DEVICES

Restoring arm function with a soft robotic wearable for individuals with amyotrophic lateral sclerosis

Tommaso Proietti[1], Ciaran O'Neill[1], Lucas Gerez[1], Tazzy Cole[1], Sarah Mendelowitz[1], Kristin Nuckols[1], Cameron Hohimer[1], David Lin[2], Sabrina Paganoni[3,4], Conor Walsh[1]*

Despite promising results in the rehabilitation field, it remains unclear whether upper limb robotic wearables, e.g., for people with physical impairments resulting from neurodegenerative disease, can be made portable and suitable for everyday use. We present a lightweight, fully portable, textile-based, soft inflatable wearable robot for shoulder elevation assistance that provides dynamic active support to the upper limbs. The technology is mechanically transparent when unpowered, can quantitatively assess free movement of the user, and adds only 150 grams of weight to each upper limb. In 10 individuals with amyotrophic lateral sclerosis (ALS) with different degrees of neuromuscular impairment, we demonstrated immediate improvement in the active range of motion and compensation for continuing physical deterioration in two individuals with ALS over 6 months. Along with improvements in movement, we show that this robotic wearable can improve functional activity without any training, restoring performance of basic activities of daily living. In addition, a reduction in shoulder muscle activity and perceived muscular exertion, coupled with increased endurance for holding objects, highlight the potential of this device to mitigate the impact of muscular fatigue for patients with ALS. These results represent a further step toward everyday use of assistive, soft, robotic wearables for the upper limbs.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease or motor neuron disease) is a neurodegenerative disease that results in a gradual loss of motor neurons in the brain and spinal cord. This condition causes muscle atrophy and weakness, resulting in loss of muscle control and disability (*1*). In the United States alone, there are about 30,000 individuals living with ALS, with about 5000 new diagnoses per year. The average life expectancy is about 3 years after disease onset, although about 20% of individuals diagnosed with ALS will live 5 or more years (*2*). The disease is relentlessly progressive despite the availability of two modestly effective U.S. Food and Drug Administration–approved medications and several ongoing clinical trials (*3*–*5*). As new treatments are developed that can effectively slow down disease progression and prolong survival, the need for technology that can support physical function in people living with ALS is expected to continue to grow. Technology has the potential to compensate for the loss of physical capabilities in everyday life that these individuals will experience, with the goal of maintaining quality of life and prolonging their independence. Robotic wearables, for example, could be used to provide motor assistance to the affected limbs, maintaining functionality by compensating for muscle weakness and atrophy.

Most research and development on upper limb robotic wearables to date have been focused on rehabilitation devices (*6*, *7*), addressing impairments whose effects can potentially be reduced with time and training. Such devices are thus focused on maximizing user activity and engagement while avoiding the rise of pathological compensation strategies. The emphasis on rehabilitation is likely driven by a larger number of individuals in need of rehabilitation [e.g., in the United States alone, there are 800,000 new instances of stroke per year (*8*)]. Another branch of wearable robotics is instead focused on assistive devices aimed at functional compensation for individuals where recovery is not possible or likely, e.g., stroke survivors after they have reached their recovery plateau (*9*) or those with degenerative diseases such as ALS. Assistive robotic wearables face major technical challenges that are not always present for in-clinic rehabilitation devices. Specifically, assistive robotic wearables must function in unstructured environments (e.g., the end user's home) and, thus, must remain both lightweight and portable to be worn and carried around. They also need to support a broader range of activities, including activities of daily living (ADLs), potentially allowing interaction with objects. Last, they need to include on-board controllers that must work robustly for extended periods of time without intervention by a clinician or therapist.

The requirement of assisting the user for multiple hours a day makes existing rigid-framed robots or exoskeletons less suitable as assistive robots, particularly for upper-limb devices. Such robotic devices use mechanisms consisting of links and joints to transfer torques to the impaired joints of the wearer and are well suited to in-clinic use. Well-known examples include the ArmeoPower by Hocoma and the InMotion by Bionik Labs, two pioneers of rehabilitation robotics for the upper limb (*6*, *7*). One of the few portable rigid robots to assist successfully part of the upper limb (elbow-wrist-hand) of people with impairment is the MyoPro by Myomo, available on the market since 2006. This robot uses surface electromyography (EMG) to modulate assistance to the wearer. A clinical evaluation of 18 individuals after stroke showed that the device improved the function of this population, as assessed by an increased Fugl-Meyer assessment score when assisted by the robot and improved ability to perform simulated ADLs (*10*). Ekso Bionics

[1]John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138, USA. [2]Center for Neurotechnology and Neurorecovery, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA. [3]Neurological Clinical Research Institute, Massachusetts General Hospital, Boston, MA 02114, USA. [4]Department of Physical Medicine and Rehabilitation Services, Spaulding Rehabilitation Hospital, Boston, MA 02129, USA.
*Corresponding author. Email: walsh@seas.harvard.edu

recently joined the market of upper extremity wearable devices for medical assistance with their EksoUE, a wearable spring-powered exoskeleton for bilateral shoulder support (*11*). The device has interchangeable springs to set different amounts of assistance, weighs about 6 kg, and requires a minimum of 20° of active shoulder flexion to be used by patients. The main advantages of such a passive (i.e., not powered) solution—frequently used for industrial applications—are that it does not need to be charged and it is inherently quiet. On the other hand, the spring-based actuation mechanism requires the user to input energy for some operations (e.g., lower the arm), which can be challenging for individuals with arm weakness. Furthermore, with a passive exoskeleton, the use of the robot as a tool to assess quality and quantity of movement is limited. This approach cannot have a transparent mode (i.e., where the user can move naturally and not be encumbered by the weight of the system on the arm), meaning changes in unassisted performance cannot be monitored, which is crucial from a clinical standpoint.

A major challenge for robotic wearables targeting shoulder assistance is the complexity of the shoulder joint itself. The glenohumeral joint is a ball and socket joint that allows for movement in three-dimensional (3D) space; it is coupled to the acromioclavicular joint, which in turn allows motion for two additional degrees of freedom. This configuration creates one of the most mobile joints in the human body (*12*). Alignment of mechanical rigid robotic joints with such an articulated biological joint is a challenge that is often addressed by exploiting redundancy and thus adding passive degrees of freedom serially to the robot kinematic chain to align the active joints to the human joints (*13*). However, this comes at a trade-off of increased complexity for robot hardware and control. To address this challenging robot-body alignment problem and achieve the lightweight portability requirements of upper limb assistive devices, a more recent trend in research is to use the wearer′s skeletal structure as the frame of the robot itself, with a trade-off on the maximum achievable torque. This design strategy has led to the development of soft robotic wearables (*14*) that combine soft, compliant, lightweight hardware with smart sensing and control strategies to support a wearer′s movements, potentially enabling assistance outside of clinical settings.

Most soft robotic wearables are prototypes (*7*, *14*), either cable-driven or pneumatically actuated, with a limited number of untethered and fully portable devices. Some of these include three cable-driven shoulder robots (*15*–*17*), one pneumatic shoulder robot (*18*), one pneumatic robot assisting either the elbow or the wrist joint (*19*), and one elbow robot using shape memory alloy springs as the actuation mechanism (*20*). In addition, most published studies have been performed on healthy individuals only, mainly demonstrating a reduction in muscle activity during weightlifting. A few studies included testing with clinical populations (mostly stroke survivors) and showed reduction of heart rate activity as a proxy for muscle fatigue during weightlifting (*16*), increased endurance time during static hold (*21*), and improved passive range of motion (i.e., when the limb is passively mobilized by the robot) (*22*, *23*). Using a pneumatic robot assisting either at the elbow or the wrist, Nam *et al.* (*19*) showed that 15 stroke survivors improved flexion/extension active range of motion (i.e., when the wearer is actively trying to reach their maximum range supported by the robot) and improved their score in standard clinical assessments after longitudinal training.

Our team has previously presented a tethered, i.e., not portable, version of a soft robot powered by a laboratory-based research platform (about 15 kg of total system weight) to assist shoulder elevation against gravity (*24*, *25*). The robot uses a pair of textile-based pneumatic actuators, anchored one per side to a custom shirt, to support the arm through inflation of the actuators based on signals from inertial measurement units on the arms and torso. With this platform, we demonstrated on healthy individuals that the device does not impede the user′s active range of motion compared with a no-suit condition in a weightlifting task. As a proof of concept, we also showed its use as a static arm support system (i.e., no dynamic control) to reduce muscle fatigue for an occupational therapist supporting the arm during simulated upper extremity rehabilitation exercises.

Here, we advance this soft wearable technology and demonstrate its utility in improving upper extremity function in individuals with ALS, a patient population underserved by assistive technologies. We demonstrate a fully portable and wearable version of this soft robot that can automatically adapt assistance on the basis of an impaired individual′s volitional movement. We show that the system can be intuitively used and provide sufficient support to improve both movement performance and the ability to perform functional tasks. In addition, when powered off, we show that this robotic wearable can be used as a tool to assess quality and quantity of upper extremity movement.

Table 1. Study participant characteristics. Information about the 10 participants with ALS enrolled in the study is shown. Individual data and averages with SDs are included.

	Sex	Age	Weight	Height	Postdiagnosis
	(–)	(year)	(kg)	(cm)	(years)
P1	M	76	108	170	5
P2	F	36	113	165	3
P3	M	52	100	182	2
P4	M	72	78	179	0
P5	M	73	82	180	2
P6	M	68	113	182	3
P7	F	53	82	160	1
P8	M	61	125	204	0
P9	M	72	125	190	0
P10	M	63	84	178	1
Avg		62.6	101.0	179.0	1.7
SD		12.5	18.3	12.5	1.6

RESULTS

To evaluate our soft robotic wearable (Fig. 1A), we recruited 10 individuals living with ALS (eight males and two females; 62.6 ± 12.5 years old on average; weight, 101 ± 18 kg; height, 179 ± 12 cm). These study participants had a wide range of upper extremity impairment: 1.7 ± 1.6 years after the diagnosis, five individuals were using a wheelchair, and two were on a ventilator. Study participant characteristics are provided in Table 1. On the first study visit, all participants performed the following experimental movements

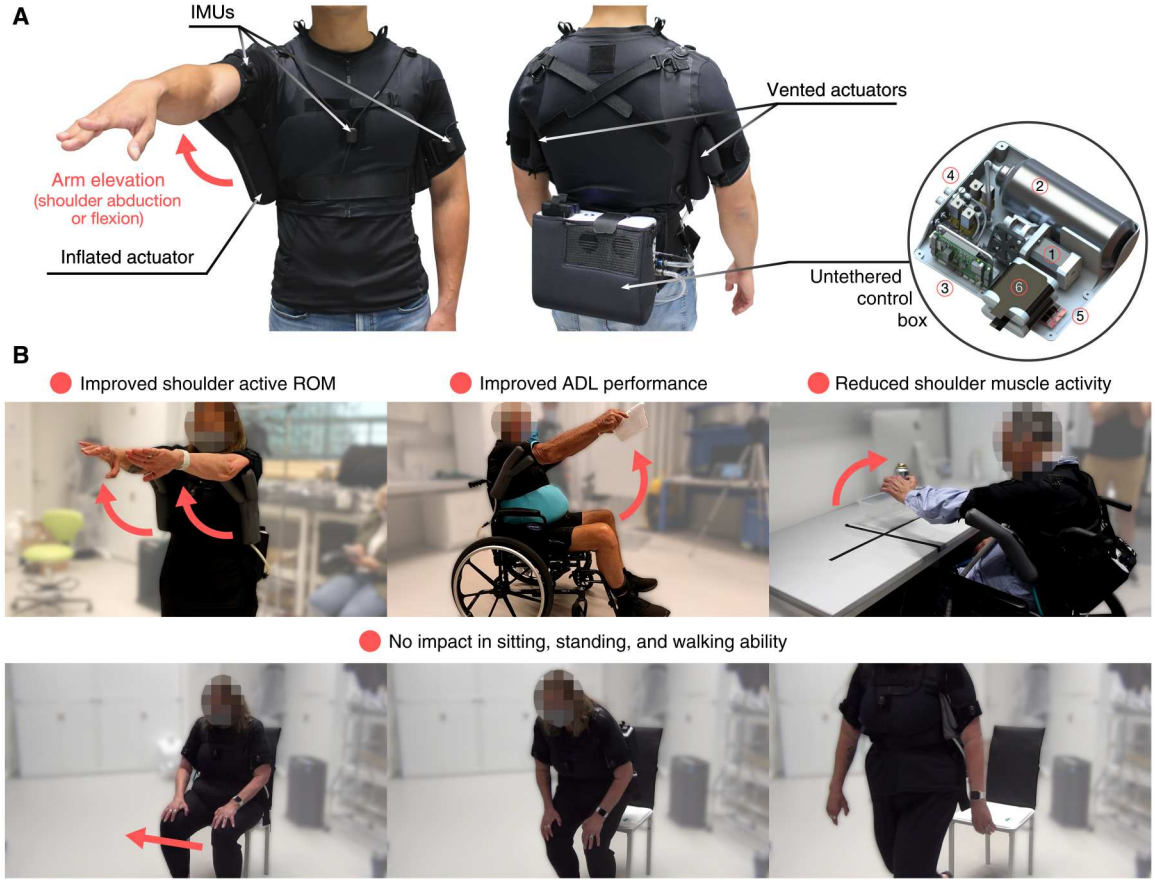

Fig. 1. Untethered, portable soft robotic wearable for shoulder monitoring and assistance. (**A**) Shown are the main robotic components of the robotic wearable shirt. Two textile-based soft actuators, anchored under the armpits, provide dynamic assistance while inflating. To assess user movement ability and assist the shoulder in an intuitive way, three inertial measurement units (IMUs), placed on the torso and both upper arms, estimate upper limb kinematics. A control box, anchored to the waist of the user (total weight, ~3.6 kg), powers the robotic wearable and runs the gravity compensation strategy. Textile components include strap-based adjustments for optimal fit. Arm elevation is defined as either shoulder abduction or shoulder flexion. Other upper limb movements, such as shoulder horizontal flexion, are not restricted. The user can actively control their motion by leveraging any residual strength or capacity as the robotic wearable helps to compensate for the effects of gravity. Control box components: (1) scroll compressor, (2) 750-ml air reservoir, (3) microcontroller and custom electronics, (4) proportional valves and custom manifold, (5) electronic speed controller, and (6) batteries. (**B**) Study participants with ALS performed a series of activities from the study protocol, including shoulder abduction and flexion, holding an object, and the 6-min walk test. Red arrows indicate direction of movement. ROM, range of motion; ADLs, activities of daily living.

(Fig. 1B): (i) unassisted versus assisted active range of motion, (ii) unassisted versus assisted simulated ADLs (reaching, holding, transferring, and manipulating an object; touching the head), and (iii) participants completed a survey about the ease of use of the robotic wearable (the system usability scale). In addition, the five ambulatory participants performed a 6-min walk test under two conditions (wearing the device or not).

To understand the technology's potential to compensate for the deterioration of physical abilities over time, two individuals representative of lower (P1) and higher (P2) residual volitional movement ability participated in a second study visit >6 months after the first visit (P1, 7.5 months; P2, 6 months). They performed three experimental tests: (i) no device versus unassisted versus assisted active range of motion, (ii) unassisted versus assisted lifting, and (iii) unassisted versus assisted box and blocks test. The box and blocks test is a standard clinical assessment of unilateral gross manual dexterity, consisting of transferring as many blocks as possible, one at a time, from one side of a box to another in 60 s.

Improved active range of motion in participants with different degrees of impairment over time

The active range of motion (for both shoulder abduction and flexion) of participants was increased when assisted by the robotic wearable, as shown in Fig. 2A. Specifically, we observed more than 95° of shoulder elevation on average when assisted by the robotic wearable, an increase of 27% (+20.4 ± 15.8°, $P < 0.01$) in abduction compared with the unassisted condition and 29% (+21.7 ± 17.4°, $P < 0.01$) in flexion. In the most extreme case, the robotic wearable was able to improve the active range of motion of a participant with residual shoulder abduction and flexion of less than 40° to more than 80°. The second active range of motion test with participants P1 and P2, 6 months after their first visit, was performed after an automatic recalibration of assistance characteristics. Physical deterioration due to ALS had occurred in both participants: For participant P1, abduction was 62° at visit 1 and 50° at visit 2, and flexion had decreased from 58° to 50°; for participant P2, abduction decreased from 96° to 86°, and flexion decreased from 85° to 83°

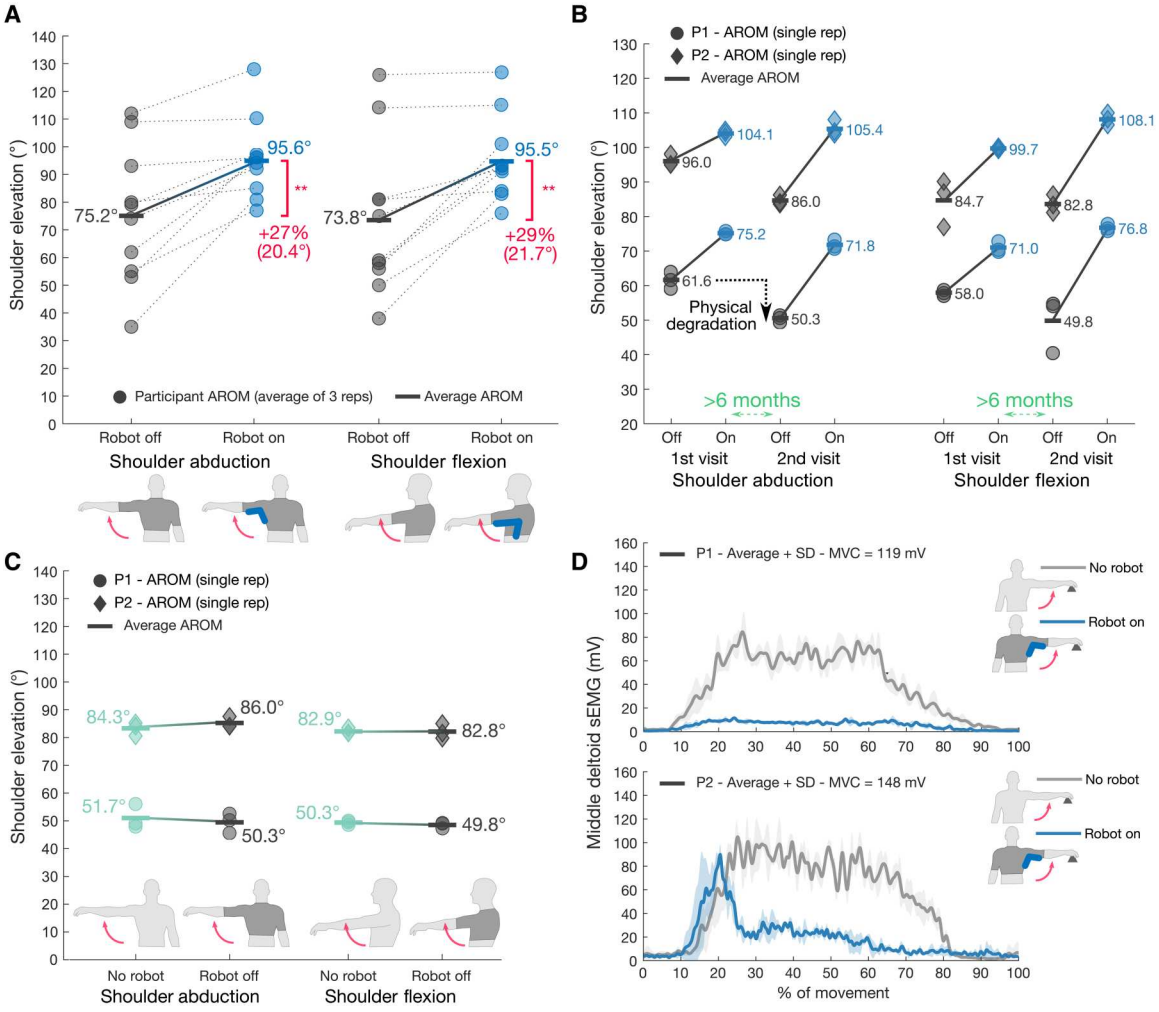

Fig. 2. Improved active range of motion, mechanical transparency, and muscle activity reduction with the robotic wearable. (**A**) Individual active range of motion (AROM) and averaged values with and without assistance from the soft robotic wearable are shown. Participants achieved >95° of shoulder elevation when assisted by the device, with an increase of 27% in abduction (+20.4 ± 15.8°, $n = 10$, $^{**}P < 0.01$, t test) and 29% in flexion (+21.7 ± 17.4°, $n = 10$, $^{**}P < 0.01$, t test). (**B**) Active range of motion comparison for participants P1 and P2 between the first study visit and the second study visit >6 months later ($n = 2$, average of three repetitions per participant). Participant P1 had a lower residual active range of motion, whereas participant P2 had a higher residual active range of motion. There was physical deterioration due to ALS disease progression between visit 1 and visit 2: Participant P1 had an unassisted shoulder abduction of 62° at visit 1 and 50° at visit 2, and unassisted shoulder flexion decreased from 58° to 50°; participant P2 had an unassisted abduction of 96° at visit 1 and 86° at visit 2, with flexion decreasing from 85° to 83°. With assistance from the robotic wearable, there were minimal changes between visit 1 and visit 2: Participant P1 had assisted shoulder abduction of 75° and 72° and flexion of 71° and 77°; participant P2 had assisted abduction of 104° and 105° and flexion of 100° and 108°. (**C**) Robotic wearable transparency, defined as no reduction in the wearer's movements, was measured by comparing no robot versus robot off conditions ($n = 2$, average of three repetitions per participant). Participant P1 had a lower residual active range of motion, and participant P2 had a higher residual active range of motion. (**D**) Reduction of middle deltoid muscle activity was measured by an EMG sensor in participants P1 and P2 during lateral weightlifting with assistance (robot on) or no assistance (robot off) ($n = 2$). The middle deltoid muscle has a primary role in shoulder abduction/adduction. The solid line represents the average of three repetitions, whereas the shaded area represents the SD. MVC, maximum voluntary contraction.

from visit 1 to visit 2. When assisted by the robot, there were only minimal changes in shoulder abduction and flexion between visit 1 and visit 2: For participant P1, abduction decreased from 75° to 72° for visit 1 versus visit 2, and flexion increased from 71° to 77°; for participant P2, abduction increased from 104° to 105° for visit 1 compared to visit 2, and flexion increased from 100° to 108° (Fig. 2B).

Mechanical transparency of the robotic wearable and its use as an assessment device

Figure 2C shows the result of the mechanical transparency test—defined as the capability of the robotic wearable not to limit the user's movements when powered off—with participants P1 and P2. The shoulder robotic wearable was a transparent device, largely due to its lightweight and compliant nature provided by its textile-based structure (Fig. 2C). This confirms previous transparency demonstrations with healthy individuals undertaking larger active range of motion tests (*25*). Transparency is important

from a medical standpoint, given that it allows the use of the soft robotic wearable as an assessment device when unpowered. As shown in Fig. 2B, the implemented sensing strategy, based on a combination of three inertial measurement units on the torso and shoulders, was able to measure baseline characteristics of the user, tracking active range of motion degradation over time. Similarly, for all the other tests in the study, kinematic baseline characteristics were measured without any external sensing device (e.g., a motion capture system). The accuracy of the inertial measurement unit–based strategy has been validated against a motion capture system elsewhere (*25*).

Shoulder muscle activity reduction with a robotic wearable

Despite the mechanical transparency, the robotic wearable was still able to reduce supported muscle activity when powered on, as measured by EMG (Fig. 2D). In a timed weightlifting task, we observed a reduction in the activity of the middle deltoid muscle, which is the main muscle responsible for shoulder abduction/adduction, when participants P1 and P2 performed a lateral lift of a lightweight object. It is interesting to observe the initial spike of activity for the higher functioning participant P2. This is due to the shoulder muscles becoming activated to raise the arm. After about 25% of the motion had been performed by participant P2 (about 2.5 s), the robotic wearable reached full inflation and started providing torque at the given pose (about 90°).

We note that the robot is controlled to assist movement, not to passively mobilize the limb. Thus, the accuracy and speed during the performance of any task are linked to the residual ability of the user. From a technical point of view, the robotic wearable control reacts within 150 ms of detecting the user's intention to move their limb (the minimum value for the valves to start opening or closing). Robotic assistance was fully deployed in 1.8 s in a worst-case scenario (step response from actuator fully vented to the maximum allowed pressure of 110 kPa; see fig. S1 and Supplementary Materials and Methods) due to the pressurized air dynamics. These reaction times are adequate when considering the usually reduced speed of movement of the user with a physical disability.

Improved ability to perform functional tasks with a robotic wearable

Figure 3 demonstrates improvement of the 10 participants with ALS in performing ADLs when assisted by the robotic wearable. We found an improved ability to hold an object with both hands (both the duration of ~+11 s and the maximum angle of ~+23°; $P < 0.05$) and improved reach for targets at various heights in front of the participants ($P < 0.05$). Specifically, for targets at head height, participants on average went from reaching one target of three to reaching 3 of 3 ipsilateral targets, 2.7 of 3 middle targets, and 2.6 of 3 contralateral targets. Furthermore, participants had a better performance on different simulated ADLs involving shoulder movements (touching the top of the head, lateral and forward transfer of a light object, and mimicking pouring of a liquid into a tall container; $P < 0.05$; Fig. 3). Eighty-two percent of these ADLs were completed successfully with robotic assistance compared with only 50% without. For the holding test, one participant did not complete the test because of shoulder pain not related to the use of the robotic wearable and was thus excluded ($n = 9$).

When assisted, all participants improved the smoothness of their movements [spectral arc length (*26*) of −6.1 ± 0.2 unassisted versus −5.2 ± 0.1 when assisted ($P < 0.05$)] and showed reduced maximum torso displacement (about 3° reduction; $P < 0.05$). These are two common negative features of upper limb impairments, and compensating for these features can counteract their worsening with time and preserve the individual's motor and functional ability. In addition to better movement and performance in functional tasks, qualitative feedback from the participants described reduced perceived fatigue in performing these activities: Rate of perceived exertion when unassisted was 6.0 ± 2.6 versus 3.4 ± 2.4 when assisted ($P < 0.05$). The reduction in rate of perceived exertion, together with the reduction of muscle activity during weightlifting and increased endurance during the holding task, points to the potential of the technology to mitigate the impact of fatigue for individuals with upper extremity impairment.

The actuators provided on average about 60% of the required torque to the shoulder joints to successfully assist participants performing ADLs (see Supplementary Materials and Methods, fig. S2, and table S1). Figure 4 shows two examples of simulated ADLs as performed by two study participants with associated values of biological torque (τ_{bio}, the torque required by the user to sustain their arm at a given pose) and the actuator torque (τ_{act}, the torque provided by the robotic wearable at that given pose). These two examples are from the 180 ADL trials performed by the pool of 10 study participants. Averaged torque profiles over the entire testing population are shown in fig. S3. Actual ADL performance is presented in movie S1.

Improved ability to perform a pick and place task and walking test with a robotic wearable

When performing the box and blocks test, participants P1 and P2 showed an increased number of blocks transferred per minute when assisted by the soft robotic wearable: +11 blocks and +50% for P1 and +9 blocks and +28% for P2 compared with the unassisted condition (Fig. 5A and movie S1). Both increases were above the minimal detectable change (+5.5 blocks or +18%) (*27*). Despite this improved performance, the activity of the anterior deltoid muscle—the main muscle responsible for this pick and place task—was reduced in magnitude as measured by EMG.

The five study participants who were not confined to a wheelchair performed a walking evaluation (the 6-min walking test). These participants did not show an increase in heart rate (used as a proxy for exertion) (*28*) or a decrease in the distance walked while wearing the device (Fig. 5B). This result confirms the limited impact of carrying such a device for those individuals with ALS who maintained the ability to ambulate.

As a proof of concept, we showed the possibility to integrate a previously developed soft wearable glove (*29*) with the soft shoulder robotic wearable presented in this work. One of the participants with the lowest residual movement at both the hand and the shoulder used both devices simultaneously to complete a pick-and-place task (Fig. 5C) otherwise unachievable without assistance.

Positive usability feedback

Last, we conducted a standard usability survey, the system usability scale (where 1 = strongly agree and 5 = strongly disagree) at the end of the testing session. The 10 participants ranked the robotic wearable as a good system (79.2 ± 9.0) (*30*). In particular, participants felt confident in using the robotic wearable (1.4), thought that the robotic wearable was easy to use (1.6), would like to use the

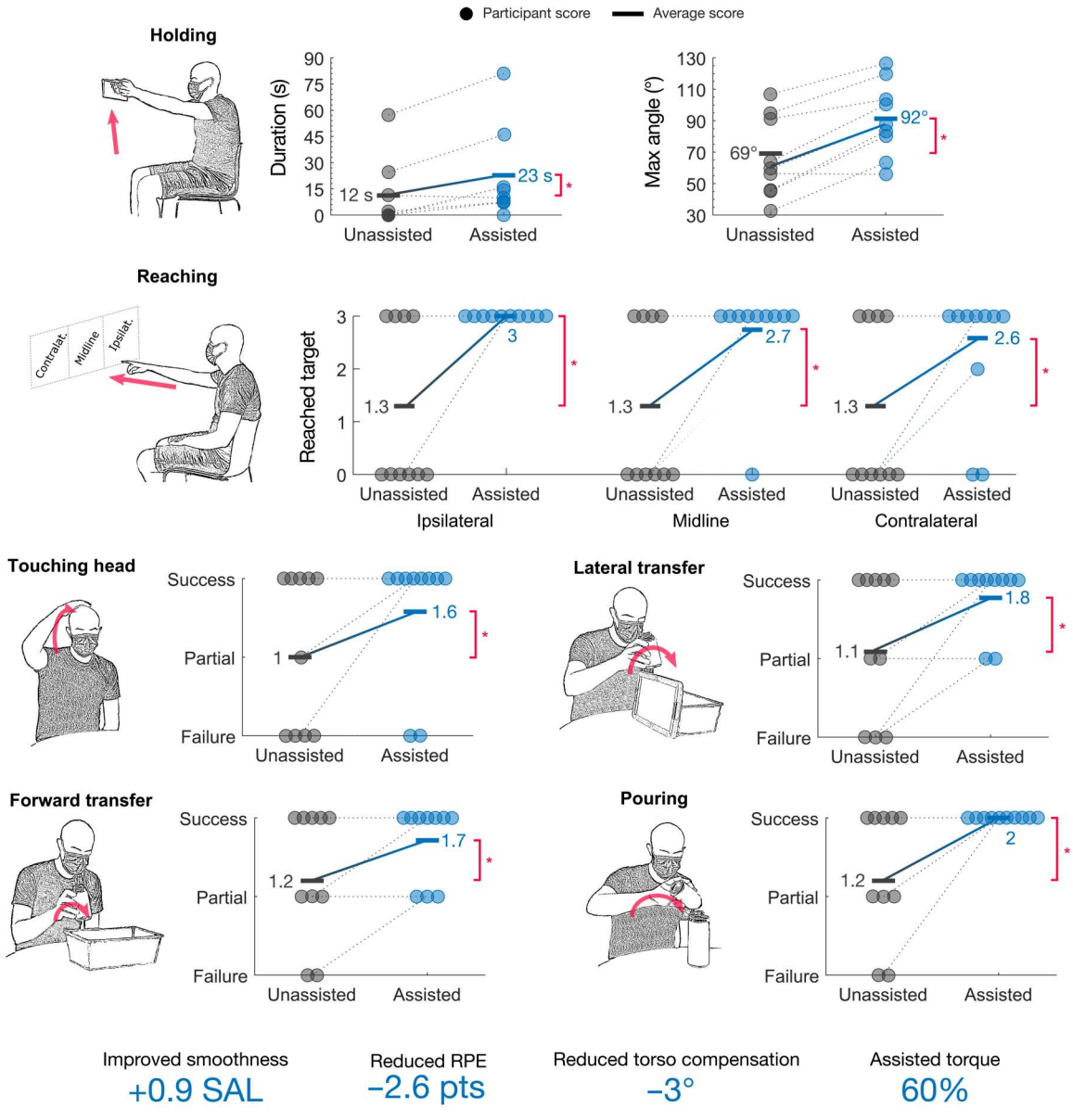

Fig. 3. Performance of simulated ADLs, with and without the assistance of a robotic wearable. Results show individual data (average of three repetitions, except for holding test) for a series of simulated ADLs (e.g., holding an object, reaching out to touch an object, touching the head, box and blocks test) and the average over the group of participants (n = 10, *P < 0.05, t test). Success score is 0 for failure to perform the ADL, 1 when partially accomplished (touching face instead of top of head, transferring object by dropping it, pouring without sustaining object for more than 3 s), and 2 when fully accomplished. One participant did not complete the holding test because of pain in one shoulder not related to the use of the robotic wearable (n = 9). Holding time was computed for angles of >60°. For reaching tasks, ipsilateral targets were located on the same side of the assisted arm, whereas contralateral targets required reaching across toward the opposite side of the body. Midline targets were in front of the faces of the participants. SAL, spectral arc length; RPE, rate of perceived exertion.

robotic wearable frequently (1.7), and believed that most people would learn to use the device very quickly (1.2). Individual participant answers are available in data file S1.

DISCUSSION

In this study, we demonstrated a fully portable and soft robotic wearable to support the shoulder for individuals with upper extremity impairment and evaluated it on 10 individuals with ALS who had different degrees of upper extremity weakness. For these individuals and for others with degenerative conditions, designing practical systems that can provide dynamic support in functional tasks is crucial, given that current therapies can only partially delay the loss of function and are unable to restore it.

Most prior research on medical robotic wearables for the upper limb has focused on stationary, clinic-based rigid robots targeting rehabilitation, in large part due to the prevalence of stroke. Assistive soft robotic wearables for the upper limb are a more recent development. So far, the focus for assistive soft robotic wearables has been on demonstrating reduced muscle activity in healthy

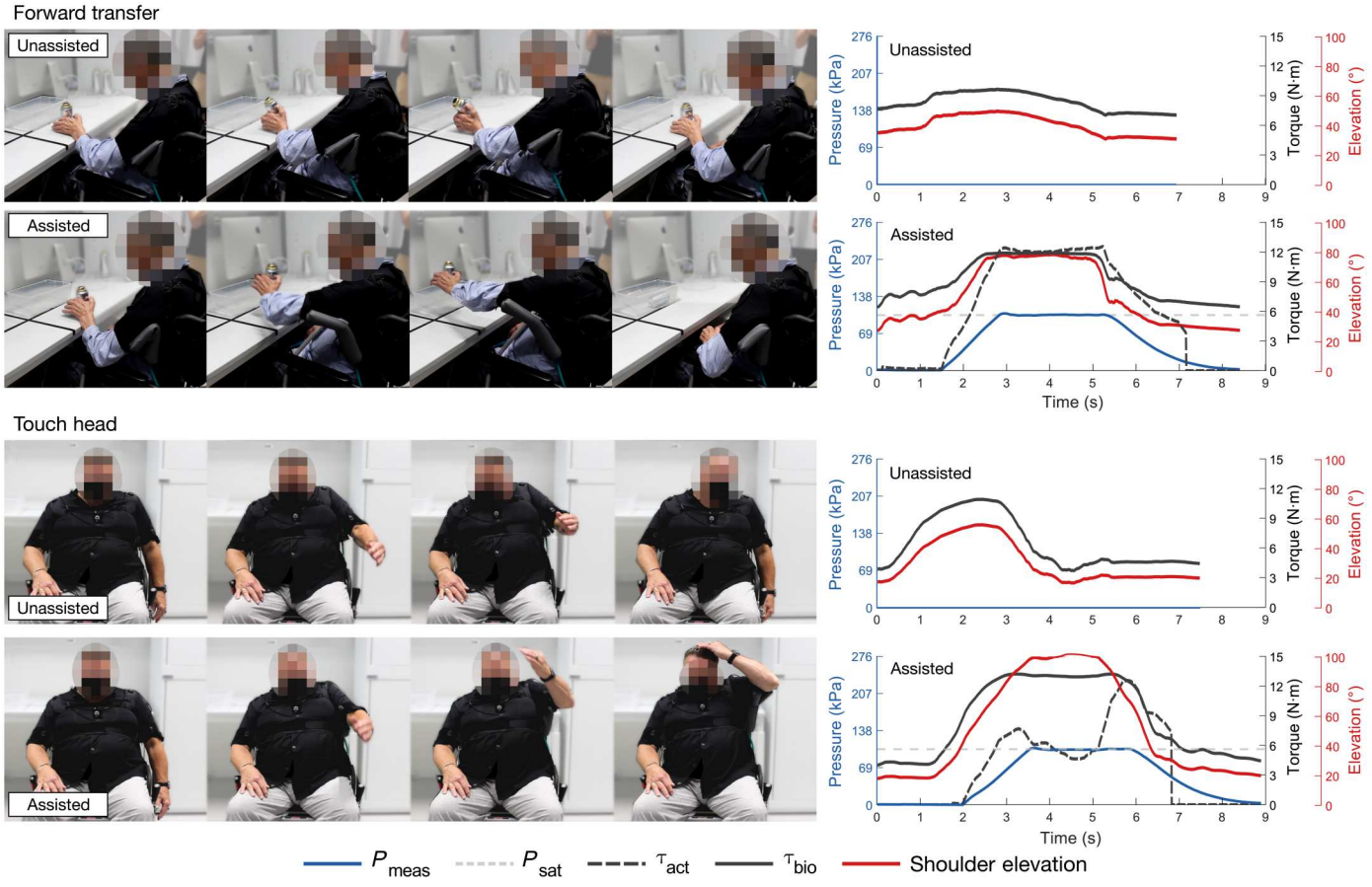

Fig. 4. Simulated ADLs performed by two participants. Photographs of two participants performing simulated ADLs are shown for unassisted (robot off) and assisted (robot on) conditions. On the right side is the actuator desired and measured pressure profiles versus the shoulder elevation and the estimated torques for both assisted and unassisted conditions. τ_{act} is the torque provided by the actuator based on the torque characteristics of the actuator; τ_{bio} is the required biological torque given the shoulder elevation and the participant's size and weight. Pressure was limited to P_{sat} ~ 110 kPa to reduce the risk of failure of the airtight bladder within the textile actuator. A minimum elevation threshold of 40° was set to trigger the compensation control intervention. For these specific movements, the robotic wearable was able to provide an estimated 76% (forward transfer) and 56% (touch head) of the required biological torque to achieve the task.

individuals, with few studies showing increased passive range of motion on an impaired population (*14*). In this study, we showed an improved active range of motion for shoulder abduction and flexion using a soft robotic wearable in 10 participants with ALS, which enabled users to better leverage any residual strength or capacity. In addition, the reduction in shoulder muscle activity and in perceived exertion, as well as increased endurance when holding a weight, highlight the potential to mitigate the effects of fatigue known to be an early challenge for this population (*31*). There is diversity in the presentation of impairment for individuals with ALS, and ability rapidly deteriorates over time; thus, we also demonstrated that the technology adapted to and compensated for a wide range of physical disability. To enable true independence, the support from the device needs to be intuitively delivered; we demonstrated that our robotic controller enabled this through improved performance in simulated functional tasks and in a clinical upper extremity function test (box and block test) at the first usage of the device and without providing any specific training. Last, beyond assistance, more frequent assessment (potentially remotely) can enable better monitoring of changes over time. Because of its mechanical transparency when unpowered (due to its light weight and nonrestrictive design), our robotic wearable allowed measurement of user ability in unsupported movements. Collectively, these findings represent a critical step toward ensuring robotic wearable usefulness in everyday life, aiming at better quality of life and extended independence.

The MyoPro exoskeleton by Myomo is the only commercially available device to show promising results as an assistive wearable device. It provides assistance to the elbow, wrist, and hand, and Peters *et al.* (*10*) demonstrated that stroke survivors could improve performance of some simulated ADLs using the robotic exoskeleton (turning on a light switch, lifting a laundry basket bilaterally, bringing a spoon to the mouth, and drinking from a cup). Regardless of its elegant design, the use of traditional robotic components means that the device adds about 1.8 kg to the arm of the user (an order of magnitude more than the solution presented in this work), a non-negligible amount for an impaired individual.

Despite the importance of the shoulder joint in performing functional tasks, little has been seen in terms of solutions for assisting this complex joint from untethered wearable devices. Likely, a reason for this is a major challenge in making traditional rigid exoskeletons able to provide sufficient assistance without adding

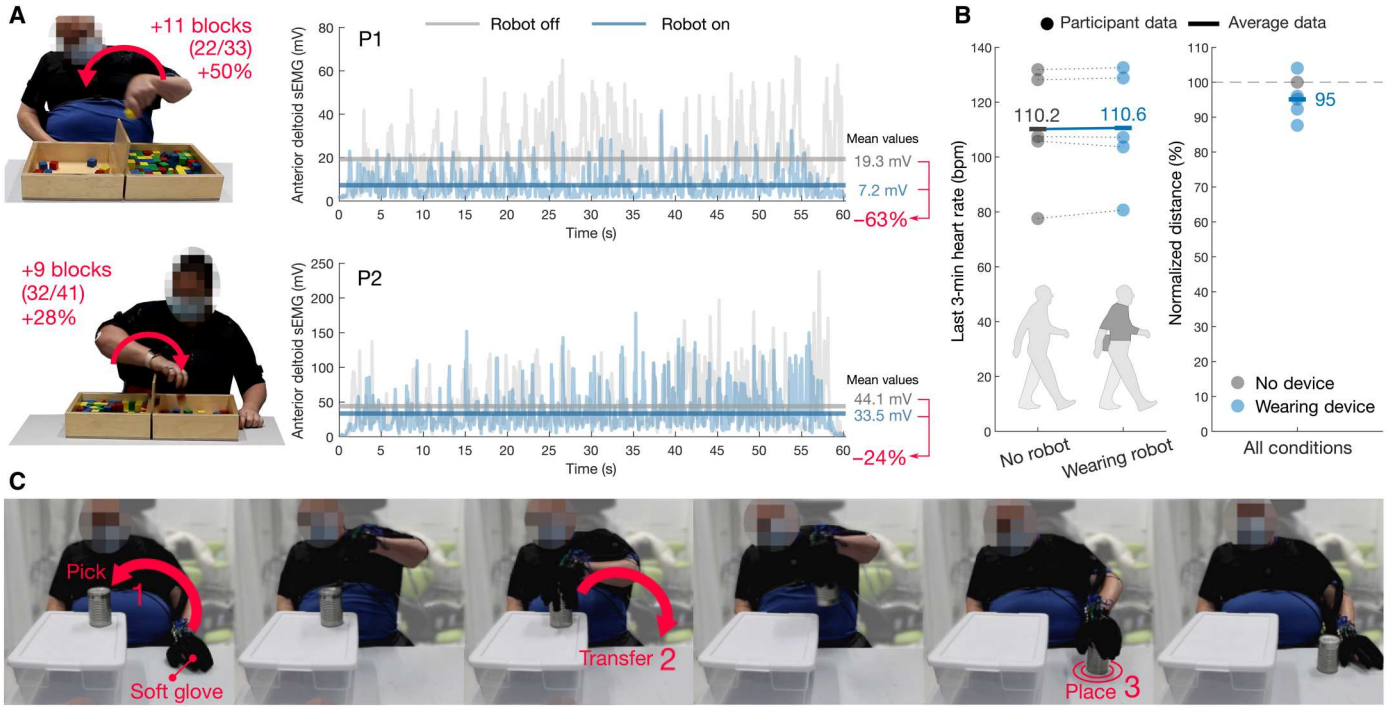

Fig. 5. Box and blocks test, 6-min walking test, and proof of concept of shoulder-glove integration. (**A**) Photographs show two participants, P1 and P2, completing the box and blocks test. EMG activity of the anterior deltoid muscle during robot off and robot on conditions while completing the test is also shown. Participant P1 had lower residual active range of motion, and participant P2 had higher residual active range of motion. The red arrows indicate direction of movement. When assisted by the robot, both participants were able to improve their performance above the minimal detectable change, that is, +5.5 blocks or +18% (*23*). (**B**) Comparison of the 6-min walk test for five study participants with and without the device is shown. Not all study participants were able to perform the 6-min walking test because of the effects of ALS. Results show the individual values and the average for the five participants who were able to perform the test. (**C**) A proof-of-concept test was conducted with the shoulder soft robotic wearable combined with a soft robotic glove previously developed in the laboratory. Photographs show a highly impaired participant with ALS using both devices simultaneously to complete a pick-and-place task, otherwise unachievable without assistance. The red arrows indicate direction of movement.

unacceptable weight and restrictions to the wearer. Using a soft inflatable robotic approach that combines textiles and pneumatics enabled us to minimize the amount of weight on the user's limb (about 150 g). Although the approach does require a control box (weight, ~3 kg), this can be worn on the waist or attached to a wheelchair. The waist, in particular, is a body location with low impact on walking ability (*32*), and this was further confirmed by our finding of a nonappreciable impact of the system in the 6-min walk test, a standard clinical assessment of mobility. Our laboratory has experience using similar waist-mounted systems of similar weight, showing that individuals with impairments are able to use and wear these systems with minimal impact (*33*). Noticeably, the robotic wearable's weight is similar to that of one of the smallest life-support ventilators on the market, the Vivo 45 LS (*34*), a typical machine needed by individuals with ALS late in the disease. Despite such a low weight on the limb, we estimated that the average delivered assistance from the robot was about 60% of the biological torque during simulated functional tasks over the full range of motion. Although a design specification was for 100% for a man with 1.75 m in height and with a body mass index (BMI) of 25, we had a wide range of body types for participants enrolled in the study (1.79 ± 12.5 m, with three individuals over 1.9 m and three below 1.7 m and an average BMI of 31.6 ± 5.2). Moreover, from past characterization studies, we expected the robotic wearable to provide minimal assistive torque beyond about 105° of arm elevation (fig. S2) (*35*). In future iterations, actuator size, geometry, or inflation pressure could be adjusted and customized to increase the level of assistance.

When considering the clinical impact that a shoulder-only device could have, with respect to a full arm device including elbow and hand, it is important to underline that there exist different phenotypes for ALS (*36*). Although a shoulder-only device would not provide sufficient support for all individuals with ALS, there are subsets of patients (e.g., those with progressive muscular atrophy) for whom this device would provide marked improvements in independence with ADLs, at least for a period of time. Extending to other diseases, e.g., myopathy (*37*), that could benefit from such a robotic wearable, the shoulder is still very important, because weakness progression often starts from this joint. Moreover, most of the work against gravity in daily activities is performed by the shoulder joint rather than the elbow and hand (i.e., if a weak arm is raised, then it can likely move in a horizontal plane). These facts highlight the importance of assisting the shoulder joint and the impact that such assistance may have on daily activities.

For all evaluations of the soft robotic wearable, participants used the device completely independently after minimal training (<15 min). This was possible thanks to our gravity compensation control scheme that enabled simple and intuitive control. After a short initial calibration (about 30 s), participants could move their arms naturally and seamlessly switch between movements

and activities. This fast calibration procedure allows the robotic wearable to tailor assistive support to the needs of the participants over time due to changes in fatigue or disease progression. This is an advantage over commercially available spring-based exoskeletons (e.g., EksoUE); for these exoskeletons, the procedure is generally slower and more complex (it requires carefully unscrewing/screwing springs in the system with an external tool) and requires the user to take off the robot, a non-negligible procedure for impaired users. It is important to underline that, similar to these exoskeletons, the torque to arm angle ratio of our robotic wearable is constant once calibrated. However, although achieving a similar amount of supported torque, the soft robotic wearable does not require particular effort to lower the arm; for example, observe in Fig. 2C the absence of spikes in the EMG signals toward the end of the motion. As soon as the robot detects the intent to lower the arm, it vents the actuators, quickly reducing the provided torque. This is fundamentally different from spring-based exoskeletons, where, to lower the arm, the user needs to input into the system a value proportional to the supported torque. Furthermore, with a passive exoskeleton, there will always be some amount of force or resistance applied to the user from either the integrated springs or the mass of the device. Because of the low weight on the upper limbs of our soft robotic wearable when unpowered (i.e., actuator fully deflated), our device is highly transparent to the wearer and allows a person to move naturally. This unique aspect opens the possibility to leverage the integrated sensors to monitor changes in a wearer′s movement performance over time, crucial from a clinical standpoint.

This study included participants with a wide range of impairments; however, we showed meaningful improvements in movement and function at both the individual and group level. Some participants had better function and could complete some of the tasks without assistance (e.g., a participant with less impairment was able to hold the object for more than 60 s unassisted). If we consider only individuals with active range of motion in the range where the actuator can apply supportive torques or ADLs for individuals who could not complete tasks unassisted, then we observed higher average improvements. For participants with less impairment, even if range of motion did not improve, we observed decreases in the rate of perceived exertion and improvements in endurance (as shown by longer duration of the hold task). Moreover, for a single participant with less impairment, we noted a marked reduction in shoulder muscle activity during both the box and block test and the weightlifting activity. These data suggest that the technology successfully assisted individuals with different degrees of impairment in different ways. Furthermore, although the consequences of ALS reduced participants' movement ability, the robotic wearable was able to compensate for motor degradation over time (in this case, >6 months from the first visit) in two selected participants, P1 and P2. This is a preliminary demonstration of the ability of the robotic wearable to adapt to changing degrees of impairment and slow the loss of functional ability, something particularly important given the degenerative nature of ALS.

Despite the promising results, this study and the proposed device have some limitations. Any solutions addressing ALS-related deficits need to be suitable across as much of the disease spectrum as possible, given the degenerative nature of the disease itself. Future work needs to address the possibility of designing and integrating additional supported joints, e.g., the hand (which was only shown as a proof of concept in one participant in this study), to support movements over a larger set of activities and with more diffuse impairments in the upper limb. Although we demonstrated that our soft robotic wearable could be used by both ambulatory and wheelchair-bound individuals, another feature that would be beneficial to add is a control mode that provides assistance to those without volitional movement. In the current version of our robotic wearable, a tunable threshold sets the minimum elevation of assistance (for this study, 40°) to avoid inflation when the arm is in a rest position (along the body). In the future, improved strategies of motion intention detection will be investigated to overcome this requirement for the user, for example, by using a brain-computer interface (*38*, *39*). The approach for estimating the amount of support from the robotic wearable using the actuator characterization and a kinematic model of the arm is an approximation that is prone to error. Further work will be needed to develop approaches for sensing and estimating directly the assistive torque generated by a soft pneumatic robotic wearable. Participants were assisted by team members to wear the robotic wearable (the whole donning process took less than 5 min to complete). Future iterations of the device will target a simpler, faster, and potentially self-donnable procedure. However, it is important to underline that despite a non-negligible donning time, the advantage of such a soft robotic wearable, made of a comfortable textile and lightweight material, is that once donned, it can be worn all day long (~12 hours), therefore reducing the impact of setup time compared with usage time.

This work represents an important step toward the development of a fully portable soft robotic wearable for assisting the upper limbs of people with arm weakness due to degenerative disease. Given the lack of robotics and wearable technology solutions available for individuals with ALS, the results of this study pave the way toward improving the functional independence and quality of life for this patient population.

MATERIALS AND METHODS

Study design

This study was designed as a proof of concept for a textile-based soft inflatable robotic wearable to support impaired upper limbs. We set out to demonstrate that such a technology could increase the upper limb motor abilities of individuals living with ALS and could support the performance of simple but frequently done ADLs. We tested the ability of this robotic wearable to track kinematic changes due to physical deterioration over >6 months and its ability to compensate for these changes and to reduce muscular fatigue, and, last, we investigated the impact that carrying such a weight could have on ambulatory individuals. One of the original design objectives was to create an intuitive technology for the user, with a control strategy that did not require a long time for training or adaptation. We verified this by collecting feedback from the study participants with a standard survey. A sample size of 10 participants was used for this study. The study was not blinded, but testing conditions (with or without the assistance of the robot) were randomized. All participants took part in a single session of tests, whereas two selected participants, P1 and P2, were invited for a second session of tests >6 months after their first evaluation.

Study participants

Ten individuals with a diagnosis of ALS (eight men and two women, 63 ± 12 years old, 101 ± 18 kg, 179 ± 12 cm, and 1.7 ± 1.6 years after diagnosis) were enrolled after passing our screening criteria (Table 1). The screening criteria were (i) 18 to 85 years old, (ii) no major visual deficits, (iii) could understand and follow simple instructions as assessed by the Mini-Mental State Examination (MMSE > 23) (*40*), and (iv) did not have joint stiffness or spasticity of the upper limbs that could prevent movement through the full range of motion. Informed consent was obtained from each participant, and the study (IRB13-3418) was approved by the Harvard Medical School Institutional Review Board.

Device design

We present a fully portable, soft robotic wearable capable of dynamically assisting the shoulders of individuals with upper extremity weakness. The robotic wearable uses a pair of textile-based pneumatic actuators anchored to a shirt, one per side, to support the arm through a gravity compensation controller that can dynamically, continuously, and intuitively modulate the assistance level to augment and restore weakened arm functionality (fig. S4). A fast (about 30 s) automatic calibration tunes the assistance level to the specific needs of the user. The soft actuators support the arm elevation in both shoulder abduction and shoulder flexion; once unloaded from gravity, the user can better leverage any residual strength or capacity to actively control other degrees of freedom, such as shoulder horizontal flexion. The fluidic supply, power, and electronics to control the system are embedded in a waist-mounted control box (that can alternatively be attached to a wheelchair), and air pressure in each of the two actuators can be independently controlled.

The actuators were designed to provide about 11.5 N·m of torque at an inflation pressure of 110 kPa at 90° of shoulder elevation (see Supplementary Materials and Methods). This value is an estimation of the biological torque required to fully sustain the arm of a male individual with a height of 1.75 m and a BMI of 25 [based on a simplified kinematic model of the arm and literature-averaged anthropometric data (*41*, *42*); table S1]. Secure anchoring of the actuators was achieved by combining an extensible textile base layer with inextensible force transmission pathways to allow transfer of the necessary torque to assist the user′s shoulder movements (similar to the textile component used in previous works) (*24*, *25*, *43*). Several strap-based adjustments were also present to allow for better fitting of the device to the user′s body and to maximize torque transmission. The system can assist individuals with widely varying body types and sizes with available textile components of different sizes (from extra small to extra large), excluding the actuators that have a fixed dimension. Zippers are included on the chest in addition to along both sleeves to aid in donning the robotic wearable shirt. Three hook and loop patches (Velcro IP Holdings LLC) on the chest and arms allowed for mounting of the inertial measuring units. Flexible 3-mm-thick nylon sheets were inserted in the sleeve and along the side seam to support the actuator anchoring and to further distribute the forces of actuation on the wearer′s body. The sheets were padded with a high-friction material (Fabrifoam, Applied Technology International Ltd.) to help stabilize the actuator placement. Close-up photographs of the robotic wearable shirt are shown in fig. S5.

By optimizing the fluidic supply design (air compressor, reservoir, and valves) to match the actuator requirements, we demonstrate a system that is compact (25.5 cm by 21.5 cm by 8.5 cm) and lightweight (control box weighs 3 kg) and, thus, suitable to be used for everyday activities in unstructured environments, from the clinic to the community. The final design consisted of a high-performance compressor (P07H015A-BLDC-C, AirSquared Inc.) providing 13 liter/min at 310 kPa and a lightweight reservoir (Crowler, Twistee Can; 750 ml of volume), pressurized in operation to 350 kPa. The pump produced about 30 dB of noise when running at full speed, thus negligibly affecting real-life usage: 30 dB is defined as a soft whisper by the Centers for Disease Control and Prevention (*44*) and is within the suggested noise limits for hospitals as defined by the World Health Organization (*45*). Pressure control of the actuators was achieved using a pair (fill valve and vent valve) of proportional valves (Polaris, IQ Valves) per channel, two channels total. The four valves were mounted onto a custom manifold for compact packaging, where they shared a common connection to the accumulator. Each pressure channel had a dedicated pressure sensor (MPX5700GP, NPX), with a third sensor monitoring the pressure in the accumulator. The fluidic supply was controlled by a microcomputer (Beaglebone Black Wireless, BeagleBoard.org Foundation) with a custom circuit board containing the proportional valve drivers, power regulation, and a controller area network (CAN-bus) to communicate with the inertial measuring units. The robot was battery powered, using a pair of 15.0-V, 3.2-A·hour batteries in series (RRC2054, RRC Power Solutions GmbH) with integrated safety circuitry. This allowed the robot to assist ~100 movements per hour per limb, with a total battery life of ~4 hours. The control box was designed to maintain surface temperatures below 41°C (as per IEC 60601-1 standard), and this requirement was achieved using three fans mounted on the cover of the box.

Intuitive gravity compensation control and calibration procedure

The gravity compensation controller was designed to offload the wearer′s limb from the effects of gravity and was introduced in (*25*). Three inertial measuring units (MTi-3 AHRS, Xsens Technologies B.V.) on the torso and upper arms detected residual volitional movements of the limbs. Briefly, the gravity compensation controller used the pose of the limb and a user-specific calibration—i.e., a mapping between arm angle, actuator pressure, and thus delivered torque—to compute a desired dynamic pressure profile, which was, in turn, tracked by a low-level pressure loop, as shown by the robotic control loop in fig. S4. With this architecture, the controller delivered assistance in an intuitive way (only based on the elevation of the user′s arm) by adjusting pressure to increase or decrease the amount of support. Once the user initiated the motion, the robot reacted in real time (any motion was detected within 10 ms by the inertial measuring units, and then assistance started to be deployed within 150 ms, limited only by the valves′ opening/closing time and the fluid dynamics; see fig. S1 and movie S2). A minimum shoulder elevation threshold was implemented to avoid assistance at very low angles (e.g., arm along the side of the body).

The specific nonlinear mapping of limb angle to actuator pressure could be achieved two ways: through an autonomous calibration procedure or through manual selection of a precalibrated profile. The autonomous calibration procedure involved slowly

ramping the pressure in the actuator up to a maximum pressure or to when the limb achieved 90° of range of motion (inflation profile) and then down to a zero-pressure condition (venting profile). The wearer was instructed to remain relaxed during this process to allow the system to support the arm's full weight. The whole calibration procedure took about 30 s. It was necessary to record both the inflation and deflation profiles because of a hysteresis in the system. To switch between the inflation and deflation profiles when the controller was active, a tunable velocity threshold must be exceeded. For this work, we customized the value of the threshold for each participant as part of a calibration routine with their help to understand the "best" trade-off between intuitiveness and maximum support. The resulting tuning was a value in the range 5° to 10°/s. The precalibrated profiles were scaled versions of profiles that were recorded on healthy individuals.

Testing protocol and metrics

In a single-day test session, six different experiments were conducted under assisted (with the device powered on) versus unassisted (with the device powered off) conditions. The order of the conditions was randomized between participants and between tests. For unilateral exercises, the side with the greater impairment was selected for assistance, as determined by a preliminary range of motion test.

The first experiment consisted of an active range of motion assessment performed to measure the maximum range of shoulder abduction and flexion. Participants were instructed to reach their maximum range of motion and briefly hold (2 s) the position before returning to rest. This pause was included to prevent ballistic trajectories typical of impaired individuals trying to achieve their maximum range of motion. Each motion was repeated three times by the target limb, with range of motion being recorded by the inertial measurement units. The maximum range of motion was averaged over the three repetitions and then over the participants.

A static hold assessment was conducted next. Under both conditions, participants were instructed to lift a box (weight 224 g) bimanually as high in flexion as possible and maintain that position for as long as possible. Both hold duration and maximum angle were measured. An elevation angle of 60° was set as the threshold for measuring the duration of the hold. No participants performed multiple crossings of the threshold. This assessment was only completed once per condition because of the fatiguing nature of the task, and a 5-min recovery was provided between both conditions.

The next experiment involved targeted reaching. A 3 × 3 grid was created, wherein the columns were aligned with the ipsilateral, central, and contralateral workspaces, whereas the rows were aligned at head, chest, and stomach height. The board was placed for each participant at a custom distance reachable with a comfortable natural extension of the arm. Each grid location was marked with a number (1 to 9), and participants were instructed to reach out and touch the correct number when asked by a team member. Each number was targeted three times under both conditions, for a total of 27 assisted and 27 unassisted reaches. During this experiment, participants' lower limbs were stationary; thus, they could only use arm and torso movement to reach the targets. Reaches were scored on a 0 to 1 scale, where 0 represented a failure to reach the target and 1 represented a successful reaching by touching the correct target on the board. Results were reported only for the reaching of the highest row (head alignment): For lower rows, chest, and stomach height, participants were able to reach 100% of targets under any conditions.

The fourth experiment involved performing four simulated ADLs similar to (*10*). In our case, the tasks were lateral and forward transfer tasks of an object (16 g) into a box, simulated pouring of fluid from one container to another, and touching the top of one's head. As with (*10*), a 0 to 2 scale was used through these tasks. For the lateral and forward transfer ADLs, two points were awarded for successfully placing the object in the box, whereas one point was awarded if the object was dropped into the box. For touching of the head, one point was awarded if the participant could reach their face without bowing their head, whereas two points were awarded for successful touching the top of the head without bowing of the head. For the simulated pouring task, one point was awarded for getting the openings of both containers in contact, whereas two points were awarded for a successful, sustained (>3 s) pouring motion. Each ADL was performed three times under both conditions.

For each ADL, the estimated biologically required torque (τ_{bio}) and the actuator torque (τ_{act}) were computed to assess the assistance provided by the robot. τ_{act} was calculated by interpolating with current measured actuator pressure and arm angle from the inertial measurement units, a 3D surface (see fig. S4), output of the characterization of the bifurcated actuator using a previously designed testing rig (*35*) on $n = 1$ healthy individual. τ_{bio} was calculated using the arm angle from the inertial measurement units, a simplified arm kinematic model, and literature-averaged anthropometric data (*41*, *42*). On completion of all ADLs, the rate of perceived exertion (10-point scale) of the participants was recorded considering holding, reaching, and ADL tasks.

A standard 6-minute walk test was the last task before the system was doffed. Participants were instructed to walk at a self-selected pace around an indoor course, whose length was measured each time with a trundle-wheel (DigiRoller Plus II, Calculated Industries). An optical heart-rate monitor (OH1+, Polar) was placed on the forearm of the participant to record the heart rate of the participant through the walk. The test was performed first while the system was worn by the participant and subsequently with the system doffed. A 10-min break was given between both conditions to ensure that participants were adequately rested. The distance traveled under both conditions was normalized with respect to the doffed condition to allow for aggregation between participants. The heart rate of the final 3 min of walking was used because this represented the steady state heart rate of the participant during the activity. Because of the progression of their ALS, several participants were wheelchair bound; therefore, only five participants were capable of free ambulation without external support and completed the 6-minute walk test. To conclude the session, we performed a system usability scale.

Two participants, selected as representative of individuals with higher and lower residual volitional movement ability, participated in a second day test session that occurred >6 months after the first visit. In this second session, three tests were conducted under no device versus worn device and unpowered versus worn device and powered conditions. As for the first session, the side with the greater impairment was selected for assistance.

The first test consisted of three repetitions of an active range of motion task (in particular, shoulder abduction and shoulder

flexion) under the three testing conditions, following the same procedure of the first testing session. This test assessed both the robotic wearable's transparency (no device versus powered off) and the ability of the robotic wearable to compensate for long-term reduction of movement ability due to ALS (device off versus device on, comparing the two study visits). Once again, the active range of motion was measured by the inertial measurement units.

The second test consisted of a timed weightlifting from an arm to the side pose to a shoulder abduction of approximately 80°, as measured by the inertial measurement units. The participants were instructed to keep the abducted pose for 2 s. The weight lift was repeated three times. For the weaker participant, we used a 0.23-kg weight. For the stronger participant, we used a 0.35-kg weight. For this test, we collected the shoulder middle deltoid muscle activity through an EMG sensor (TeleMyo 2400 T G2, Noraxon). The muscle was chosen given its primary role in the shoulder abduction/adduction motion. Sensor placement was determined according to surface EMG for the noninvasive assessment of muscle recommendations (*46*). The EMG data were sampled at 2 kHz, then bandpass-filtered (fourth order, 10 to 400 Hz), rectified, and lastly low pass–filtered (fourth order, 10 Hz). For each participant, maximum voluntary contraction of the middle deltoid muscle was also recorded and processed in the same way. To compare different testing conditions, we did not perform preliminary EMG normalization (e.g., with the square of the movement time) given that the motion duration was very similar among repetitions (duration, 10 ± 0.3 s).

Last, the third test consisted of a standard box and block test. Each participant had 60 s to move as many blocks as possible from one side to the other of the box equipment. For this test, the nodevice condition was not performed given the challenging activity and the risk of overly fatiguing the participants. We collected the shoulder anterior deltoid muscle activity through an EMG sensor. The muscle was chosen given its primary role in the shoulder flexion/extension motion. Sensor placement was kept from the second test and processed following the same abovementioned pipeline.

The highly impaired participant performed a fourth test at the end of the study protocol. The test consisted in performing a proof of concept of the integration of our soft wearable shoulder robot with a previously developed soft glove robot manually controlled by a team member. With the participant sitting at a desk, the test included a few basic ADLs, such as reaching and grasping a lightweight object (~0.5 kg) on a box (height, ~30 cm) and then moving and placing the object on the desk. For this proof of concept, only video recording of the performance was collected.

Statistical analysis

A paired-sample *t* test was conducted to compare the unassisted versus assisted conditions for each of the specific metrics (active range of motion, ADLs, 6-min walk test) on the first day of testing. Measurements were taken repeatedly (three times) for all the metrics but the 6-min walk test, the statistical analysis of which was based on distinct samples. Significance level is reported when exceeding standard P values of significance ($^{*}P < 0.05$) and high significance ($^{**}P < 0.01$) after a post hoc power analysis (required power ≥ 0.80, effect size using Cohen's criteria). Because of the limited amount of data for the second visit (only two participants), no statistical analysis was run on these data. The analysis was performed on MATLAB 2022a (MathWorks).

Supplementary Materials

This PDF file includes:
Materials and Methods
Figs. S1 to S5
Table S1

Other Supplementary Material for this manuscript includes the following:
Data file S1
Movies S1 and S2
MDAR Reproducibility Checklist

View/request a protocol for this paper from *Bio-protocol*.

REFERENCES AND NOTES

1. The ALS Association (28 July 2021), www.als.org/.
2. H. Mitsumoto, D. A. Chad, E. P. Pioro, *Amyotrophic Lateral Sclerosis* (F.A. Davis Company, 1998).
3. R. H. Brown, A. Al-Chalabi, Amyotrophic lateral sclerosis. *N. Engl. J. Med.* **377**, 162–172 (2017).
4. O. Hardiman, A. Al-Chalabi, A. Chio, E. M. Corr, G. Logroscino, W. Robberecht, P. J. Shaw, Z. Simmons, L. H. van den Berg, Amyotrophic lateral sclerosis. *Nat. Rev. Dis. Primers* **3**, 17071 (2017).
5. M. C. Kiernan, S. Vucic, K. Talbot, C. J. McDermott, O. Hardiman, J. M. Shefner, A. Al-Chalabi, W. Huynh, M. Cudkowicz, P. Talman, L. H. Van den Berg, T. Dharmadasa, P. Wicks, C. Reilly, M. R. Turner, Improving clinical trial outcomes in amyotrophic lateral sclerosis. *Nat. Rev. Neurol.* **2**, 104–118 (2021).
6. P. Maciejasz, J. Eschweiler, K. Gerlach-Hahn, A. Ansen-Troy, S. Leonhardt, A survey on robotic devices for upper limb rehabilitation. *J. NeuroEng. Rehabil.* **11**, 3 (2014).
7. T. Proietti, E. Ambrosini, A. Pedrocchi, S. Micera, Wearable robotics for impaired upper-limb assistance and rehabilitation: State of the art and future perspectives. *IEEE Access* **10**, 106117–106134 (2022).
8. Stroke Facts, CDC (28 July 2021), www.cdc.gov/stroke/facts.htm.
9. S. Demain, R. Wiles, L. Roberts, K. McPherson, Recovery plateau following stroke: Fact or fiction? *Disabil. Rehabil.* **28**, 815–821 (2006).
10. H. T. Peters, S. J. Page, A. Persch, Giving them a hand: Wearing a myoelectric elbow-wrist-hand orthosis reduces upper extremity impairment in chronic stroke. *Arch. Phys. Med. Rehabil.* **98**, 1821–1827 (2017).
11. Ekso Bionics EksoUE, (5 October 2021), https://eksobionics.com/eksoue/.
12. L. R. Chang, P. Anand, M. Varacallo, *Anatomy, Shoulder and Upper Limb, Glenohumeral Joint* (StatPearls Publishing, 2021).
13. N. Jarrasse, G. Morel, Connecting a human limb to an exoskeleton. *IEEE Transact. Robot.* **28**, 697–709 (2012).
14. M. Xiloyannis, R. Alicea, A. M. Georgarakis, F. L. Haufe, P. Wolf, L. Masia, R. Riener, Soft robotic suits: State of the art, core technologies, and open challenges. *IEEE Trans. Robot.* **38**, 1343–1362 (2022).
15. I. Gaponov, D. Popov, S. J. Lee, J. H. Ryu, Auxilio: A portable cable-driven exosuit for upper extremity assistance. *Int. J. Control Automat. Syst.* **15**, 73–84 (2017).
16. S. Lessard, P. Pansodtee, A. Robbins, J. M. Trombadore, S. Kurniawan, M. Teodorescu, A soft exosuit for flexible upper-extremity rehabilitation. *IEEE Trans. Neural Syst. Rehabil. Eng.* **26**, 1604–1617 (2018).
17. L. Samper-Escudero, A. Giménez-Fernandez, M. Á. Sánchez-Urán, M. Ferre, A cable-driven exosuit for upper limb flexion based on fibres compliance. *IEEE Access* **8**, 153297–153310 (2020).
18. R. A. Shveda, A. Rajappan, T. F. Yap, Z. Liu, M. D. Bell, B. Jumet, V. Sanchez, D. J. Preston, A wearable textile-based pneumatic energy harvesting system for assistive robotics. *Sci. Adv.* **8**, eabo2418 (2022).
19. C. Nam, W. Rong, W. Li, C. Cheung, W. Ngai, T. Cheung, M. Pang, L. Li, J. Hu, H. Wai, X. Hu, An exoneuromusculoskeleton for self-help upper limb rehabilitation after stroke. *Soft Robot.* **9**, 14–35 (2022).
20. S. J. Park, K. Choi, H. Rodriguez, C. H. Park, Soft exosuit based on fabric muscle for upper limb assistance, in *IEEE/ASME Transactions on Mechatronics* (IEEE, 2022), pp. 1–12.

21. A. M. Georgarakis, M. Xiloyannis, P. Wolf, R. Riener, A textile exomuscle that assists the shoulder during functional movements for everyday life. *Nat. Mach. Intell.* **4**, 574–582 (2022).
22. N. Li, T. Yang, P. Yu, J. Chang, L. Zhao, X. Zhao, I. E. Elhajj, N. Xi, L. Liu, Bio-inspired upper limb soft exoskeleton to reduce stroke-induced complications. *Bioinspir. Biomim.* **13**, 066001 (2018).
23. C. Simpson, B. Huerta, S. Sketch, M. Lansberg, E. Hawkes, A. Okamura, Upper extremity exomuscle for shoulder abduction support. *IEEE Trans. Med. Robot. Bionics* **2**, 474–484 (2020).
24. C. O'Neill, T. Proietti, K. Nuckols, M. E. Clarke, C. J. Hohimer, A. Cloutier, D. J. Lin, C. Walsh, Inflatable soft wearable robot for reducing therapist fatigue during upper extremity rehabilitation in severe stroke. *IEEE Robot. Autom. Lett.* **5**, 3899–3906 (2020).
25. T. Proietti, C. O'Neill, C. J. Hohimer, K. Nuckols, M. E. Clarke, Y. M. Zhou, D. L. Lin, C. Walsh, Sensing and control of a multi-joint soft wearable robot for upper-limb assistance and rehabilitation. *IEEE Robot. Autom. Lett.* **6**, 2381–2388 (2021).
26. S. Balasubramanian, A. Melendez-Calderon, E. Burdet, A robust and sensitive metric for quantifying movement smoothness. *IEEE Trans. Biomed. Eng.* **59**, 2126–2136 (2012).
27. H. M. Chen, C. C. Chen, I. P. Hsueh, S. L. Huang, C. L. Hsieh, Test-retest reproducibility and smallest real difference of 5 hand function tests in patients with stroke. *Neurorehabil. Neural Repair* **23**, 435–440 (2009).
28. L. R. Keytel, J. H. Goedecke, T. D. Noakes, H. Hiiloskorpi, R. Laukkanen, L. van der Merwe, E. V. Lambert, Prediction of energy expenditure from heart rate monitoring during submaximal exercise. *J. Sports Sci.* **23**, 289–297 (2005).
29. C. Correia, K. Nuckols, D. Wagner, Y. M. Zhou, M. E. Clarke, D. Orzel, R. Solinsky, S. Paganoni, C. Walsh, Improving grasp function after spinal cord injury with a soft robotic glove. *IEEE Trans. Neural Syst. Rehabil. Eng.* **28**, 1407–1415 (2020).
30. A. Bangor, P. Kortum, J. Miller, Determining what individual SUS scores mean: Adding an adjective rating scale. *J. Usability Studies* **4**, 114–123 (2009).
31. C. Gibbons, F. Pagnini, T. Friede, C. A. Young, Treatment of fatigue in amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst. Rev.* **2018**, CD011005 (2018).
32. S. Faraji, A. R. Wu, A. J. Ijspeert, A simple model of mechanical effects to estimate metabolic cost of human walking. *Sci. Rep.* **8**, 10998 (2018).
33. L. N. Awad, J. Bae, K. O'Donnell, S. De Rossi, K. Hendron, L. H. Sloot, P. Kudzia, S. Allen, K. G. Holt, T. D. Ellis, C. Walsh, A soft robotic exosuit improves walking in patients after stroke. *Sci. Transl. Med.* **9**, eaai9084 (2017).
34. Vivo 45 LS techincal specs (11 April 2022), www.breas.com/products/vivo/vivo-45-ls.
35. C. O'Neill, C. McCann, C. J. Hohimer, K. Bertoldi, C. Walsh, Unfolding textile-based pneumatic actuators for wearable applications. *Soft Robot.* **9**, 163–172 (2022).
36. B. Swinnen, W. Robberecht, The phenotypic variability of amyotrophic lateral sclerosis. *Nat. Rev. Neurol.* **10**, 661–670 (2014).
37. E. Suresh, S. Wimalaratna, Proximal myopathy: Diagnostic approach and initial management. *Postgrad. Med. J.* **89**, 470–477 (2013).
38. F. R. Willett, D. T. Avansino, L. R. Hochberg, J. M. Henderson, K. V. Shenoy, High-performance brain-to-text communication via handwriting. *Nature* **593**, 249–254 (2021).
39. M. J. Young, D. J. Lin, L. R. Hochberg, Brain-computer interfaces in neurorecovery and neurorehabilitation. *Semin. Neurol.* **41**, 206–216 (2021).
40. M. F. Folstein, S. E. Folstein, P. R. McHugh, Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* **12**, 189–198 (1975).
41. P. de Leva, Adjustments to Zatsiorsky-Seluyanov's segment inertia parameters. *J. Biomech.* **29**, 1223–1230 (1996).
42. S. Plagenhoef, F. G. Evans, T. Abdelnour, Anatomical data for analyzing human motion. *Res. Q. Exerc. Sport* **54**, 169–178 (1983).
43. Y. M. Zhou, C. Hohimer, T. Proietti, C. O'Neill, C. Walsh, Kinematics-based control of an inflatable soft wearable robot for assisting the shoulder of industrial workers. *IEEE Robot. Autom. Lett.* **6**, 2155–2162 (2021).
44. Center for disease control and prevention: What noises cause hearing loss? (11 April 2022); shorturl.at/oHMU9.
45. B. Berglund, T. Lindvall, D. H. Schwela, World Health Organization, Occupational and Environmental Health Team. *Guidelines for Community Noise*, (World Health Organization, 1999).
46. Recommendations for sensor locations on individual muscles (2022); http://seniam.org/sensor location.htm.

Acknowledgments: We thank all of the participants who volunteered for the study for willingness to help and insightful feedback. We thank D. Williams, A. Huang, and S. Sullivan, the research coordinators who assisted in enrolling and consenting the participants and scheduled the visits. We also thank L. Hochberg for discussions and J. Grupper for video collection during some of the study sessions. **Funding:** This research was supported by the National Science Foundation EFRI Award (no. 1830896), the Cullen Education and Research Fund (CERF) Medical Engineering Prize for ALS, and the Harvard School of Engineering and Applied Sciences.
Author contributions: T.P., C.O., L.G., S.M., and C.H. built the control box. T.C. built the textile components with the assistance of C.O., T.P., and C.H. T.P. wrote the software controlling the robot with the assistance of C.O. T.P., C.O., K.N., D.L., S.P., and C.W. developed the study protocol. T.P., C.O., T.C., and S.M. ran the protocol. T.P. processed the data and ran statistical analysis. T.P. wrote the manuscript with the assistance of the other authors. **Competing interests:** C.W. and C.O. are coinventors on U.S. patent application US2022047444A1 filed by Harvard University that describes the inflatable soft robotic components tested in this study. **Data and materials availability:** All data associated with this study are present in the paper or the Supplementary Materials.

Submitted 24 May 2022
Resubmitted 09 September 2022
Accepted 13 January 2023
Published 1 February 2023
10.1126/scitranslmed.add1504

Science Translational Medicine

Restoring arm function with a soft robotic wearable for individuals with amyotrophic lateral sclerosis

Tommaso Proietti, Ciaran ONeill, Lucas Gerez, Tazzy Cole, Sarah Mendelowitz, Kristin Nuckols, Cameron Hohimer, David Lin, Sabrina Paganoni, and Conor Walsh

Sci. Transl. Med., **15** (681), eadd1504.
DOI: 10.1126/scitranslmed.add1504