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ORIGINAL ARTICLES

AUTOMA: a wearable device to assess the upper limb muscular activity in patients with neuromuscular disorders

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Inherited muscular dystrophies and congenital myopathies present in early childhood with progressive muscle weakness, determining severe motor limitations. Active surveillance and management of associated complications have improved ambulation, function, quality of life and life expectancy. The need for repeatable, objective and quantitative measures to monitor the clinical course of the disease is a current issue, particularly in the new era where new flows of therapies are proposed to the patients. In this scenario, we designed and tested a wearable device termed AUTOMA that is able to provide quantification of the muscular impairment in the upper limb upon isokinetic tests through the integration of a force sensor and an electric goniometer. This allows qualitatively estimating the muscular functions with a systematic procedure. We carried out a preliminary pilot study on 9 patients that revealed the suitability of AUTOMA as an objective measurement tool for diagnosing and monitoring neuromuscular disorders, and opens to a more extensive clinical study in which to test and validate our platform intensively.

Key words: neuromuscular disorders, wearable devices, upper limb function, sensing, clinical monitoring, rehabilitation

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Introduction

Neuromuscular disorders (NMDs) are a group of rare genetic diseases that induce a progressive disability in patients by affecting the muscular functionality. Duchenne Muscular Dystrophy (DMD) is one of such diseases that affects 1 in 3500 new-borns [1]. This idiopathic progressive pathology affects muscles from early life, threatening the ability to walk, to perform daily tasks with upper limbs, and inducing severe failures of the cardio-respiratory apparatus thus limiting life expectancy. Individuals with Becker muscular Dystrophy (BMD) have a more variable presentation and may continue to walk well into their fourth decade or later with a variable and partially unknown natural history.

Improved standards of care and the regular early-use of steroid treatments in DMD have changed the natural history of the disease, affecting both survival and time of loss of functional milestones [2,3]. More recently, there has been an increasing evidence of an additional benefit from new therapeutic approaches based on mechanisms targeting specific types of mutation [1,4]. To monitor the effect of such a therapy and to study the natural history of these young patients, over the last few years there has been an increasing attention to the identification of suitable outcome measures for clinical trials. At first, clinical research has focused on ambulant children only but, more recently, many studies have been carried out to reduce the existing gap in identifying suitable measurements for assessing upper limb functions across all stages of the disease.

In 2012, an international group of clinicians, physical therapists, patients, advocacy groups and industries developed the so-called Performance of the Upper Limb (PUL), a functional scale, based on scores awarded by operators, specifically designed for assessing upper limb function in DMD or BMD [5]. Meanwhile, a correlation was demonstrated between muscle strength and motor function among children and in the adult population [6]. An example of such score-based method is given by the Medical Research Council (MRC) index. This parameter ranges from 0 – no appreciable muscular contraction – to 5 – full muscular strength (normal power). The numerical value is subjectively assigned after detecting the muscular strength upon the application of a manual concentrated load on the limb [7]. However, is important to consider that the relationship between muscle strength and functionality is not linear. In general, upper limb functions become increasingly influenced by weakness in conjunction with contractures and/or growth, resulting in compensatory strategies and, ultimately, loss of function.

Finally, while several efforts have been made to identify outcome measures for DMD, other NMDs are still orphaned of functional measures and, there are still no measures capable of evaluating motor impairments of the upper limb in daily life. In fact, none of the routine rating scales captures the progressive muscle weakness representing the entire spectrum of the disease, in particular for patients at the weak end of the spectrum with low gross motor functions.

To overcome those limits, a large body of research has been carried out to develop equipment and devices able to perform motor tests, also in weak patients [8].

However, several limitations still exist in the use of such devices: i) a high level of subjectivity in the assessment of tests; ii) biased/incidental errors in positioning the devices on soft tissues of the patient (e.g., incorrect perpendicularity of the tools with respect to the direction-ality of the loads); iii) high footprint and invasiveness of isokinetic platforms for assessing force; iv) limited naturalness of the gesture [9,10].

In our work, we present the design and preliminary validation of a wearable mechatronic device named AUTOMA. Such a device is able to quantitatively assess upper-limb muscle strength upon quasi-static isokinetic loads and simultaneous determination of range of movements (ROMs) and motor functionality. This is a first step towards the definition of a set of wearables, non-invasive instruments to monitor DMD and, more broadly, NMDs.

Materials and methods

Hardware

AUTOMA is conceived as a measurement tool to be worn by a patient and to be used by the therapist to evaluate in real time the impairment level of the upper limb muscles upon quasi-static loads.

Figure 1 reports the hardware parts that compose AUTOMA (Fig. 1A): i) two sensorized units (Fig. 1B1 and 1B2) to classify the typology of the limb movements and to measure the relative angle between the arm and the forearm; ii) a thermoformed polymeric bracelet to measure the external force applied by the therapist to the patient (Fig. 1C1 and 1C2) during the manual muscle test; iii) a wearable elbow sleeve or a shawl made of a washable material (e.g., lycra) on which the components are assembled to avoid a direct contact with the skin and to ensure a safe and comfortable wearability (Fig. 1D and 1E).

In detail, each sensorized unit is composed of a shell containing one endblock of a biaxial electro-goniometer SG150 (Biometrics Ltd, Newport, UK), and the predisposition for a 9-axis inertial platform ADATEC (Fig. 1B2) - for the classification of the upper limb movement but not implemented in the present study. The bracelet, fabricated in stereolithographic resin and thermoplastic polymer (Aquaplast®), shown in Figure 1C1-C2, serves as a holder for a uniaxial load cell FX1901-0001-0010 (Measurement Specialties Inc., Hampton, VA, USA). To improve comfort and to avoid a slippery direct contact between the polymeric structure and the elbow sleeve, we applied an internal coating made of polyurethane.

A first calibration of the sensors was performed on a bench by testing the loading cell and the electro-goniometer with calibrated weights applied by means of a dedicated indentation machine (Fig. 2A) and with a manual goniometer commonly used by therapists (Fig. 2B), respectively. In the first case, the calibration shows high linearity (error ~ 2%), while the angular resolution reaches values of 4°-5° due to the analogic/digital conversion (Fig. 2C). The correct donning of the device was checked

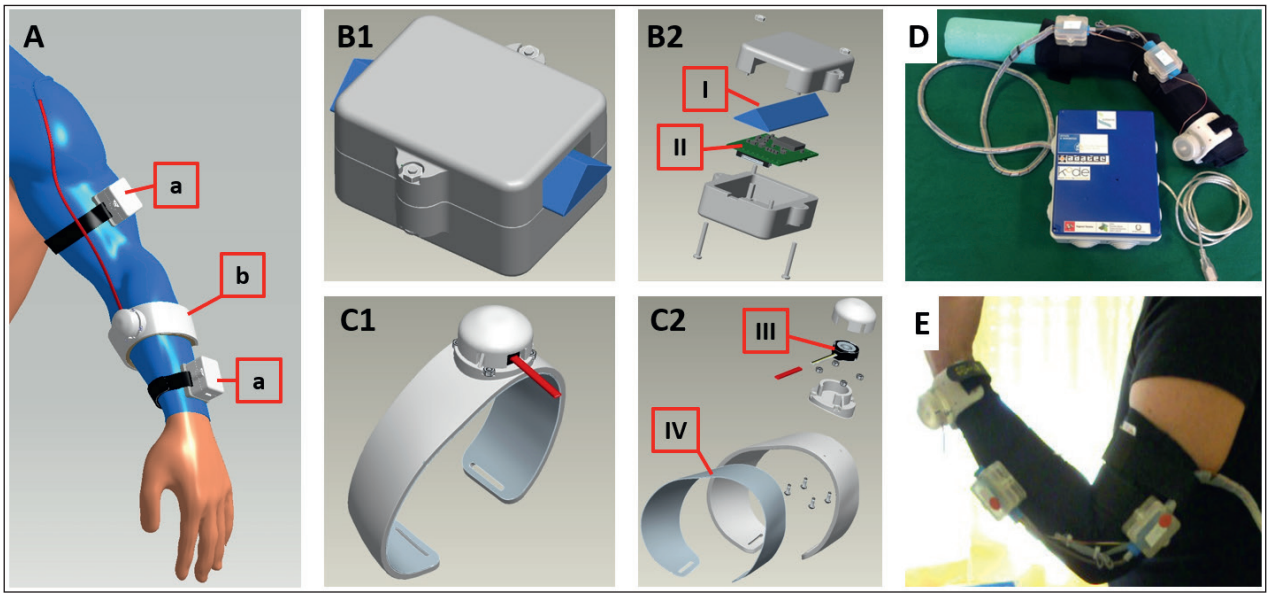

Figure 1. AUTOMA: hardware components. Panel A. 3D CAD model of AUTOMA composed of an elastic sleeve (in blue) and two types of sensors (a – electro-goniometer case; b – force sensor). Panels B1-B2: case for the electro-goniometer (I) and for the addition of a potential inertial unit - IMU (II) (not used for the validation in this study). Panels B3: Biometrics electro-goniometer SG150 model. Panels C1-C2: case (bracelet) for the force sensor (III) with an internal coating of polyurethane (IV) to assure comfort and to prevent slippage between the bracelet and the sleeve. Panel D. The complete system assembled on a dummy including the box containing the electronics. Panel E: AUTOMA worn by a subject: the bracelet was placed close to the wrist as specified by MMTs protocols implemented in the experiments.

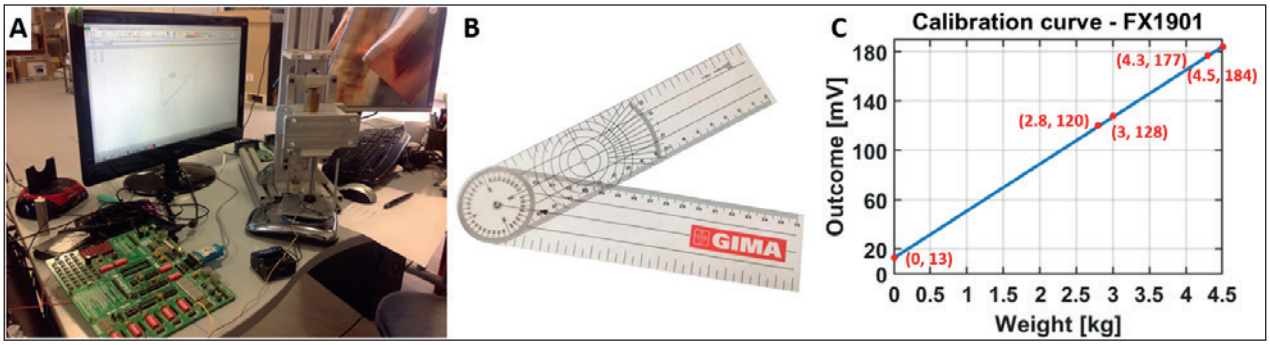

Figure 2. Calibrating AUTOMA. Panel A. Indentation machine. Panel B. Manual goniometer used by therapists. Panel C. Calibration curve. The red dots resemble the check-points for the calibration.

before the clinical trial. Within this phase, the electro-goniometer calibration was verified by means of a manual goniometer with AUTOMA already worn by the subject.

Software

Within the project developed, we implemented a platform named Health 360 to collect clinical data from AUTOMA and other sources. Health360 possesses a web-based modular architecture provided by a Software-as-a-Service (SaaS) model [11]. Data from AUTOMA can be embedded into Health360 in two manners, in both cases via communication through Application Programming Interface (API). The first approach, less computationally burdensome, relies on the communication of off-line previously analysed data; the second approach, computationally heavier, foresees the possibility of hosting data processing algorithms directly on the platform, therefore communicating raw data between AUTOMA and Health360. In both cases, Health360 will then merge data from AUTOMA with those from other sources, making them easy to be processed by Machine Learning algorithms and similar approaches. Data collected with

AUTOMA were processed using the R software (R Development Core Team) and later visualized using MATLAB (MathWorks, Inc., USA).

This will ultimately allow clinicians to collect, manage, and store data in the Cloud from tests that involve analogic and digital devices. Further details can be found in literature [12].

Pilot study in patients

We enrolled 9 subjects with neuromuscular issues (4 DMD patients, 3 BMD patients and 2 patients with a myopathic disorder, all males, age ranged 8-24 years) homogenously distributed across the MRC scale considering the upper limb performance. After being informed about AUTOMA and the procedures involved in the experimental design, patients provided a written consent to participate in the research program. With ethical approval (protocol 136/17, Tuscany Region Ethics Committee), the study took place at IRCCS Stella Maris Foundation (Pisa, Italy) and it was performed by professional therapists. Protocols included a first assignment of the PUL scores for the upper limb functionality and, using AUTOMA, the assessment through two specific items of the manual muscle test (MMT), namely MMT9 and MMT10, related to the extension and flexion of the elbow. Those exercises were independently evaluated by two operators and were repeated five times for each evaluator in a same session.

For each item, each trial was composed of three steps:

- first, the registration system is enabled with the operator supporting the subject's upper limb in the initial position without applying force on the load cell of the bracelet (time = 2 s);
- then, an isokinetic limb movement (to reduce force measurement artefacts due to inertial loads) was performed in elbow extension / flexion against operator resistance on the load cell, up to the patient's maximum range of motion for 2 s;
- after the completion of the test, the upper limb was brought to the initial position and the test repeated from point i.

Figure 3 depicts the phases of the tests on a subject. Compatibly with the patient's state of fatigue, both items were performed with 5 repetitions.

Data analysis

The experimentation and the analysis that follows focus on data recorded with the AUTOMA electro-goniometer and the load cell, while IMUs have not been preliminarily implemented since we decided to use these sensors in a future study, too, being AUTOMA designed to include them.

For each test, raw sensors signals have been initially processed using the R software off-line to identify the time interval in which the actual movement, and thus the force peak of interest, occurs. The data cleaning process consists of excluding force values below the threshold of 100 g (a threshold selected to exclude any accidental contact with the load cell), and then focusing on the angle signal *vs* time to select the interval in which test trend is similar to isokinetic trends as much as possible. Angle vs. time curves were firstly smoothed to estimate their first derivative. After that, we deemed the movements start when the angle first derivative respect to time falls over a selected threshold value of +25/-25 °/ms for MMT10 and MMT9, respectively. Finally, a linear regression model with time as the regressor was then elaborated in order to evaluate the angle *vs* time curve linearity, a benchmark meaning that the movement occurred uniformly and the test was isokinetic: when the R2 was greater than, or equal to, 0.8 the acquisition was considered adequately filtered, otherwise the acquisition was discarded (Fig. 4).

Results

In this paper, we discuss the development of AUTO-

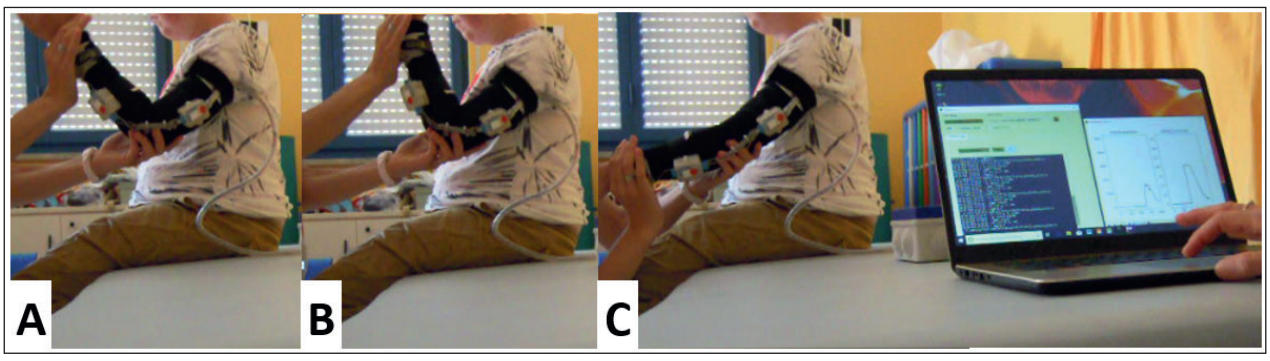

Figure 3. Isokinetic tests. Panels A to C show three different steps of the test with AUTOMA and the simultaneous data collection.

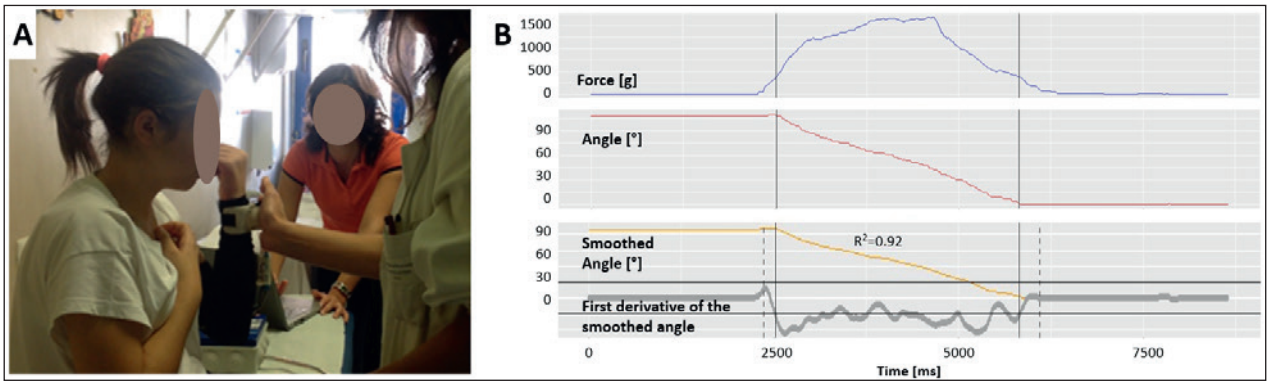

Figure 4. Gathering data with AUTOMA. Panel A. Using AUTOMA to perform MMT10. Panel B. Example of the acquisitions, showing the raw measured Force (g), raw angular displacement (degrees - °) and, in the bottom panel, the smoothed angle curve after filtering the signal (yellow line) and the first derivative of the smoothed signal. Note. Dashed lines are in correspondence of the first and the last Force numerical value above 100 g. Solid horizontal lines represent the bounds (+25/-25 °/ms) for the smoothed Angle derivative values. Solid vertical lines represent the first and the last value where the Angle derivative crosses the thresholds.

MA, a wearable device to assess the impairment level of the upper limb in patients with neuromuscular disorders.

We selected 9 patients with NMDs, previously classified with MRC scores of arms between 2 and 4, who agreed to participate to a pilot study designed to assess the capabilities of AUTOMA. We selected two specific tasks, namely the flexion and extension of the elbow (MMT9 and MMT10), to assess the muscular performance of the subjects, previously scored using PUL test. Following the criteria set by the experimental protocol, we had to discard part of the collected data (14% for MMT9 and 27% for MMT10), being not sufficiently linear, thus remodeling the structure of the dataset. Moreover, concerning MMT10, two subjects were not able to perform the MMT10 task due to their conditions and, therefore, were excluded from the statistical analysis. The final dataset is reported in Table I, where we also outline the average score assigned by the operators upon the items F to L (regarding elbow movements) of the PUL tests carried out before using AUTOMA. It is worth noting that the PUL score was not assigned to the 2 patients with myopathy since such a test is not standardized for this disorder.

Once the peak-force and mean angular velocity values were collected, they were compared across different levels of disease severity. Normality and homoscedasticity assumptions for both force and mean angular velocity were verified using Shapiro and Levene tests, respectively, separately for each disease severity and item (Tabs. II-III). Homoscedasticity assumption was accepted in all the cases at 5% significance level, but the Normality assumption was rejected in some disease severity groups for the mean angular velocity at 5% significance level. Thus, in order to perform comparisons across disease levels concerning the force, we used the ANOVA analysis that rejected the null hypothesis of no difference between different disease levels with an F value of 41.9 on 2 and 70 degrees of freedom (p-value 1.09e-12) and 61.59 on 1

Table I. Number of patients available for each disease severity level, ranging from 2 to 4 in the MRC scale and average PUL score for the upper limb tasks.

MMT item	MRC score			Number of patients examined
	2	3	4	
MMT10	0	4	3	7
MMT9	1	5	3	9
Average PUL score	17/34	32/34	34/34	-

Note. The average PUL score is not given for the patients with myopathy since the PUL test is not standardized test for such a disorder.

Table II. Shapiro-Wilk normality test p-values.

MMT item	Index	MRC scale		
		2	3	4
MMT9	Force	0.583	0.400	0.241
	Angular velocity	0.0376	0.00572	0.446
MMT10	Force	-	0.316	0.184
	Angular velocity	-	0.00215	0.362

Table III. Levene homoskedasticity test p-values.

Index	MMT9	MMT10
Force	0.583	0.400
Angular velocity	0.0376	0.00572

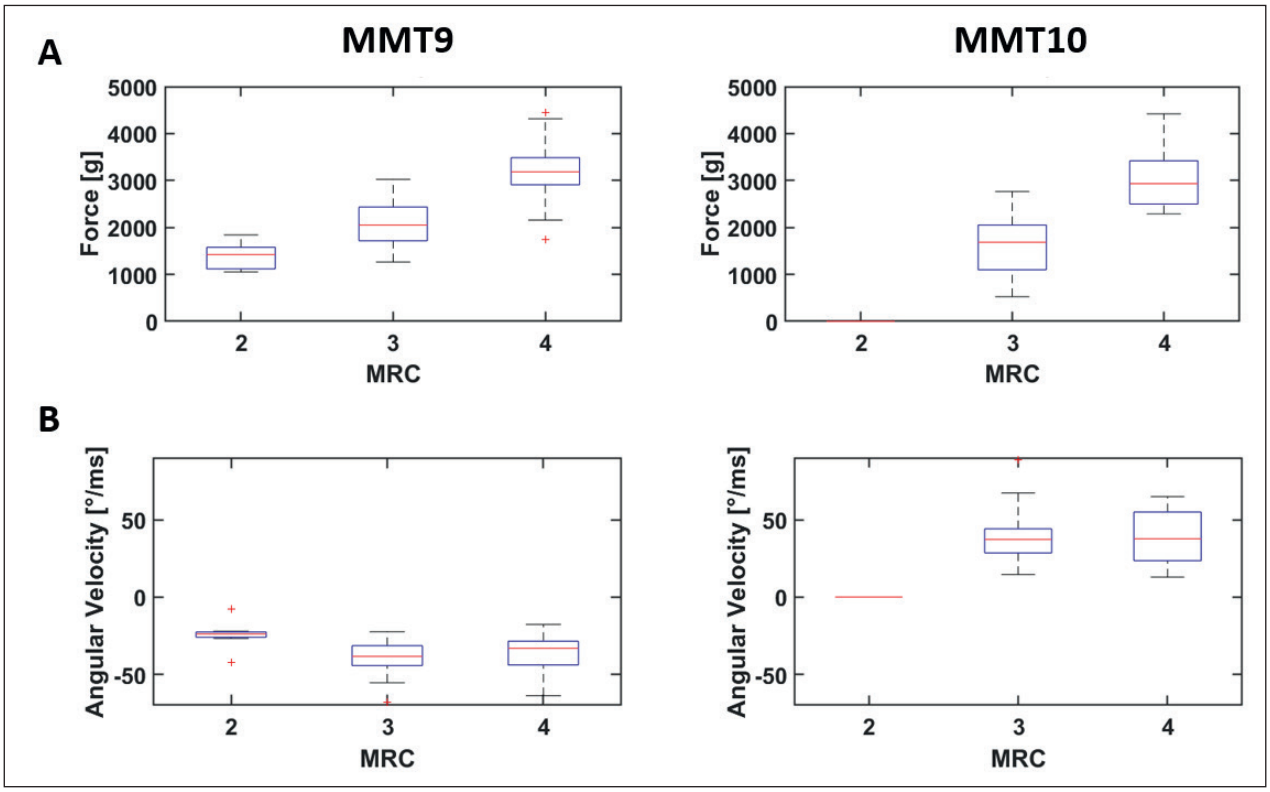

Figure 5. Whisker plots for the Force (Panel A) and the Mean Angular Velocity (Panel B) for each item in relation to the MRC.

Table IV. Results table of Tukey's method of honestly significant differences adjusted with the Bonferroni method for the force index in MMT9.

Linear hypothesis	Estimate	Std. error	t-value	Pr(>|t|)
MRC 2 – MRC 4 = 0	-1816.2	219.5	-8.276	1.70e-11
MRC 3 – MRC 4 = 0	-1137.8	150.7	-7.551	3.67e-10
MRC 3 – MRC 2 = 0	678.5	193.7	3.503	2.42e-03

and 49 degrees of freedom (p-value 3.27e-10) for MMT9 and MMT10, respectively. Conversely, concerning the non-parametric Kruskal-Wallis rank sum test for the angular velocities, we accepted the null hypothesis of no difference (significance at 5%) between disease levels with a chi-squared value of 0.019, with 1 degree of freedom (p-value 0.89) for MMT10, and rejected it with a chi-squared value of 14.645 with 2 degrees of freedom (p-value 6.61e-04) for MMT9.

Since the MMT9 presents three distinct disease severity levels and both the ANOVA and the Kruskal-Wallis rank sum test highlighted significant (at 5% significance level) differences between groups, post-hoc tests were carried out using the Tukey's method with the Bonferroni correction and the Mann-Whitney test, respectively (Tabs. IV-V). All the post-hoc tests rejected the hypothesis (significance at 5%) of equality of mean/location shift of each disease severity group, except for the comparison between groups 3 and 4 for the mean angular velocity (see Figure 5).

Table V. Results table of Mann-Whitney test for angular velocity in MMT 9.

Hypothesis tested (True location shift is not equal to 0)	W	p-value
MRC 2 *vs* MRC 3	383	2.5e-05
MRC 2 *vs* MRC 4	118	2.5e-02
MRC 3 *vs* MRC 4	312	0.19

The ANOVA/Kruskal-Wallis and post-hoc tests results, along with the plots in Figure 5, show a significant

stratification of the force levels reached by the patients with different disease severity, but not a significant difference between the angular velocities related to the movement.

Discussion

AUTOMA is a device that belongs to the family of non-invasive platforms for collecting biophysical parameters. To date, a number of studies have been published demonstrating the capability of sensing systems of providing reliable datasets about signals like tongue muscle activity [13], blood pressure [14], presence of glucose in blood [15], heart rate [16], or sweat monitoring [17]. Novel hardware designs, along with the advent of artificial intelligence and cloud computing, have brought new opportunities for clinicians and operators to quantitatively diagnose and monitor diseases, giving new quantitative data cleaned from any subjective evaluation of biophysical parameters [18]. From a rehabilitation standpoint, such new approaches can lead to a paradigm change. In fact, by integrating these advanced and, often interactive, technologies, it is possible to create a renewed patient-specific awareness on the physiological conditions and, if applicable, to easy teach specific behavioral changes with low costs and intrusion [19].

Recently, Molina-Molina et al. published a work about a wearable system to perform surface electromyography to assess muscle activity. Their platform includes surface electrodes and a mobile computing to perform a cloud data analysis. Similar to AUTOMA, the authors carried out the experimental campaign by performing a set of isokinetic tests, thus minimizing the inertial artifacts. In contrast to AUTOMA that requires an elastic sleeve without a direct contact with the skin, their system requires a specific preparation of the muscle surface (e.g., shaved skin, cleaning with alcohol) that can affect the collection and reliability of the measurements. In addition, while AUTOMA has been preliminarily tested against traditional approaches for monitoring DMDs, Molina-Molina et al. did not report any comparison with other datasets [20]

The preliminary statistical analysis of the data collected with AUTOMA suggests that the device is capable of efficiently performing an objective quantification of muscle strength in the upper limb muscles. In particular, the plots reported in Figure 5 display a relationship between the peak force and the MRC scores, while they are not correlated with angular velocity. Therefore, we can conclude that the peak force can be considered an index for classification, independently of the numerical value of the angular velocity that is always kept constant (i.e., isokinetic test) by expert operators.

In view of this, AUTOMA is to be considered a sensorized tool that might assist clinicians to objectively detect the strength deficit and to monitor the evolution of all muscular pathologies including those, such as myopathies, for which PUL tests are not standardized. Thanks to its portability and to the integration of different sensors, AUTOMA could be considered easy to adapt in the clinical practice and can be customized directly onto the patient to optimize its ergonomic fit.

From the performance perspective, AUTOMA will enhance an unbiased evaluation of the health status of a patient, delivering a more precise classification of the disorder stages without discrepancies given by a subjective evaluation from different operators. Using such a device, clinicians will have the possibility to design customized therapies based on quantitative data that, as demonstrated, reflect and improve the outcomes from the subjective scores usually attributed by the operators to the patients.

Conclusions

In the last decade, research studies have focused on quantitative measures that describe disease progression in the upper limbs, from early ambulant stages over transition stages to non-ambulant stages. Such approaches can be useful to trace the course of muscle weakness and to allow a better understanding of disease evolution and efficacy of interventions throughout the lifespan [21].

AUTOMA appears as a promising tool for monitoring NMDs from the early stages, since it is able to estimate, through a sensorized sleeve, variations of the muscle performance that could be difficult to discriminate manually based only on the experience of an operator. Moreover, being a simple and relatively cheap platform with low need for maintenance, AUTOMA could truly integrate the currently available bulky platforms, with the possibility to be easily transported and also used as a point-of-care solution for an in-home monitoring of NMDs.

From a technical standpoint, next steps include the addition of IMUs to better discriminate the angular displacements and to classify movement and fix the limitations observed in the present study. Such a methodology will include the implementation of wireless force/angular sensors to optimize portability and to increase the number of measured joints, together with the integration of other sensors (i.e., EMG, ECG, PZT Respiration) to monitor other key physiological parameters. Concerning the clinical side, we plan to start a new recruitment campaign with a larger number of patients in order to collect more data to stress the device and to perform a more robust statistical analysis, also including a correlation with the PUL scores.

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Ethical consideration

All tests were carried out following an explicit ethical approval (protocol 136/17, Tuscany Region Ethics Committee).

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Conflict of interest

All the authors declare no conflict of interest.

Author contributions

All Authors gave their approval.

References

1 Mendell JR, Shilling C, Leslie ND, et al. Evidence-based path to newborn screening for Duchenne muscular dystrophy. Ann Neurol 2012;71:304-313. https://doi.org/10.1002/ana.23528

2 Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77-93. https://doi.org/10.1016/S1474-4422(09)70271-6

3 Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol 2010;9:177-189. https://doi.org/10.1016/S1474-4422(09)70272-8

4 McDonald CM, Campbell C, Torricelli RE, et al. Ataluren in patients with nonsense mutation Duchenne muscular dystrophy (ACT DMD): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2017;390:1489-1498. https://doi.org/10.1016/S0140-6736(17)31611-2

5 Mayhew A, Mazzone ES, Eagle M, et al. Development of the Performance of the Upper Limb module for Duchenne muscular dystrophy. Dev Med Child Neurol 2013;55:1038-1045. https://doi.org/10.1111/dmcn.12213

6 Pangalila R, Bartels B, Bergen M, et al. Upper limb function in adults with Duchenne muscular dystrophy. J Rehabil Med 2011;43:770-7755. https://doi.org/10.2340/16501977-0841

7 Hough CL, Lieu BK, Caldwell ES. Manual muscle strength testing of critically ill patients: feasibility and interobserver agreement. Crit Care 2011;15:R43. https://doi.org/10.1186/cc10005

8 Gotthelf M, Townsend D, Durfee W. A video game based hand grip system for measuring muscle force in children. J Neuroeng Rehabil 2021;18:1-15. https://doi.org/10.1186/s12984-021-00908-1

9 Aramaki H, Katoh M, Hiiragi Y, et al. Validity and reliability of isometric muscle strength measurements of hip abduction and abduction with external hip rotation in a bent-hip position using a handheld dynamometer with a belt. J Phys Ther Sci 2016;28:2123-2127. https://doi.org/10.1589/jpts.28.2123

10 Feiring DC, Ellenbecker TS, Derscheid GL. Test-retest reliability of the Biodex isokinetic dynamometer. J Orthop Sport Phys Ther 1990;11:298-300. https://doi.org/10.2519/jospt.1990.11.7.298

11 Sun W, Zhang K, Chen S-K, et al. Software as a service: an integration perspective. International Conference on Service-Oriented Computing 2007:558-569. https://doi.org/10.1007/978-3-540-74974-5_52

12 Conte R, Tonacci A, Sansone F, et al. NeuroExam: a tool for neurological examination in neuromuscular diseases. 2019 IEEE 23rd International Symposium on Consumer Technologies (ISCT), 2019, pp. 5-10. https://doi.org/10.1109/ISCE.2019.8901045

13 Milazzo M, Panepinto A, Sabatini AM, et al. Tongue rehabilitation device for dysphagic patients. Sensors 2019;19:4657. https://doi.org/10.3390/s19214657

14 Luo H, Yang D, Barszczyk A, et al. Smartphone-based blood pressure measurement using transdermal optical imaging technology. Circ Cardiovasc Imaging 2019;12:e008857. https://doi.org/10.1161/CIRCIMAGING.119.008857

15 Tura A. Noninvasive glycaemia monitoring: background, traditional findings, and novelties in the recent clinical trials. Curr Opin Clin Nutr Metab Care 2008;11:607-612. https://doi.org/10.1097/MCO.0b013e328309ec3a

16 Rachim VP, Chung W-Y. Wearable-band type visible-near infrared optical biosensor for non-invasive blood glucose monitoring. Sensors Actuators B Chem 2019;286:173-180. https://doi.org/10.1016/j.snb.2019.01.121

17 Lee YK, Jang K-I, Ma Y, et al. Chemical sensing systems that utilize soft electronics on thin elastomeric substrates with open cellular designs. Adv Funct Mater 2017;27:1605476. https://doi.org/10.1002/adfm.201605476

18 De Fazio R, De Vittorio M, Visconti P. Innovative IoT solutions and wearable sensing systems for monitoring human biophysical parameters: a review. Electronics 2021;10:1660. https://doi.org/10.3390/electronics10141660

[19] Santos OC. Training the body: the potential of AIED to support personalized motor skills learning. Int J Artif Intell Educ 2016;26:730–55. https://doi.org/10.1007/s40593-016-0103-2

[20] Molina-Molina A, Ruiz-Malagón EJ, Carrillo-Pérez F, et al. Validation of mDurance, A Wearable surface electromyography system for muscle activity assessment. Front Physiol 2020;11:1556. https://doi.org/10.3389/fphys.2020.606287

[21] Melo FCM, de Lima KKF, Silveira APKF, et al. Physical training and upper-limb strength of people with paraplegia: a systematic review. J Sport Rehabil 2019;28:288-293. https://doi.org/10.1123/jsr.2017-0062