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RESEARCH

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A personalized clinical assessment: multi-sensor approach for understanding musculoskeletal health in the frail population

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Abstract

Background: Sarcopenia is a muscle disorder causing a progressive reduction of muscle mass and strength, but the mechanism of its manifestation is still partially unknown. The three main parameters to assess are: muscle strength, muscle volume or quality and low physical performance. There is not a definitive approach to assess the musculoskeletal condition of frail population and often the available tests to be performed in those clinical bedridden patients is reduced because of physical impairments. In this paper, we propose a novel instrumental multi-domain and non-invasive approach during a well-defined protocol of measurements for overcoming these limitations. A group of 28 bedridden elder people, subjected to surgery after hip fracture, was asked to perform voluntary isometric contractions at the 80% of their maximum voluntary contraction with the non-injured leg. The sensor employed before and/or during the exercise were: ultrasound to determine the muscle architecture (vastus lateralis); force acquisition with a load cell placed on the chair, giving an indication of the muscle strength; surface electromyography (EMG) for monitoring muscular electrical activity; time-domain (TD) near-infrared spectroscopy (NIRS) for evaluating muscle oxidative metabolism.

Results: A personalized "report card" for each subject was created. It includes: the force diagram (both instantaneous and cumulative, expected and measured); the EMG–force diagram for a comparison between EMG derived median frequency and measured force; two graphs related to the hemodynamic parameters for muscle oxidative metabolism evaluation, i.e., oxy-, deoxy-, total-hemoglobin and tissue oxygen saturation for the whole exercise period. A table with the absolute values of the previous hemodynamic parameters during the rest and the ultrasound related parameters are also included.

Conclusions: In this work, we present the union of protocols, multi-domain sensors and parameters for the evaluation of the musculoskeletal condition. The novelties are the use of sensors of different nature, i.e., force, electrical and optical, together with a new way to visualize and combine the results, by means of a concise, exhaustive and personalized medical report card for each patient. This assessment, totally non-invasive, is focused on a bedridden population, but can be extended to the monitoring of rehabilitation progresses or of the training of athletes.

Keywords: Time-domain NIRS, EMG, Median frequency, Musculoskeletal impairment, Surgery, Ultrasound, Oxidative metabolism, Sarcopenia, Rehabilitation

Background

Physical inactivity contributes to the impairment of the whole musculoskeletal system. It was demonstrated that only 5 days of sedentarism in healthy subjects cause endothelial dysfunction, arterial stiffening, vascular inflammation and changing in muscle skeletal characteristics [1]. Furthermore, physical inactivity not only leads to muscle atrophy, but also can cause damage to the peripheral nervous system that innervates skeletal muscles [2]. In addition, if considering an elder population, there are age-related factors such as frailty and sarcopenia [2, 3], which can be added to physical inactivity. Sarcopenia is a muscle disorder causing a progressive reduction of muscle mass and strength, but the mechanism and timing of its manifestation are still partially unknown [4]. These factors increase hospital stays, re-admission risks, and costs, worsening patient conditions. A personalized medicine approach has been proposed [5] to aid in assessing frailty during rehabilitation. In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP2) suggested that muscle quality and volume are parameters hard to identify, in particular in a clinical setting, also if they could be important to diagnose sarcopenia. The three main parameters for assessing sarcopenia are: low muscle strength, reduced muscle volume or quality, and low physical performance [6]. The available measurements techniques recommended for muscle strength include measurement of grip strength with a calibrated handheld dynamometer [7], which is easy to use but it is a surrogate of the condition of the different limbs; isometric torque methods or the chair stand test are also used. For measuring muscle volume, the gold standard techniques are magnetic resonance imaging (MRI) or computed tomography (CT), which are non-invasive but bulky and expensive. Always in the group of non-invasive imaging techniques, more recently, ultrasound (US) was employed, and a parameter called “ultrasound sarcopenia index” (USI) was proposed, where the ratio of the fascicle length to muscle thickness is increased in sarcopenic patients [8]. Dual-energy X-ray absorptiometry (DXA) is also used since it is fast but there is no homogeneity in the results from different devices and measurements are influenced by the hydration status of the patient. Similar problems can be found for the bioelectrical impedance analysis (BIA), which thanks to its high simplicity, portability and affordability is at the moment the most spread technique in the clinical environment [4, 6], also if the outcomes refer to a global parameter for the whole body and not for a specific muscle. For assessing physical performance, the gait speed is the most common test, being fast and affordable.

Considering that there is not a definitive approach to assess the musculoskeletal condition of frail population and that the above-mentioned tests cannot be performed in bedridden patients after surgery or in case of other physical impairments. In this study, we propose a methodology, which integrates the use of multiple sensors to provide a comprehensive evaluation of musculoskeletal health during a well-defined protocol of measurements [9]. The multi-sensor approach is based on the combination of: (1) US: used to determine muscle architecture (specifically the vastus lateralis). This allows for the assessment of muscle volume and quality; (2) force acquisition with load cell: measures muscle strength by capturing the force exerted during voluntary isometric contractions at 80% of the maximum voluntary contraction (MVC) using the non-injured leg. The MVC is a standard measure of muscle strength defined as the highest voluntary force that can be achieved by the participant; (3) surface electromyography (EMG): monitors muscular electrical activity, providing insights into muscle activation and neuromuscular function; (4) time-domain near-infrared spectroscopy (TD NIRS): evaluates muscle oxidative metabolism by measuring hemodynamic parameters, such as oxy-hemoglobin, deoxy-hemoglobin, total hemoglobin, and tissue oxygen saturation. The use of sensors of different natures (force, electrical, optical) and the integration of their data represent a significant advancement in the assessment of musculoskeletal conditions in frail populations.

The neuromuscular system resulted to be the main contributor to sarcopenia pathogenesis. Indeed, the loss of muscle strength and muscle mass that characterize sarcopenia may be related to the degeneration of the neuromuscular junction (NMJ) function and structure [10]. In this context, the use of the EMG is crucial as it is an easy-applicable, non-invasive technique for the analysis of muscular activity [11]. EMG recordings represent a weighted integration of the electrical activities associated to muscular contraction below the electrodes [12], and EMG magnitude increases with muscle contraction strength, even if in a not linear way [13]. For the characterization of the skeletal muscle of sarcopenic patients, it is worth noting that the frequency components of EMG signals can be associated to the phenomenon of muscle fatigue. In static conditions, when a given level of effort/exerted force is sustained, a decrease of the median frequency (MF) measured in consecutive time windows is a typical biomarker indicating muscle fatigue [14]. Often, the decrease of MF is also associated to an increase of the magnitude of time-domain measures such as the signal root mean square (RMS) [15].

NIRS is a non-invasive optical technique employing light in the red and near-infrared region (400–900 nm), able to penetrate up to few centimeters (2–3 cm under the skin) in the limbs reaching muscular tissue [16]. The parameters that can be extrapolated during the acquisitions are the oxygenated- (O_2Hb), deoxygenated- (HHb) and total- (tHb) hemoglobin concentrations and the tissue oxygen saturation ($SO_2 = O_2Hb$ /tHb). NIRS allows to measure mainly the musculoskeletal oxidative metabolism during exercises through the measurement of skeletal muscle fractional O_2 extraction, typically represented by a concomitant increase in HHb and decrease in O_2Hb [17]. It was demonstrated that in elderly population the NIRS-derived indices of microvascular function are reduced compared with younger one [18]. We believe that these parameters are important to be acquired not only to have a comprehensive overview of the physical performance during the exercise, the loss of muscle oxidative capacity is associated with physical inactivity indeed, but also because both ageing and inactivity cause a chronic reactive oxygen species (ROS) overproduction in skeletal muscle leading to atrophy [9]. NIRS was successfully used to assess longitudinal changes due to aging, response to training or the occurrence of disease [19]. In this work, the time-domain (TD) modality for NIRS acquisitions was employed, with respect to the more spread continuous-wave (CW) one allowed for the calculation of absolute values for the hemodynamics parameters (not only relative variations with respect to a baseline) without the need of performing vascular occlusion test (VOT) [20] and allowed for a better depth discrimination, avoiding the confounding effect of the more superficial skin and fat layer [21, 22].

In this work, we test the proposed approach on a group of 28 bedridden elder people, subjected to surgery after hip fracture, performing voluntary isometric contractions at the 80% of their MVC with the non-injured leg. Before the test a US exam was performed to determine the muscle architecture (vastus lateralis, VL). The exerted force was measured with a load cell placed on the chair, on which the patient sat, giving an indication of the muscle strength. During the measurements, EMG and TD NIRS sensors were placed on the VL.

In Sect. "Methods", an overview of the involved population, the protocol followed and of the overall sensors employed will be given. In Sect. "Results", we will propose a quick and informative way to look at the data obtained. The aim of the graphs proposed is to create a personalized medical report card, which can give an overview of the actual condition of the patient's musculoskeletal system. In Sect. "Discussion", the advantages and limitations of the employment of the above-mentioned protocols and sensors will be discussed from both technical and clinical point of view. Furthermore, the possibility of using the medical report cards also in the rehabilitation field will be explored. The idea of this paper is then to determine a multi-modal approach for musculoskeletal health assessment integrated with an easy and novel way to summarize the outcome parameters in personalized patients' card.

Results

In this paragraph, the parameters acquired and the elaborations made in the multi-domain assessment are shown. The parameters we show as averages are PA and ATT, to provide the main architectural characteristics of the investigated muscle. For the VL, the average PA was $7.54 \pm 4.18°$ and the ATT was 11.08 ± 5.65 mm. All other parameters were considered individual and unique to each subject evaluated. After presenting all the assessments separately (force and contractions; EMG and Force; TD NIRS), we offer a new combined view in order to provide a comprehensive perspective to the multi-domain approach and an aggregated summary of the outputs of these acquisitions to give to the physician a rapid and effective way to read and interpret them all at once. In order to give a better overview about the studied population, we report, in Table 1, the main characteristics of the 28 subjects: age, gender, MVC, number of the maximum contraction performed, ATT and PA.

Force and contractions

In the graph in Fig. 1, all the extrapolated parameters from the load cell for subject #1 are shown in the different contractions performed. On the right axis, with the black dots, the mean nominal force (Goal) is shown. It corresponds with the 80% of the MVC, which subjects were requested to exert. The measured force in each contraction is represented with the open dots. For the first 6–7 contractions, the subject performed the exercise at a higher force with respect to the goal. During the 8–14th contractions, it was able to maintain the desired force, but after the 15th contraction until the end, the force was lower with respect to the goal. On the left axis, the cumulative force is expressed. The goal is shown with the black diamonds and the

Table 1 Describing parameters of the 28 subjects involved

Subject [#]	Age [Year]	Gender	MVC [N]	Contraction [#]	ATT [mm]	PA [deg]
1	91	F	240	20	7.85	6
2	86	F	283	20	9.16	6
3	64	F	300	20	3.53	16
4	79	F	230	20	7.5	23
5	74	F	240	20	9.93	8
6	73	F	268	20	9.91	9
7	72	F	660	20	18	7
8	76	F	170	20	8.6	7
9	85	F	141	20	32.1	2
10	80	F	326	20	8.72	12
11	77	F	211	20	7.72	5
12	87	F	226	20	9.4	4
13	79	M	568	14	4.09	6
14	83	F	239	20	12.6	6
15	81	F	275	20	7.39	11
16	84	F	201	20	9.7	8
17	85	F	264	20	9.96	5
18	76	M	550	20	5.85	7
19	86	F	247	20	15.2	10
20	87	F	252	19	15.1	8
21	80	F	321	20	12.7	6
22	77	F	301	20	9.05	5
23	81	F	447	20	14.6	7
24	75	F	306	20	8.61	3
25	82	F	390	20	16	5
26	64	F	N/A	20	18.5	9
27	77	F	N/A	20	12.4	6
28	75	F	263	20	5.96	4

Main characteristics of the 28 subjects: age, gender, maximum voluntary contraction (MVC), number of the maximum contraction performed, adipose tissue thickness (ATT) and pennation angle (PA)

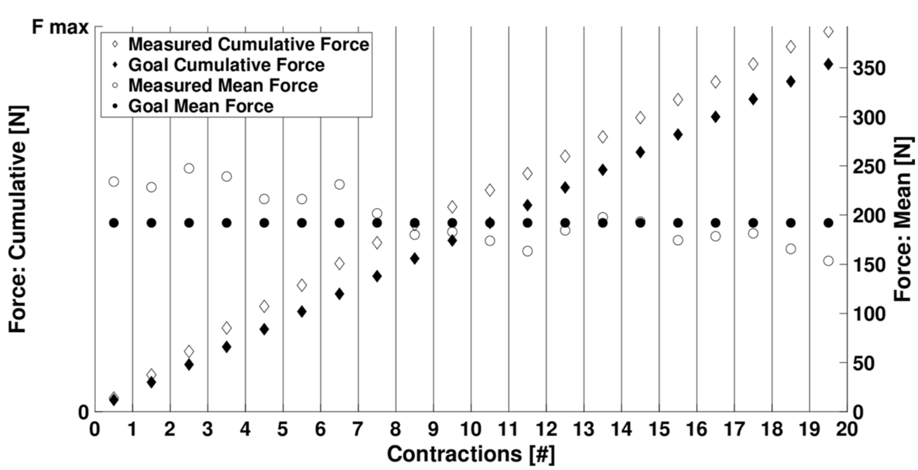

Fig. 1 Force diagram for subject #1. Left axis: cumulative force (diamonds), right axis: mean force (dots). Expected values (Goal): black, measured values: white

measured cumulative force with the white diamonds. At the end of the 20th contraction, if the exercise was performed according to the experimenters' requests, the cumulative force goal should be the maximum value reached. We can observe that the white diamonds, starting from the 3rd contraction, are always higher than the black ones, showing that, also if the mean force started to decrease, the expected total force exerted in the exercise was always higher than the expected one, showing a good performance during the exercise.

In Fig. 2, referred to Subject #2, it is possible to notice that starting from contraction 7, the mean force measured (white dots) starts to decrease and the subject was not able to maintain the goal (black dots) for the rest of the exercise. Consequentially, the cumulative measured force (white diamonds) is lower than the expected one (black diamonds) starting from the 10th contractions.

EMG and force

In Fig. 3, we report on the right axis the main metrics from the EMG signal analysis, i.e., the value of the MF for each contraction (stars), obtained as the mean of 5 epochs (2 s per epoch). To offer a practical and effective visual guide, a solid black line has also been drawn, corresponding to the initial value of the MF, and a dashed black line representing a 10% decrease in the MF with respect to the value calculated in the first contraction. We can observe that from the contractions 3–4, the MF starts to decrease, maintaining its value lower for the rest of the task, indicating a condition of muscular fatigue. On the same graph, for further clarity, the mean exerted force is also shown, on the left axis (black dots). In this way, it is easier to correlate the decrease in force with the onset of the muscular fatigue (starting at about contraction 7).

In subject #2, as shown in Fig. 4, the MF time course is less clear, alternately decreasing and increasing during the sequence of contractions. This trend is not that typical of muscle fatigue, and it is coupled with a decrease in the force exerted (i.e., the patients could not be fully compliant with the requested task).

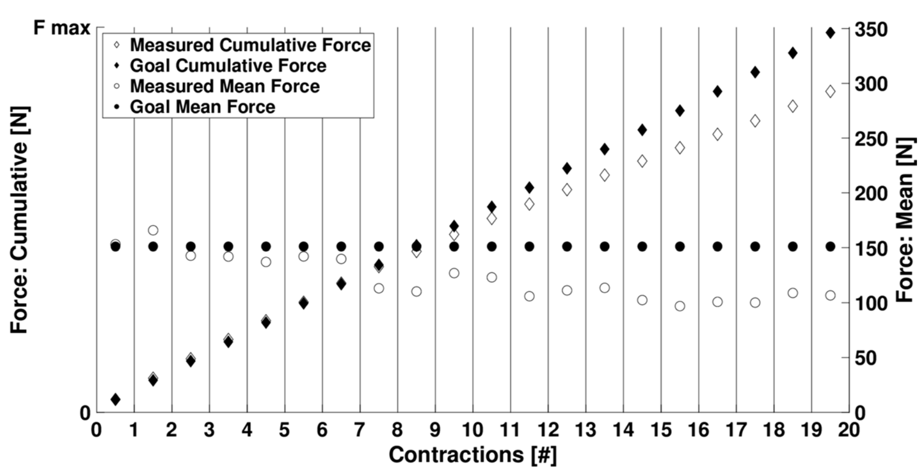

Fig. 2 Force diagram for subject #2. Left axis: cumulative force (diamonds), right axis: mean force (dots). Expected values (Goal): black, measured values: white

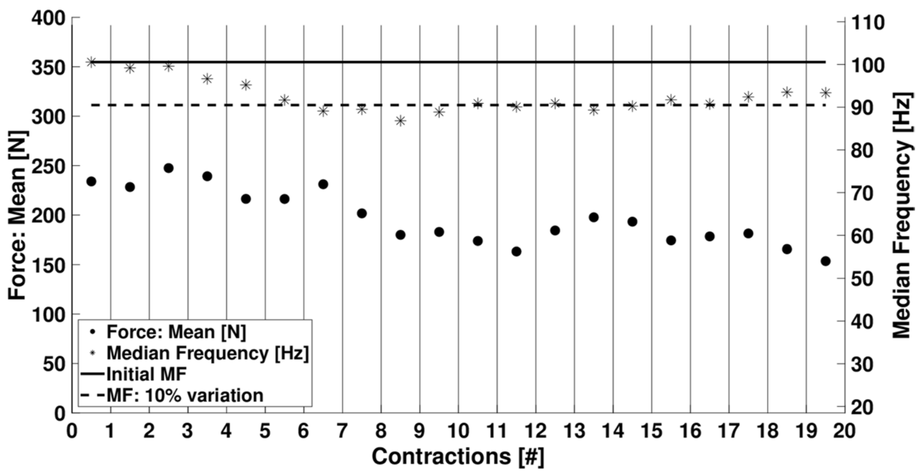

Fig. 3 EMG–force diagram for subject #1. Left axis: mean measured force (black dots), right axis: median frequency (MF, black star). Black solid line: Initial MF; black dashed line: reduction of the 10% for the MF

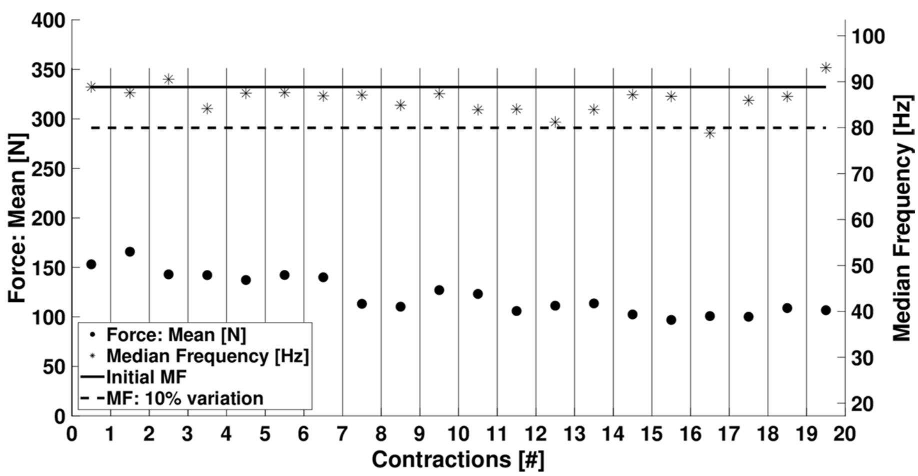

Fig. 4 EMG–force diagram for subject #2. Left axis: mean measured force (black dots), right axis: median frequency (MF, black star). Black solid line: initial MF; black dashed line: reduction of the 10% for the MF

TD NIRS

The outcome of the TD NIRS acquisitions are the time courses for the concentrations of O_2Hb, HHb, tHb and SO_2, respectively, shown in red, blue, black and green in Fig. 5. These parameters are represented in panel (a) as a normalization with respect to the first second of the exercise. In this way, it is easier to observe the typical behavior of the muscular oxidative metabolism, which is an increasing of the HHb and a contextual decreasing in O_2Hb during the exercise. Consequently, tHb should be constant during the exercise, while the SO_2 (see panel b) decreases as the effect of the muscular metabolism. Dashed vertical lines indicates a 15-s period, related to contraction–relaxation phase. In Fig. 6, the same graphs are presented for subject #2. These patterns are not typical of the oxidative metabolism. In addition, if it is possible to observe changes in the whole exercise at the level of the single contraction, there

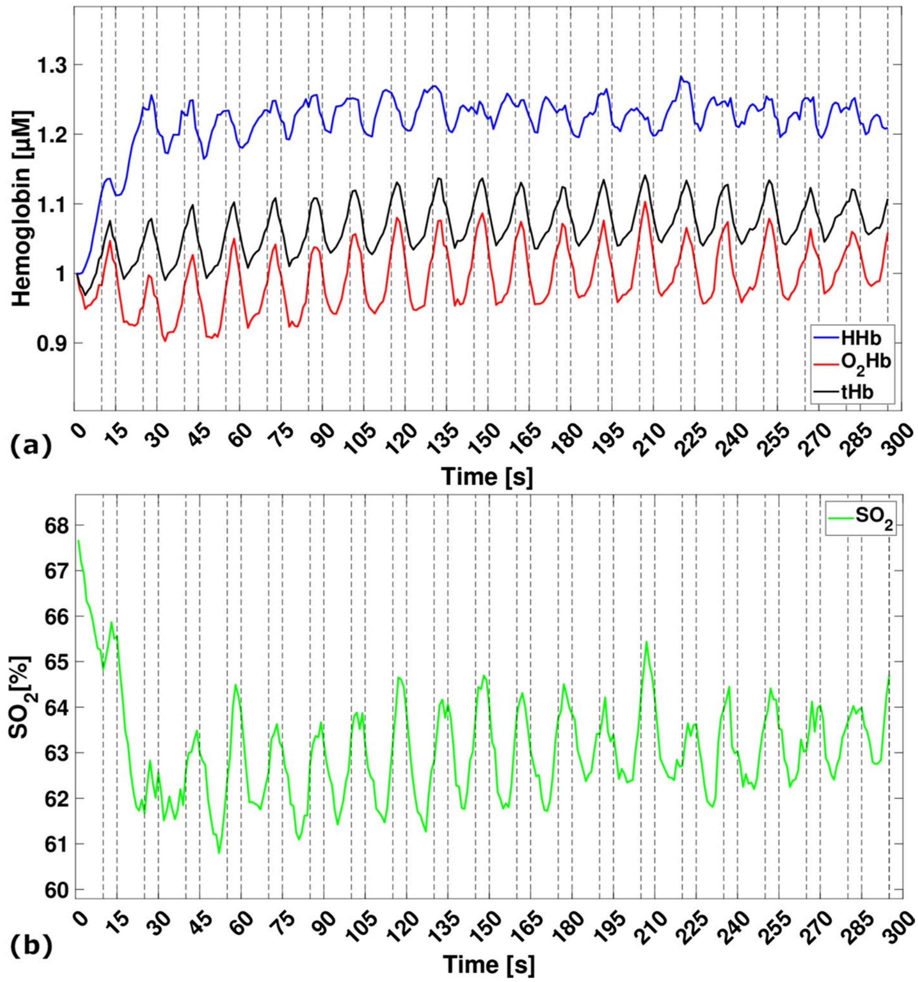

Fig. 5 TD NIRS time courses for subject #1 during the exercise. **a** Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. Results are normalized with respect to the first second of the exercise. **b** Tissue oxygen saturation (SO_2, green)

is no evidence of the global trend, which should be an increase (decrease) in HHb (O_2Hb).

In the same way we did for the FORCE and EMG signals, we calculated the mean of the hemodynamic parameters in each contraction. We normalized them with respect to their baseline values and plotted against the contraction number, as shown in Fig. 7 for subject #1. A dashed horizontal line was added to better underline differences with respect to the baseline value.

Medical report card

For a better interpretation of the previous outcomes, we propose to organize them on a unique sheet record, personalized for each patient. In Fig. 8, the “report card” for subject #1. On the top is possible to insert information about the patient ID (here Subject: 1), the date of birth and some notes (here, as example, “PRE Rehabilitation”). The four graphs inserted are, respectively, Figs. 1, 3, 7a and b. In Fig. 9, the “report card” for subject #2 is presented as a second example. In addition, all the parameters, calculated during the

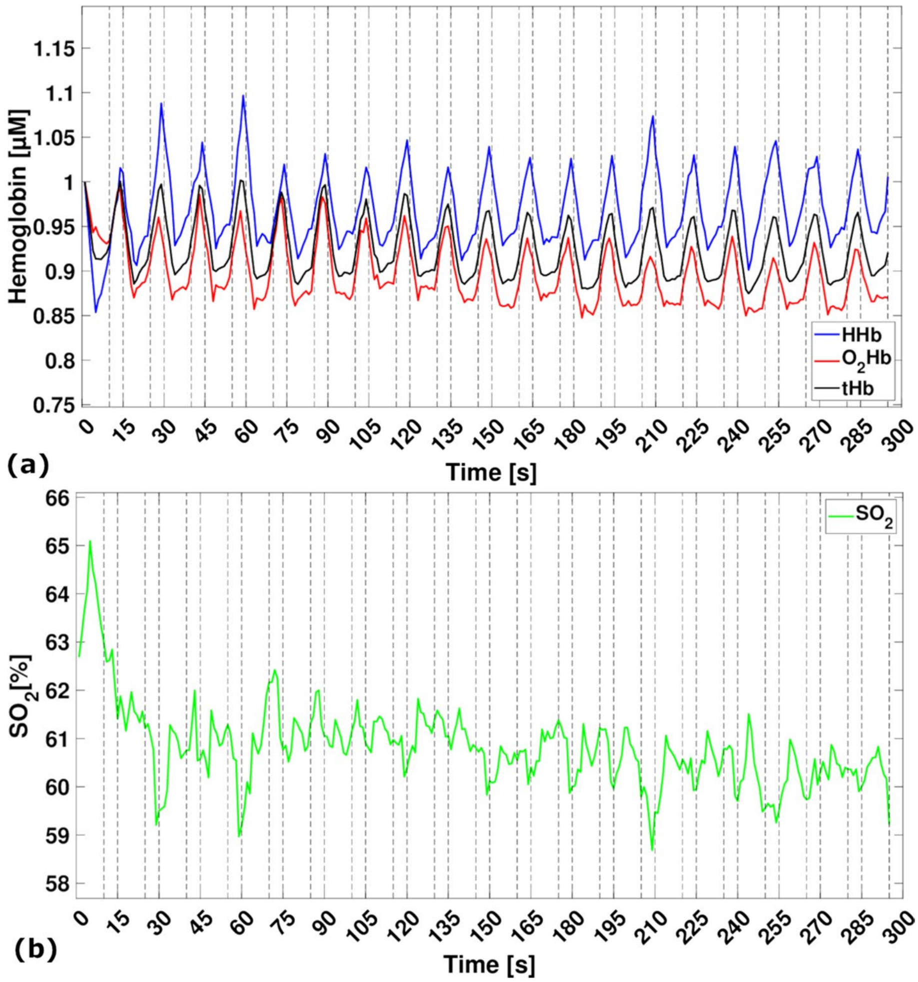

Fig. 6 TD NIRS time courses for subject 2 during the exercise. **a** Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. Results are normalized with respect to the first second of the exercise. **b** Tissue oxygen saturation (SO_2, green)

initial baseline of the acquisition can be inserted in a dedicated table, placed on the back of the personal "report card", as shown in Table 2, together with US images of the vastus lateralis.

Discussion

In this paper, we propose an ensemble of protocol, sensors, data analysis and methodology to represent results for a better understanding and representation of the musculoskeletal status in the specific case of bedridden patients. In the following paragraph, we will discuss the main results achieved and the different aspects related with this topic.

Protocol

The choice of an exercise protocol to test the physical performance of a bedridden population is not easy, particularly in cases of recent fractures and/or musculoskeletal impairments. This particular demographic is vulnerable, not just in terms of physical condition, but also from a psychological perspective. Encouraging bedridden elderly

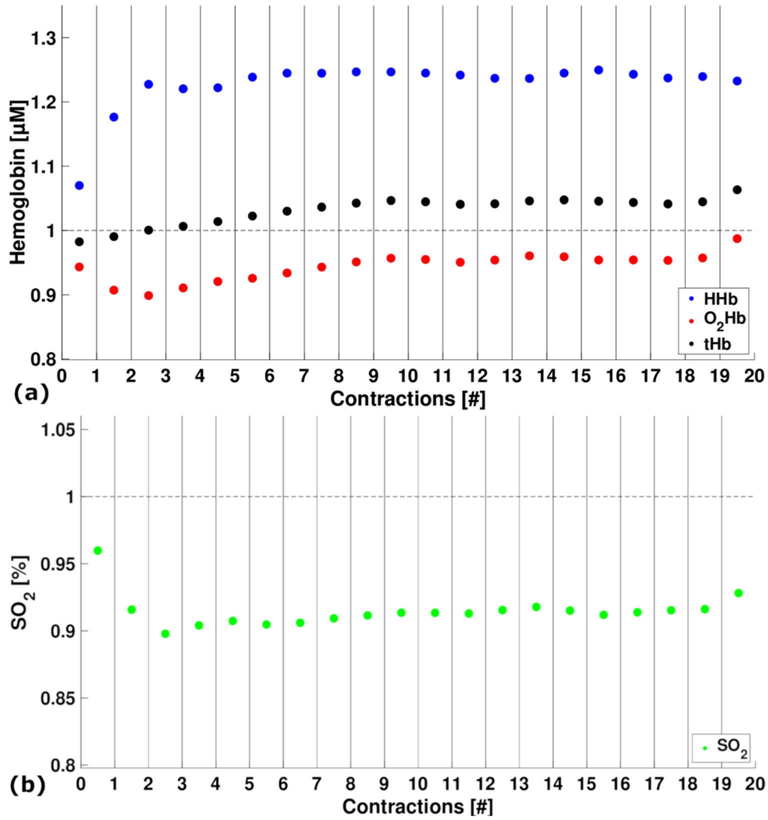

Fig. 7 TD NIRS mean values inside each contraction for subject #1. **a** Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. **b** Tissue oxygen saturation (SO_2, green). Results are normalized with respect to the initial baseline (dashed horizontal line)

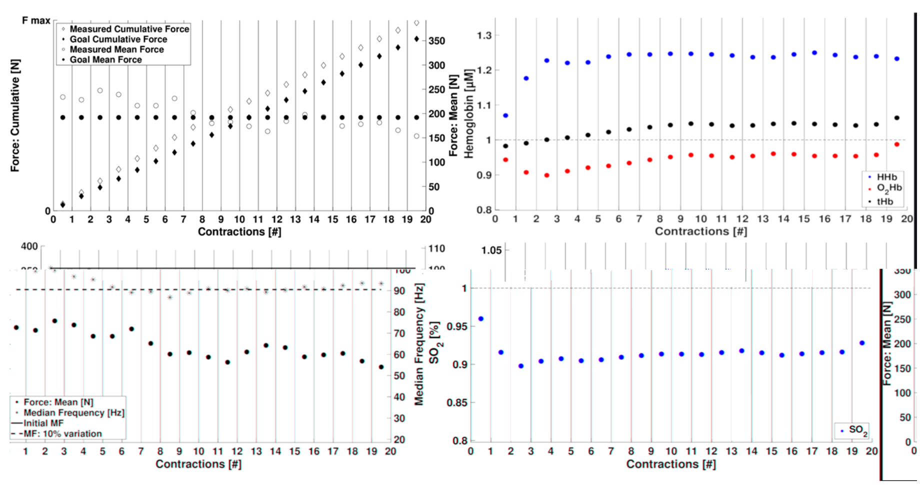

Fig. 8 Example of medical report card for subject #1. It is a combination of the previous Figs. 1, 3, 7a and b. Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. Tissue oxygen saturation (SO_2, green). Results are normalized with respect to the initial baseline (dashed horizontal line)

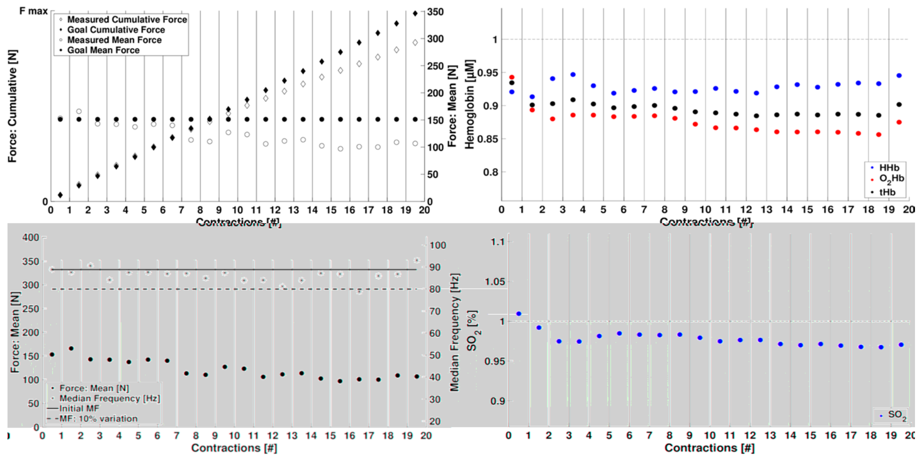

Fig. 9 Example of medical report card for subject #2. Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. Tissue oxygen saturation (SO_2, green). Results are normalized with respect to the initial baseline (dashed horizontal line)

Table 2 Table of parameters that can be added to the report card acquired during an initial baseline. Example related to subject #1

Parameter	Value	Unit
TD NIRS		
Average O_2Hb	33.8	[μM]
Average HHb	15.2	[μM]
Average tHb	49.0	[μM]
Average SO_2	69.0	[%]
US		
ATT	9.93	[mm]
PA	8	[deg]

Example of parameter acquired during the baseline period before the exercise that can be added in the back of the personal "report card" for each subject. TD NIRS: time domain near-infrared spectroscopy, oxygenated- (O_2Hb), deoxygenated- (HHb) and total- (tHb) hemoglobin concentrations and the tissue oxygen saturation ($SO_2 = O_2Hb$ /tHb), US: ultrasound, ATT: adipose tissue thickness, PA: pennation angle

patients to engage in exercise can often be challenging due to their apprehension, making it difficult to gauge the appropriate exercise intensity, as they may perceive it as more demanding than it actually is. Therefore, to enhance the effectiveness of rehabilitation efforts, it is crucial to prioritize the unaffected leg initially, striving to maintain or enhance its strength and mobility while simultaneously addressing the injured area. This approach can lead to an overall improvement in the individual's musculoskeletal health, thereby supporting their recovery and overall quality of life [33]. We choose to personalize the maximal force to exert based on literature, where the 80% of the MVC is indicated as a typical threshold to hold during training. Recently, it was demonstrated that it is possible to identify the external load as the highest SO_2 or to a specific percentage of a maximal SO_2 measured for cerebral oxygenation during graded exercise to exhaustion. This external load (i.e., workload) can then, in turn, be used to set the initial exercise intensity in an exercise session [34]. On the direction of having more personalized interventions, it could be possible to include this brain-derived indicator of internal load, employing the same TD NIRS device presented in this paper for acquiring the cerebral SO_2, as already demonstrated in previous literature [35, 36].

Analyzing more in depth the outcome of our study, we can affirm that the exercise performed was well tolerated from our population. Only two subjects were not able to perform all the 20 contractions indicating that the combination of the movement request together with the percentage of the MVC chosen is a good combination to be asked to bedridden patients. In particular, patients confirmed the crucial importance of the real-time visual feedback showing a line to follow (i.e., mimicking the contraction) and the actual force exerted by the limb.

The choice of testing the non-surgical leg allows to extend this protocol also to all the population, which underwent lower/upper limb surgery. In fact, the decision to give precedence to the uninjured leg was primarily influenced by the nature of the injury, which in this case is a hip fracture, preventing immediate application of rigorous rehabilitation tests to the injured leg post-surgery. Additionally, the uninjured leg serves as a useful benchmark for evaluating the injured leg's progress. Other research studies have shed light on the significance of rehabilitation following a hip fracture, the consequences of immobilization on muscle strength and mass, and the overall importance of addressing musculoskeletal health throughout the rehabilitation process [23, 37].

Furthermore, the choice to acquire patients' data 3 days after the surgery was justified by the fact that it was already shown that in a group of young men, muscle atrophy was already present after 2 days of leg immobilizations and in particular in the quadriceps muscle [38]. In these studies, it has been convincingly demonstrated that the process of muscle atrophy sets in remarkably early, becoming discernible within just 2 days of leg immobilization. This rapid onset of muscle wasting is particularly pronounced in the quadriceps muscle, which plays a pivotal role in lower limb function. In this direction it is suggested to have a "zero" time-point as close as possible to the immobilization event, in particular, if other patient's evaluation is planned in following time points to monitor a rehabilitation program (see par. "Other applications of the medical report card").

The implications of this research are of paramount importance for post-surgical rehabilitation strategies. It stresses the urgency of commencing assessments and intervention protocols as soon as practically possible after hip fracture surgery. Tailoring the rehabilitation plan based on the type of surgery, closely monitoring the post-operative course, addressing complications proactively, and optimizing hospitalization time are all vital components of ensuring the best possible recovery and musculoskeletal health for patients undergoing rehabilitation [39]. By doing so, healthcare providers can proactively address the potential consequences of muscle atrophy, which can include not only loss of muscle mass, but also decreased muscle strength and function. This early intervention approach is instrumental in mitigating the extent of muscle deterioration and facilitating a more effective rehabilitation process.

Moreover, recognizing the significance of these findings, it becomes evident that the timeframe for post-surgery assessments should be carefully considered, bearing in mind the vulnerability of patients, especially in the context of hip fractures. Initiating rehabilitation and muscle preservation efforts early on can contribute to enhanced overall musculoskeletal health, expedited recovery, and an improved quality of life for patients undergoing rehabilitation after hip fracture surgery.

Force measurements

The force measures give a quantitative assessment of the muscle strength. In the graphs proposed, we show the mean value of the force exerted in each contraction, in order to have a better comprehension of how the exercise was executed. We also introduced the cumulative force as a measure of the total force performed during and at the end of the whole exercise. In fact, it was demonstrated that in a group of sarcopenic subjects a significantly lower total work was performed during exercise compared to normal lean counterparts [40]. In Fig. 1, it is shown how the cumulative force measured is higher with respect to the expected one at the end of the exercise, even if during some contractions the mean measured force becomes lower than the expected one.

US measurements

The assessment of PA and ATT within the vastus lateralis muscle before and after a rehabilitation program in individuals recovering from hip fractures constitutes a pivotal component of clinical research and practice. This evaluation yields critical insights into muscle architecture and composition, offering valuable data for gauging muscle strength, function, and quality. The pennation angle serves as a proxy for muscle strength, with changes indicating improvements or declines in functional capacity. Concurrently, monitoring adipose tissue infiltration within the muscle elucidates the muscle's quality and potential hindrances to mobility. Establishing baseline measurements before commencing rehabilitation is paramount, as it enables the precise tracking of changes throughout the rehabilitation process. The PA and the muscle volume are reduced in the sarcopenic population [41]. By evaluating these parameters, healthcare professionals can tailor rehabilitation strategies, gauge the effectiveness of interventions, and contribute to enhanced patient outcomes. Moreover, research in this realm advances our comprehension of hip fracture consequences and rehabilitation practices, facilitating the development of improved clinical protocols.

EMG measurements

Time to fatigue is inversely related to the intensity of the effort [42]. The decrease of MF of EMG is a biomarker of muscular fatigue in isometric contractions. In our experiment, the decrease of MF could be used as a biomarker for fatigue only if the force was almost invariant and, therefore, the task requirements (isotonic contraction) are hold within the trial. When such condition is met, the decrease in MF indicates the presence of fatigue [43]. Otherwise, when the force was not invariant, MF could not be used as a reliable indicator of muscular fatigue because the request to hold a static condition with a stationary effort was not fulfilled [14]. In this case, the force parameter can be a measure of fatigue [44], indicating that the patient cannot sustain the effort requested in the experiment and is not fully compliant with the task. In Fig. 3, the decrease of MF can be considered as a biomarker for muscular fatigue since the decrease of MF can be clearly detected while the force is almost stationary. In Fig. 4, instead, the time course of MF cannot be clearly interpreted since it is associated to a decrease of the exerted force. Therefore, MF cannot be used as a biomarker of fatigue and the comparison with force measure can be crucial to identify the presence of fatigue.

TD NIRS measurements

NIRS technique allows for the determination of biomarker for the muscular oxidative metabolism [45]. Most of the protocols present in literature for the evaluation of bedridden population, needs to perform a VOT [18], since with the traditional CW approach, no quantitative information can be retrieved, but just relative variations with respect to a reference period. From a technological point of view, the quantification of the muscle's capacity to extract oxygen from blood, together with a good depth selectively (i.e., to be able to distinguish between systemic microcirculation and muscle vasculature) can be achieved with TD approach [20] allowing to execute a protocol where exercises are presented. In sarcopenic patients the aerobic metabolism during low-intensity steady-state exercise is impaired [40]. This could be highlighted by the graphs in Fig. 6, where the common oxidative metabolism pattern is not followed, i.e., an increase in HHb and decrease in O_2Hb, as in Fig. 5. In this sense, it could be useful to have in the report card the whole time courses for the hemodynamic parameters. SO_2 is the most common parameter evaluated during NIRS exercises, since it is the outcome of the commercial CW devices. It should decrease in the initial part of the exercise for then reaching a plateau towards the end, when there is a switch between oxidative (type I) and non-oxidative (type II) muscular fibers [46]. With TD NIRS, is possible to decouple the contribution of the O_2Hb and HHb from the whole SO_2, adding information to the execution of the exercise from a metabolic point of view. Furthermore, tHb gives an information about the total volume of hemoglobin inside the muscle and can be used to assess muscle volume not only during rest but also during exercise. The TD NIRS device employed has a good repeatability in the assessment of the musculoskeletal hemodynamic parameters [29] and the variations among the instruments are quite negligible [47] with respect to the traditional technique such as DXA and BIA.

Medical report card

In Fig. 8, we observe that the MF is decreasing during the contractions indicating that the subject is performing a fatiguing exercise. In order to understand if the fatigue is influencing the capability to exert the proper force, we can refer to the first graph of the report card, observing that the force is decreasing with the contractions. Nevertheless, the total force among the contractions is higher than the expected one. The metabolic parameters, showing the typical pattern, demonstrate that the muscle is working properly from an oxidative point of view. On the other hand, to understand if a decreasing in the exerted force is due to a muscular fatigue rather than a patient unwillingness or psychological discomfort, the EMG parameters had to be considered.

In the second example, in Fig. 9, we do not observe the typical oxidative metabolism patterns for the hemodynamics parameters. To understand the reason, we need other parameters that indicate, in an objective way, if the exercise is performed according to the requests. In this sense, the exerted force confirms that all the contractions were performed, even though, after the 7th contraction, their intensity start to decrease. The decreasing was not caused by an increase of muscular fatigue (the MF has not a decreasing trend among the contractions), indicating that probably the exercise was not performed with a sufficient care or the demands of the exercise were too high for the patients with respect to their muscular possibilities.

It is then clear that a multi-parameter and multi-sensors approach offers objective interpretations of the musculoskeletal apparatus, enhancing the comprehension of the mechanisms underlying pathologies and clinical decision-making. A key-point of multi-modal assessments is to find to right equilibrium between number of sensors (and parameters) and usability in clinical practice. Multiple sensors require longer preparation, higher costs and time for training personnel in using and interpreting the results. These three techniques were already employed in the clinical settings [48] showing an excellent compatibility and a reasonable preparation time, but there was still a lack in the organization of the outcomes of the measurements both in terms of best parameters to compare and easiness of results presentation. These limitations can be overcome with the brief but exhaustive report presented in this paper. The protocols, the multi-sensor acquisitions and the report as well were tested on 28 patients in the PRE phase. In addition, a subgroup of 15 patients was evaluated in POST period, after rehabilitation, as discussed later. Both in PRE and POST evaluation, the outcome of the employment of the method proposed was successful.

Additional sensors and parameters

From the previous examples it is then clear how is important to give a multi-parameters overview of the exercise performances: only the combined reading of all the parameters can give a complete overview of the musculoskeletal condition. Of course, even though the parameters investigated in this work can provide a comprehensive description of the status of a patient, they are only a subset of the assessments available that can potentially be exploited in this scenario. It is in principle useful to add further sensors/parameters to the assessment. However, it is difficult to define when the advantages of a multi-domain investigation may conflict with the discomfort caused to the patients during the movements to the encumbrance of the sensors. In the vastness of the possible sensors and parameters that could be added, we would like to mention some that, in our opinion, might be relevant for further work. This is the case of another optical technique, the diffuse correlation spectroscopy (DCS) [49], which could be easily integrated in the same TD NIRS probe [27, 50] and allows for the determination of the blood flow index (BFI) [51]. NIRS data are limited by the impossibility of distinguishing between perfusion factors (O_2 delivery) and mitochondrial function (O_2 uptake), while the union of TD NIRS and DCS could help to distinguish them. Since the hemodynamic parameters evaluated with NIRS and DCS, reflect directly skeletal muscle fractional O_2 extraction and blood flow, respectively, these techniques are well suited for identifying and evaluating the oxidative metabolism in humans at rest or during exercise and could eventually be used also in the assessment of the endothelial and microvascular dysfunction [52]. If the integration of DCS in the same NIRS sensor was already demonstrated elsewhere and does not add discomfort for the patient [27, 50], from the point of view of the presentation of the result, we should add a graph for the BFI in the medical report card, making the whole page more complex to be read. Further developments of our work may include presenting the results in the form of gamification or even using the equipment with an interface to control a serious game, as in a similar setup conceived for post stroke patients [53].

Considering EMG parameters, we reported only the MF as the most used assessment measure for fatigue in clinical studies. However, the field of EMG signal processing includes several parameters that exploits analysis in the time domain and in the frequency domain. In the time domain, the RMS is an estimate of the EMG signal amplitude and is computed as the square root of the average power of the raw EMG signal over a specific time period [54]. In static conditions, the increase of the RMS amplitude may reflect the fatigue of the measured muscle [55], even though it is not the most reliable biomarker of fatigue. Another time-domain parameter is the mean absolute value (MAV) that is the average of the absolute EMG signal value. When MAV increases, muscle fatigue is found [56]. In frequency domain, muscle fatigue can be identified also when there is a decrease in mean power frequency (MPF) in time. Using MPF leads to results similar to those achieved with MF [14]. Future developments of this study could include the assessment of muscle fatigue in dynamic motor tasks. These different conditions might require to adapt the methods presented in this work for the analysis of non-stationary signals. Standard indices used for static postures, such as MAV, MF and mean power frequency, might be use also in non-stationary conditions in high-intensity tasks [57]. In dynamic tasks, fatigue can be identified also with a decrease in the conduction velocity of the muscle [58]. However, in order to perform this kind of assessment, it is necessary to use of high-density multi-channel sensors to overcome the additional technical issues deriving from the dynamic measurement [12]. Finally, increasing the number of EMG sensors can add information about muscular assessment. This can be useful to extend metabolic, force and fatigue assessment with measurements related to the coordination of many muscles in a variety of postures and gestures. A multi-sensor mapping allows to analyze motor or postural synergies, integrating kinetic and orthopedic assessment with neurologic evaluations in order to understand if the intervention modifies not only muscle force and metabolic parameters, but also motor control [59].

These advancements in sensor technology and data analysis techniques offer promising avenues for enhancing our understanding of musculoskeletal function and improving rehabilitation strategies [60], also considering the evaluation of gender-related differences [61].

Other applications of the medical report card

The medical report card presented here, together with a proper protocol and a set of multi-domain sensors, was created to give a real-time immediate picture of the musculoskeletal condition of a bedridden patient towards a personalized medicine intervention. For this population, or for not trained elder population, the benefits of regular exercise on physical and mental health counteract the risks of damage induced by oxidative stress [62]. In this context, it could be useful to monitor also how the exercise are performed before, during and after a rehabilitation program, in order to tune the therapeutic and physiotherapeutic intervention in a personalized way. This can be used, in particular at the beginning of the rehabilitation course, when the musculoskeletal changes are not macroscopic and clearly visible. We think that our report

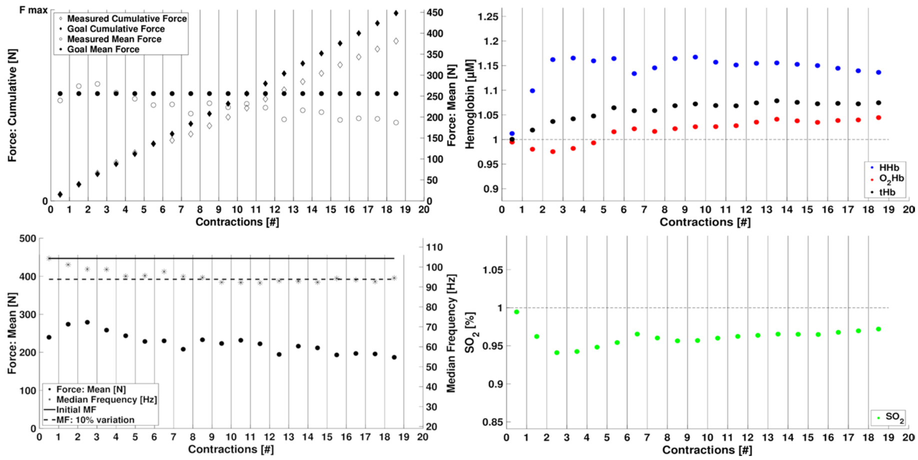

Fig. 10 Example of medical report card for subject #1, POST rehabilitation. Oxy- (O_2Hb, red), deoxy- (HHb, blue) and total- (tHb, black) hemoglobin. Tissue oxygen saturation (SO_2, green). Results are normalized with respect to the initial baseline (dashed horizontal line)

card can represent a precious tool for clinicians. A subset of the patients involved in this study underwent 15 days of rehabilitation program, as described in paragraph 5.1 and 5.2. In Fig. 10, we show the report card for subject #1 after the rehabilitation (POST). Comparing it with the clinical status before the rehabilitation (PRE, Fig. 8), we can observe that the subject is able to perform all the contractions and starting from the 5th–6th, the force starts to decrease with respect to the expected one.

Probably, this is due to the rising of the muscular fatigue, i.e., the MF starts to decrease as well. The observation regarding the goal force having a nominal value higher than that of the PRE period is indicative of the significant improvement in muscle strength achieved after the rehabilitation program. This increase in the target force level suggests that the subject's muscles have become notably stronger because of the rehabilitation efforts. Furthermore, the analysis of the hemodynamic time courses reveals intriguing insights. Specifically, the measurement of oxygen saturation (SO_2) displays a noteworthy difference when compared to the PRE period. During the rehabilitation phase, SO_2 exhibits a lower amplitude, primarily attributable to the reduced amplitude observed in oxygenated hemoglobin (O_2Hb) levels. This decrease in O_2Hb amplitude signifies that, in contrast to the PRE period, the muscular fibers are more efficient in utilizing and delivering oxygen. In essence, this observation underscores the positive physiological changes that have occurred within the subject's musculature during the rehabilitation process. The heightened goal force values signify improved muscle strength, while the altered hemodynamic patterns, with reduced O_2Hb amplitude, suggest enhanced oxygen utilization and circulation within the muscles. These findings collectively reflect the effectiveness of the rehabilitation program in not only strengthening the muscles but also optimizing their oxygen supply, both of which are pivotal factors in facilitating the subject's recovery and overall physical well-being. In general, there is an inverse relationship between SO_2 and exercise intensity in healthy individuals, both young and older. More specifically, SO_2 decreases in response to increasing exercise intensity. However, this effect appears to be more pronounced due to the aging process [63]. On the contrary, no significant differences were found for the basal hemodynamics parameters.

In addition to the rehabilitation field, there are other circumstances where it can be useful the monitoring of the musculoskeletal condition in time. Is the case of the understanding of the mechanism of aging muscles, where longitudinal studies are required or, again, when monitoring the athletes training [64]. For example, the EMG parameters can be used for the evaluation of the decrease of muscle strength in older adults. Indeed, with aging a process of remodeling of motor units can be observed in which type II muscle fibers (fast-twitch) are reinnervated by small neurons that, usually, innervate type I motor units [65]. Type II fibers generate higher maximum force level and, therefore, this reinnervation may cause the loss muscle strengths in older adults [66]. This process can degenerate in atrophy in sarcopenic patients when the denervation rate outpaces the reinnervation one and some muscles remain denervated [67]. The decrease of muscle strength results also in a decrease in exerted force and a decrease in the EMG signal amplitude.

Conclusion

In this work, we present the union of protocols, multi-domain sensors and parameters for the evaluation of the musculoskeletal condition applied to bedridden patients after hip fracture. Even if this assessment is focused on the bedridden population, it can be extended to the monitoring of the rehabilitation progresses in other diseases or to the training of athletes. The novelties is the use of sensors of different nature, i.e., force, EMG and TD NIRS, together with a new way to visualized combined retrieved parameters. At this purpose, the possibility to have a concise but exhaustive and personalized medical report card for each patient is also presented. It is then clear that a multi-parameter and multi-sensors approach offers objective interpretations of the musculoskeletal apparatus, enhancing the comprehension of the mechanisms underlying pathologies and clinical decision-making.

Methods

Subjects

All the participants signed the informed consent and took part in this study, conducted in accordance with the Declaration of Helsinki, approved by Ethical Committee of "Milano Area B" (prot. n. 14386, 16/11/2015) and coordinated by Istituto Ortopedico Gaetano Pini. Twenty-eight subjects (age: 78 ± 6.5 years old, 2 male and 26 female) were enrolled at the Rehabilitation Department for a rehabilitation program after surgery of the locomotor system for hip fracture. The exclusion criteria encompassed individuals with neoplastic conditions and significant neurological, psychiatric, cardiovascular, or pulmonary disorders. All the subjects were tested before the beginning of the rehabilitation (PRE) program and after a couple of weeks of the rehabilitation program (POST). The physical therapist administered an exercise program prescribed by specialist physicians for rehabilitation. This program aimed to address leg edema, improve quadriceps control and hip abduction strength, and normalize gait. Patients followed a daily 60-min physical therapy regimen, which could be divided into two sessions if needed. After surgery, patients began with ankle pumps to move their ankles. They also started knee extension strength training for the injured limb during the early phase. The main goal was to enhance muscle strength and control, especially in the gluteal and quadriceps muscles. Early mobilization involved activities like getting in and out of bed, sit-to-stand, sitting from a chair with arms, and walking with mobility aids. The program included weight-bearing exercises, gait training with assistive devices, lower extremity isometrics, range of motion activities, physical therapy methods, stretching, resistance exercises, balance training, proprioception activities and conditioning.

Experimental protocol

To guarantee safe and controlled experimental conditions, subjects were seated on a custom designed chair, equipped with safety belts, handlebars, and a leg holder to maintain a knee angle of 60°. The ankle was fixed onto a holder, connected to a load cell for measuring the traction force exerted. The subject had to perform voluntary isometric contractions pulling the holder with the leg. The fixation system ensured that the contraction was mainly performed with the quadriceps muscle. The experimental protocol consisted in a first assessment of the MVC, calculated as the maximum of three consecutive trials. Pain was monitored, and participants were advised to perform contractions at tolerable effort levels to avoid exacerbating discomfort. The second part of the protocol required the subject to perform a series of 20 sustained isometric contractions at the 80% of MVC, lasting 10 s each and followed by 5 s of relaxation. The contraction–relaxation sequence was dictated by an auditory stimulus (Presentation®, Neurobehavioral Systems Inc.), synchronized with the other instrument employed. In addition, also an initial baseline (60 s) and a recovery period after the exercise (300 s) were acquired. In Fig. 11a, the timeline of the experiment is shown.

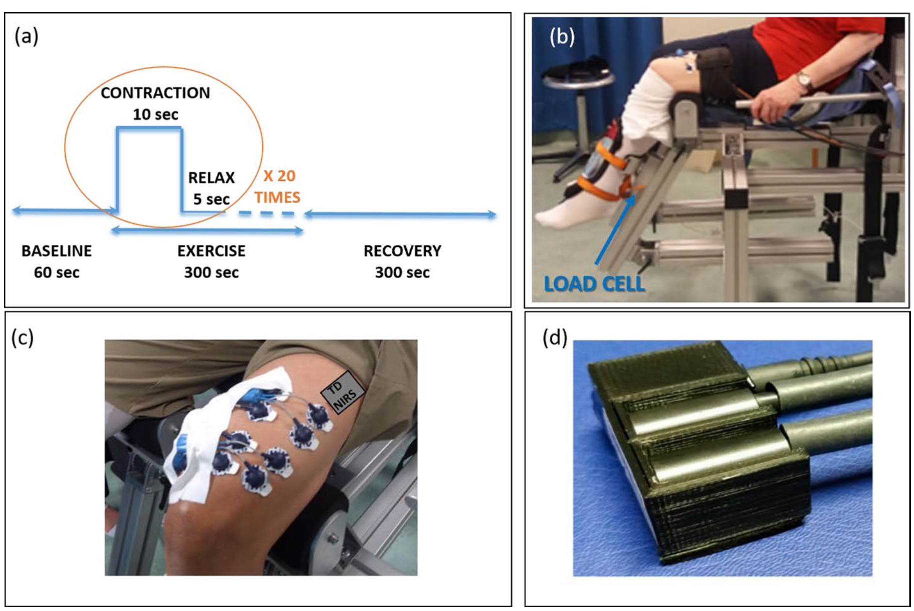

Fig. 11 Acquisition protocol and sensors detailed. Timeline of the acquisition protocol (**a**). Picture of the whole setup (**b**). Details about sensor positioning: electromyography sensors (EMG) and time domain (TD) near-infrared spectroscopy (NIRS) sensor (**c**). Zoom on the innovative optical TD NIRS sensor (**d**)

Sensors setup

In Fig. 11b, a scheme of the sensors positioning is shown. In the following section, the characteristics and the data extrapolation for each sensor/acquisition are detailed. For further details about the setup and a picture of the experimental setting, the reader can refer to reference [23]. EMG and TD NIRS devices were synchronized with a TTL signal sent by the EMG (acting as master) to the TD NIRS instrument (acting as slave). The procedure for the software synchronization will be explained in the following dedicated sections of the data analysis, and will allow to determine a common "start" and "stop" period for the signal coming from different sensors.

EMG. EMG acquisitions were performed with a 16-channel wireless commercial system (Cometa, Milan, Italy). The superficial EMG of five parts of the muscle heads of the quadriceps muscle were registered by means of five bipolar electrodes at a sampling frequency of 2 kHz. The following repere points were chosen for EMG recordings: 2 probes were on the vastus lateralis (VL) muscle (proximal and distal parts of the heads), 2 on the rectus femoris (proximal and distal parts of the heads), 1 on the vastus medialis. This multi-channel mapping was chosen to account for multiple muscle heads contracting during isometric tests, since it is not a priori possible to address all muscle torque at knee level to a single muscle head. The electrodes on the distal head of the VL muscle were put at about 2/3 distance from the anterior superior iliac spine (ASIS) to the lateral condyle of the femur, as suggested by the SENIAM guidelines and as close as possible below the TD NIRS electrode. The distal electrode on the rectus femoris was placed at about at 60% on the line from the anterior spina iliaca superior to the superior part of the patella. The vastus medialis electrode was placed at 80% on the line between the anterior spina iliaca superior and the joint space in front of the anterior border of the medial ligament. Two additional proximal electrodes were placed at the same level of the vastus medialis electrodes on the rectus femoris and vastus lateralis. Electrodes were circular (radius 8 mm) and the center to center electrode distance was 24 mm.

Force. The force sensor was placed on the chair holder and consists on a load cell. The outcome of the measure is the force, exerted by the subject's leg during the isometric contraction. A visual feedback of the actual force exerted by the limb and measured by the load cell was real-time presented to the subject during the experiment onto a screen. After three consecutive trials, the MVC is calculated as the maximum among the trials. During the second protocol, where the subject had to exert the 80% of the MVC.

US. We placed the US probe (Pro Focus Ultrasound, BK Medical, Burlington, Massachusetts, USA) perpendicular to the skin surface considering one-third distance from the anterior superior iliac spine (ASIS) to the lateral condyle of the hip. We measured one-third of the distance between these two points, and placed the ultrasound probe at that location on the thigh. We asked patients to stay in a comfortable sitting position, preferably with their thigh muscles relaxed and applied a water-based ultrasound gel to the skin over the area of the vastus lateralis. This gel improves the acoustic coupling between the skin and the ultrasound probe [24].

TD NIRS. TD NIRS measurements were performed with a home-built medical device, previously developed at the Department of Physics, Politecnico di Milano [25]. It is provided with a custom probe [26] with two channels (source–detector distances: $\rho_1 = 15$ mm and $\rho_2 = 30$ mm) for an accurate estimation of the hemodynamic parameters of the muscular tissue, avoiding their contamination by the adipose tissue [21, 22, 27–29]. The probe should be positioned at a standardized location on the thigh to ensure consistent measurements, exactly where the US exam was performed.

Data analysis

Each signal was extrapolated and treated as reported below.

EMG. The first step for signal processing was to filter raw data with a bandpass filter (10–450 Hz). Then, the EMG envelope was achieved by filtering the signal low-pass, cut-off frequency 10 Hz. The envelope was used to identify the onset and offset of each of the 20 contractions with a double threshold algorithm [24]. This procedure allowed synchronizing and comparing the electrical signal to the corresponding TD NIRS and force signal acquired with the load cell. The bandpass-filtered EMG signal was further analyzed to extract the median frequency on each contraction epoch and their time course, as biomarkers related to muscle fatigue.

Contractions. Based on the processed EMG signal, the number of contractions effectively performed by the subject were determined, as well as the exact start and stop time for each contraction. Since all the sensors during the acquisitions were synchronized by a TTL signal, these time intervals were employed as start and stop of the contraction for the FORCE and TD NIRS signal as well.

Force. The mean force inside each contraction was calculated. The cumulative force among the contractions was also computed.

US. With US measurements, the adipose tissue thickness (ATT) and the pennation angle (PA) in the site of the measurements were evaluated (proximal head, VL). The ultrasound measurements allowed us to assess muscle architecture, including parameters related to muscle thickness and cross-sectional area, which are indicative of muscle volume [30].

TD NIRS. The acquired TD NIRS reflectance curves at each wavelength were fitted with the solution of the diffusion equation for a semi-infinite homogenous medium after the convolution with the instrument response function [31]. From the absolute values of the absorption coefficient, knowing the extinction coefficients at the given wavelengths, it is possible to calculate the absolute values during the whole acquisition for O_2Hb, HHb and tHb, expressed in µM, and SO_2, expressed in %, for the VL muscular tissue [32]. The time courses were smoothed with a moving average method with 5/sample span. Furthermore, we also calculated: the basal absolute value for each hemodynamic parameters as the average of the last 10 s of the period before the exercise. During the exercise, the start and stop time for each contraction were calculated as already done for the EMG and FORCE parameter. For each parameter, inside each contraction, the average value was then calculated (data not smoothed).

Abbreviations

MRI	Magnetic resonance imaging
CT	Computed tomography
DXA	Dual-energy X-ray absorptiometry
BIA	Bioelectrical impedance analysis
US	Ultrasound
USI	Ultrasound sarcopenia index
MVC	Maximum voluntary contraction
VL	Vastus lateralis

sEMG or EMG	Surface electromyography
NIRS	Near-infrared spectroscopy
NMJ	Neuromuscular junction
MF	Median frequency
RMS	Root mean square
O_2Hb	Oxygenated hemoglobin
HHb	Deoxygenated hemoglobin
tHb	Total hemoglobin
SO_2	Tissue oxygen saturation
ROS	Reactive oxygen species
PRE	Before the rehabilitation
POST	After the rehabilitation
TD NIRS	Time domain near-infrared spectroscopy
TTL	Transistor–transistor logic
ATT	Adipose tissue thickness
PA	Pennation angle
ASIS	Anterior superior iliac spine
VOT	Vascular occlusion test
CW NIRS	Continuous wave near-infrared spectroscopy
DCS	Diffuse correlation spectroscopy
BFI	Blood flow index
MAV	Mean absolute value
MPF	Mean power frequency

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Author contributions
RC, AT, LS, DC, AVC, RR and AS: conception of the work; design of the work RR, AT, DC, LS, AS, AT: acquisition on patients RR, AS, CB: data analysis, RR, AS, CB OA, AT, DC, LS: interpretation of data; RR, AS, CB OA, AT, DC, LS, AF: Writing and revision of the work.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All the participants signed the informed consent and took part in this study, conducted in accordance with the Declaration of Helsinki, approved by Ethical Committee of "Milano Area B" (protocol n°14386/2015) and coordinated by Istituto Ortopedico Gaetano Pini.

Consent for publication
Written informed consent has been obtained from all participating patients, which includes their explicit agreement to the publication of this paper. This consent encompasses the use of their anonymized data and any related information necessary for the dissemination of the study's findings in scientific journals, presentations, or educational materials**.**

Competing interests
A.T. and D.C. are cofounders of PIONIRS S.r.l. (Italy).

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