classifier with a linear kernel to map the co-activity pattern of a muscle group associated with a virtual movement of the phantom limb to a corresponding movement of the robotic hand. More specifically, multiple classifiers were trained to selectively recognize an equal number of classes, and a one versus all approach was applied at the training stage to determine the class with the highest score. At testing time, the latter was determined based on a majority voting approach, according to which the class that obtained the highest score in at least three out of five previous iterations was ultimately selected as the winner. The same GUI was used to acquire the data for training the models, which consisted of a number of individually acquired movements alternating 5s seconds of muscle contraction with 5s of muscle relaxation (rest). To increase the robustness of the classifier, the movements were acquired while keeping the limb in different positions, including elbow extended on the side, elbow flexed at 90°, reaching front (i.e. as to pick up an object on the table), and shoulder flexed at 135° (as to grasp an object placed on top). The GUI temporized the contraction and relaxation phases and saved the output of the localization in a text file.

Subsequent offline analysis was implemented to extract 30 time series describing the linear and angular distances between all possible magnet pairs. Due to a limitation of the CU hardware resources, 18 out of the 30 series, corresponding to nine magnet pairs which showed observable patterns associated with muscle activation, were empirically selected for model training and testing. To ensure that training was performed on the steady portion of the signal, the central 2.5s of the contraction and rest intervals of each selected time series were extracted and concatenated. The feature set was ultimately obtained by normalizing the median value of the samples contained in windows of 200-ms, with a 150ms overlap. These features were used to train the classifiers on Matlab 2017b (MathWorks Inc.), and subsequently derive the SVM parameters to be transmitted to the CU that implemented the embedded classifier. During real-time operation, the latter provided new predictions every 50ms.

We tested the real-time performance of the classifier by implementing a three-class model able to discriminate hand opening (trained on wrist supination data), hand closing (trained on wrist pronation or radial deviation data), and rest. The trained classifier was used to control the robotic hand and perform the same functional tests (including the BAT) and ADLs carried out with the EMG controller and the myokinetic direct controller, including the NASA TLX at test completion. In addition, the real-time performance of the classifier were assessed through a modified Motion Test carried out in two different configurations: (i) with the participant sitting and resting the arm on a support; (ii) with the participant

standing and performing different movements in six different arm positions. The training dataset acquired for configuration (i) included three repetitions of two movements, i.e. radial deviation and wrist supination. The training dataset acquired for configuration (ii) included three repetitions of six movements, i.e. radial deviation, wrist supination, wrist extension, ulnar deviation, middle finger extension, and hand closing. The latter were repeated holding the arm in six different positions, namely: shoulder flexed at 45°, 90°, and 135°, elbow flexed at 90°, and reaching front obliquely to the left and to the right (Extended Data Fig. 2). Different combinations of the movements acquired in (ii) were used to train three classifiers, respectively including: radial deviation and supination; the previous plus middle finger extension and ulnar deviation; the previous with hand closing in place of middle extension. According to this, the test evaluated the feasibility of discriminating in real-time a maximum of classes. During the test, the participant was asked to wear the robotic hand in order to reproduce realistic loading conditions on the stump. In line with previous studies from the literature^{15,30}, the Motion Test required 20 correct predictions within 10s to consider a motion completed. Standard metrics were employed to evaluate the test outcomes, namely: the completion time, consisting of the time between the first prediction different from rest and the 20th correct prediction; the completion rate, consisting of the number of completed motions over the total number of motions attempted. The deviation from the standard test was that, unlike what is generally reported in the literature, the completion time also included the time to reach the target position from rest (i.e. arm extended on the side).

Finally, larger datasets comprising up to 16 movements, including grasps, wrist movements, single finger flexion/extension, and thumb adduction/abduction, were acquired with the arm at rest, to assess offline the feasibility of discriminating many classes.

Figures

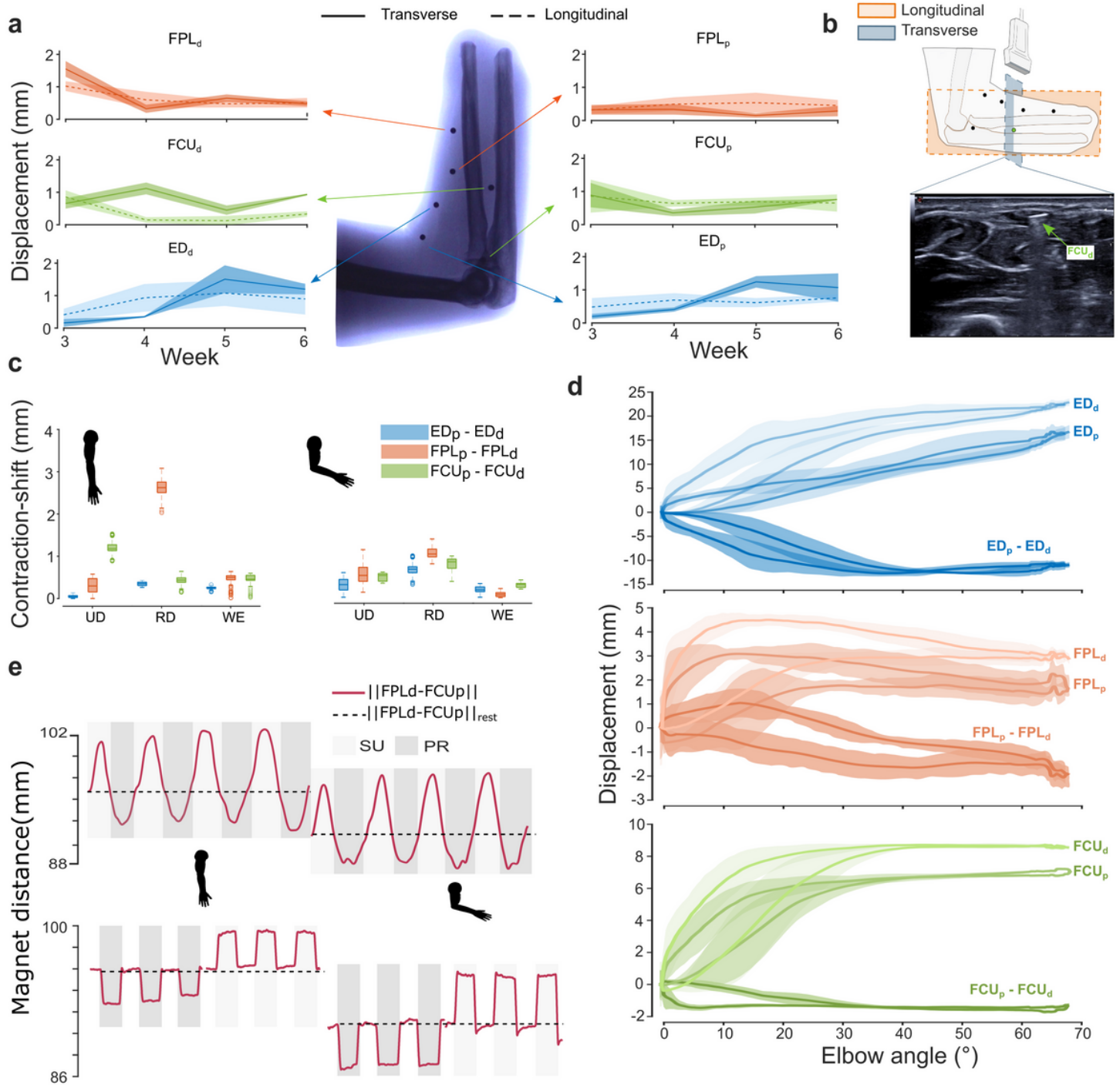


Figure 1

Clinical implementation and signal characterization. **a**, Displacement of each magnet from rest following prevalent activation of each of the three implanted muscles (namely, thumb flexion for FPL, ulnar deviation for FCU, and four-digit extension for ED), derived through periodic ultrasound imaging throughout the implantation period. Stable patterns of displacement were found both in the longitudinal and the transverse muscle plane. **b**, Example frame extracted from a video acquired with the ultrasound probe in the transverse plane of FCU. The frame captures the magnet implanted distally in the muscle. **c**, The boxplots represent the contraction-shifts relative to each magnet pair in the same muscle, caused by

ulnar deviation (UD), radial deviation (RD), and wrist extension (WE), both with extended and flexed elbow. **d**, Mean and standard deviation of the displacement from the rest position for each magnet, and from the rest distance for each magnet pair in the same muscle, caused by elbow flexion/extension. **e**, Distance between FPL_d and FCU_p while matching sinusoidal waves (above) and sequences of steps (below) by performing wrist pronation and supination, with both extended and flexed elbow. The graphs show that the rest distance between the magnets was affected by the elbow movement (dashed line).

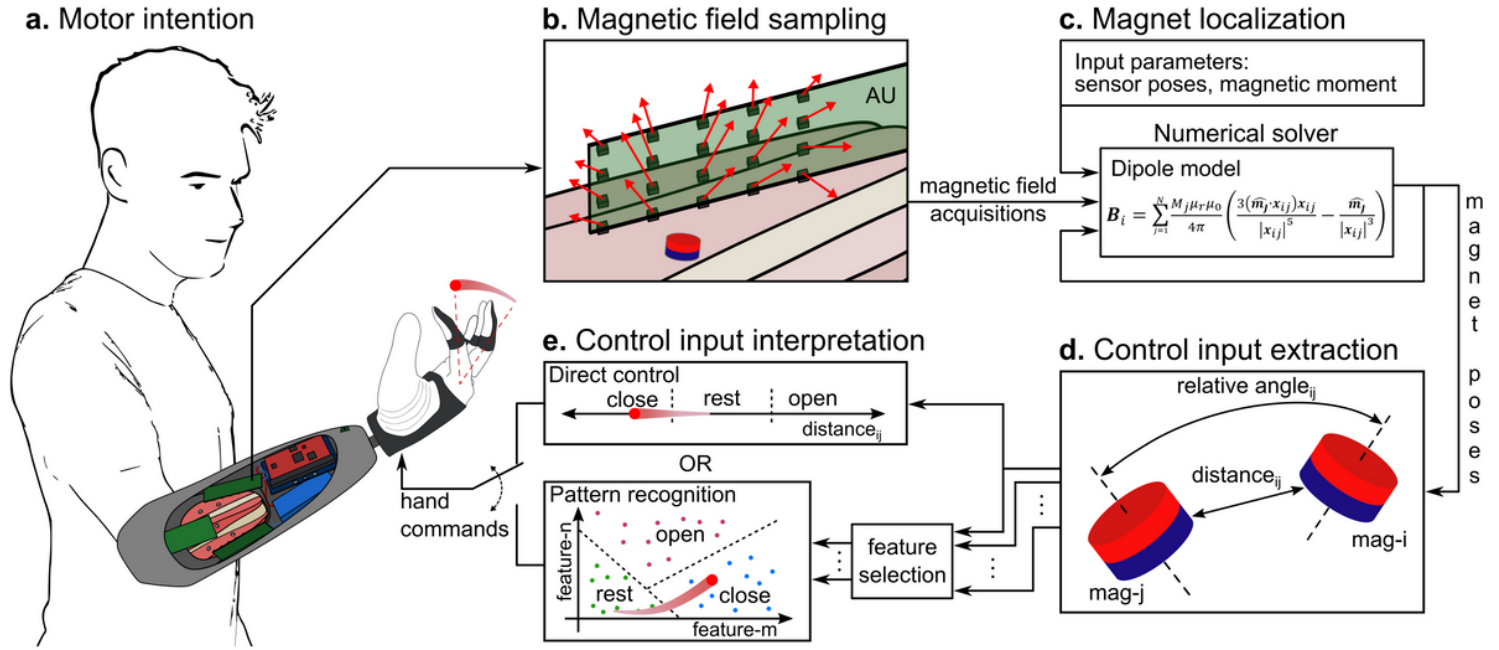


Figure 2

The myokinetic prosthetic hand. **a**, The user's motor intention travels from the brain to the muscles through the efferent neural pathways, inducing muscle deformation. **b**, Magnetic field sensors sample the magnetic field generated by the implanted magnets and transmit the acquisitions to an embedded computing unit. **c**, An iterative numerical solver retrieves the poses (position and orientation) of the six magnets by modeling the sensed magnetic field as a superimposition of magnetic dipoles. **d**, The candidate control inputs are computed from the retrieved poses as the distances and relative angles between all magnet pairs. **e**, The control inputs are interpreted through a direct or pattern recognition control strategy and translated into commands for the robotic hand.

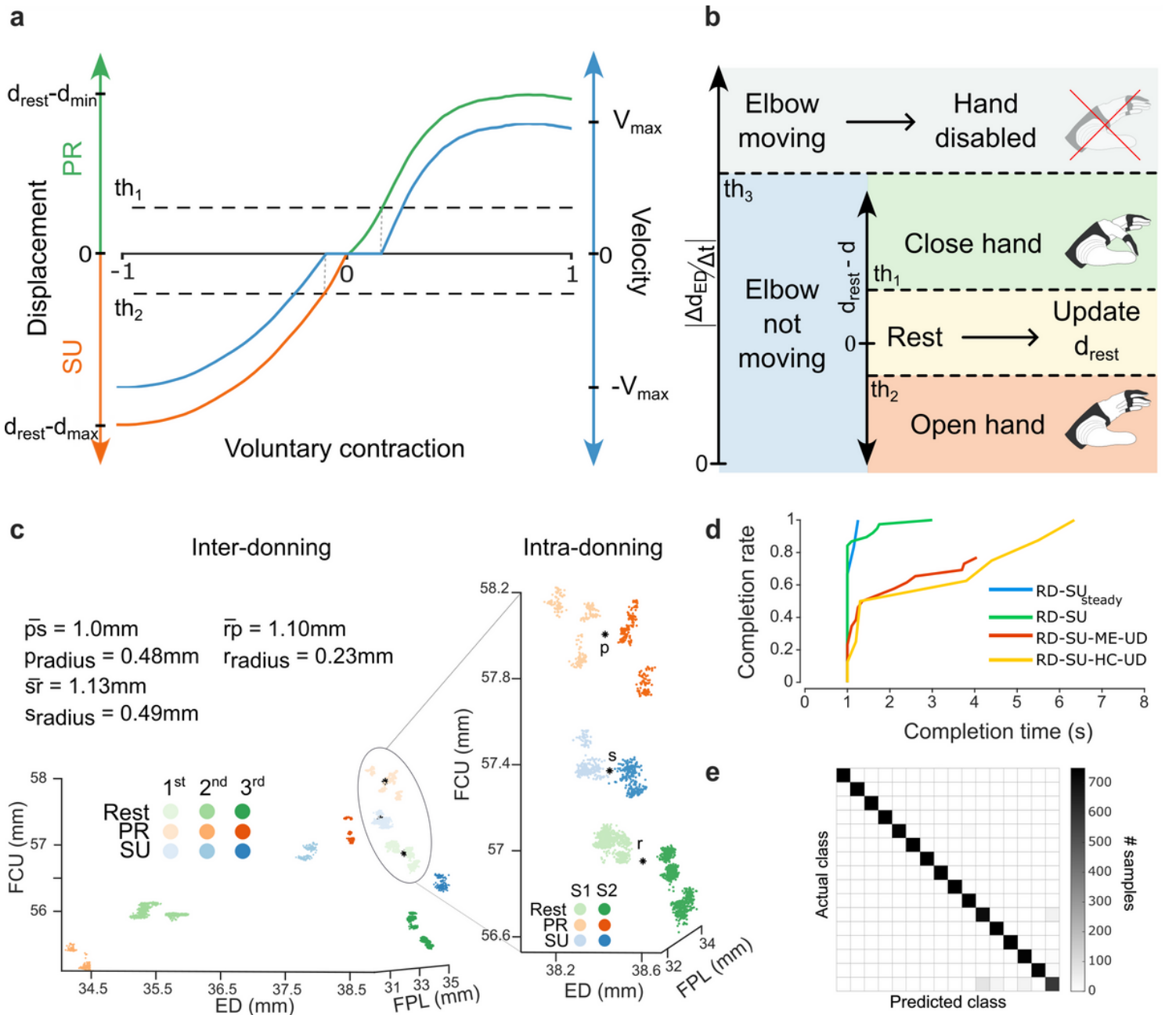


Figure 3

Direct control (a, b) and Pattern Recognition (c, d, e). **a**, The contraction-shift between FPL_d and FCU_p ($d_{rest} - d$) during supination (SU) and pronation (PR) of the wrist was mapped to the opening ($d_{rest} - d < th_2$) and closing ($d_{rest} - d > th_1$) of the robotic hand. Proportional control was implemented by linear mapping to the corresponding speed of the robotic hand. **b**, Direct control strategy. An enable/disable switch was implemented by setting a threshold th_3 on the slope of the rest distance between ED_p and ED_d (d_{ED}/t), to counteract elbow artifacts. If the elbow was not moving ($d_{ED}/t < th_3$), direct control was implemented according to **a**. **c**, In intra-donning data, contraction patterns related to PR, SU, and rest resulted into linearly separable clusters in terms of distances between magnet pairs. This held true across multiple sessions (S1, S2), i.e. acquisitions performed before and after asking the participant to

repeatedly move the elbow. On the contrary, cluster separation proved not stable across multiple donnings. **d**, The Motion Test proved completion rates of 100% when the SVM was trained to discriminate radial deviation (RD) and SU, both with the arm in a fixed position (RD-SU_{steady}) and with the arm reaching six different target positions (RD-SU). In this latter case, when retrained with two sets of five classes (RD-SU-ME-UD and RD-SU-HC-UD), the SVM yielded to completion rates of 77% or 98%, although with an increase in completion time. **e**, When assessed offline, the pattern recognition approach could discriminate up to 16 classes with accuracies greater than 94% for all movements and equal to 77.5% for the rest. Misclassifications consisted mainly in individual finger movements recognized as rest. Actual classes (from up to down): palmar, lateral, and precision grasp, hand opening, wrist flexion and extension, wrist pronation and supination, radial and ulnar deviation, index and thumb flexion, thumb opposition, middle and little finger flexion, rest.

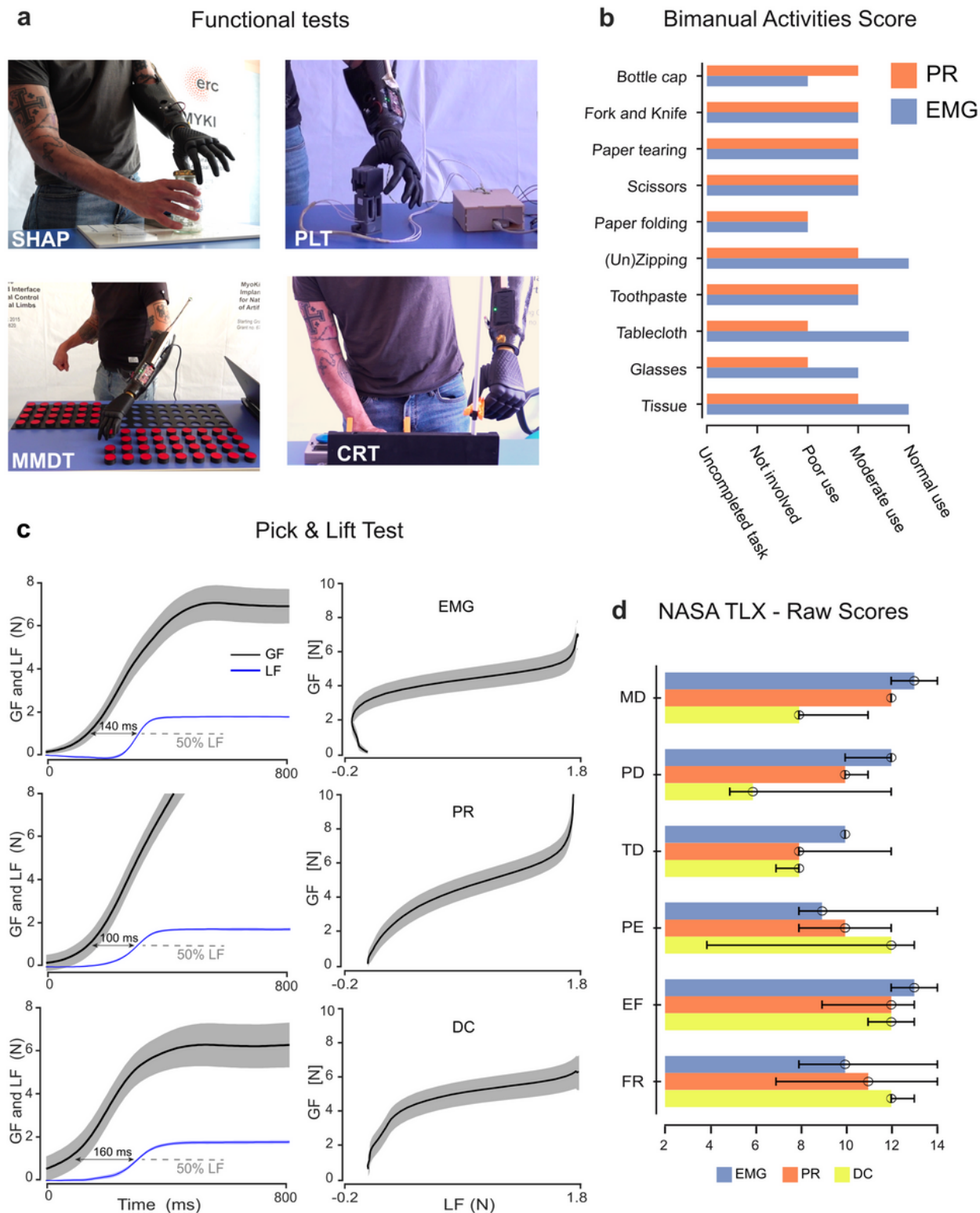


Figure 4

Functional tests and questionnaire. **a.** Representative pictures of the participant carrying out the SHAP, PLT, MMDT, and CRT. **b.** Scores of the BAT test, performed with the EMG and the pattern recognition (PR) controllers. The obtained scores proved similar, and showed that in most cases the impaired limb was moderately engaged in bimanual activities, which included: unscrewing and screwing the cap of a water bottle; slicing a soft object using a fork and a knife; tearing a sheet of paper; cutting a sheet of paper in

two with scissors; folding a sheet of paper and putting it in an envelope; opening and closing the zip of a pencil case; squeezing toothpaste onto a toothbrush; laying a tablecloth on a table; opening a case and taking out a pair of glasses; opening a tissue package and taking out one tissue. **c.** Motor coordination during the pick and lift test for the EMG controller, the myokinetic direct controller (DC), and the pattern recognition controller (PR). The temporal delay between the instants when the *grip force* (GF) reached 50% of the *load force* (LF) was lower with the used of PR (left graphs), for which the GF vs LF profile (right graphs) also proved better motor coordination. On the contrary, PR demonstrated a poorer controllability on the GF value after lifting the object compared to EMG and DC. **d.** Raw scores of the NASA TLX questionnaire for all three controllers, which showed that the latter demanded similar (and generally low) physical and mental workload to complete functional tasks.

Supplementary Files

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