NIRS-EMG for Clinical Applications: A Systematic Review

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Abstract: In this review, we present an overview of the applications and computed parameters of electromyography (EMG) and near-infrared spectroscopy (NIRS) methods on patients in clinical practice. The eligible studies were those where both techniques were combined in order to assess muscle characteristics from the electrical and hemodynamic points of view. With this aim, a comprehensive screening of the literature based on related keywords in the most-used scientific data bases allowed us to identify 17 papers which met the research criteria. We also present a brief overview of the devices designed specifically for muscular applications with EMG and NIRS sensors (a total of eight papers). A critical analysis of the results of the review suggests that the combined use of EMG and NIRS on muscle has been only partially exploited for assessment and evaluation in clinical practice and, thus, this field shows promises for future developments.

Keywords: NIRS; EMG; rehabilitation; patients; clinical practice; muscles; review

1. Introduction

In a clinical setting, it is often important to obtain feedback about the muscular status of a patient; in particular, during the rehabilitation of patients after a stroke or neurological impairments, or after orthopedic surgery [1]. In these cases, it is essential to have an indication of the progress of the rehabilitation process for motor function recovery. Another field where physicians need an indication of the muscular status is in the treatment of chronic pain, either post-surgery or caused by wrong movements or posture due to repetitive work or sports injuries [2]. Furthermore, there are also other clinical aspects where the muscle is not the main focus of a pathology, but its assessment plays a relevant role, such as in case of patients with cardiovascular or blood diseases [3]. In all of these scenarios, the muscle activity and functional progresses of patients need to be monitored.

In clinical practice, several techniques have been employed for muscle monitoring during movements, as reported by Lobo-Prat et al. [4]. To provide an assessment of muscular contraction, mechanomyography (MMG), miokinemetric (MK), sonomyography (SMG), and electric impedance evaluations are typically employed. However, muscular activation and contraction is more often assessed with electromyography (EMG) and near infrared spectroscopy (NIRS), which allow a continuous monitoring of the muscle during motor activities or rehabilitative exercises [5,6]. Other techniques, such as ultrasonography and lactate sampling, provide only a picture of the muscular status at the moment of the exam, and not a functional trace in time.

A multi-parameter assessment of patients may investigate several levels of the hierarchical organization of the neuro–musculo–skeletal system, assessing correlations within the neural, the muscular, and the kinematic activity. Such results can be achieved by coupling techniques such as EEG and EMG (as well as with kinematics tracking) or MEG and EMG, in order to investigate neural processes and their motor correlates [7]. The advantage to adding NIRS into this framework is to assess neurovascular coupling during exercises [8]. However, techniques can also be combined to assess the same domain under different perspectives. In a similar manner to the analysis of brain tissues and activity when coupling EEG and NIRS, which has been recently discussed [9], in this review, we focus on EMG and NIRS techniques which, when combined together, can simultaneously assess the electrical and hemodynamic activity of the working muscle, providing a strong characterization of muscles under multi-variate perspectives, which cannot be provided with the other mentioned techniques. At the same time, as far as muscle evaluations are needed, these two techniques allow the investigation of muscle activity in detail and with relatively rapid monitoring procedures which are compliant with clinical treatments and investigations.

A surface EMG signal represents the linear transformation of motor neuron discharge times by the compound action potentials of innervated muscle fibers and it is used as a source of assessment of neural activation in muscle. However, retrieving the embedded neural code from a surface EMG signal is extremely challenging [10]. Several time domain, frequency domain, and time-frequency methods for analyzing EMG, especially related to rehabilitative purposes, have been evaluated in recent works [11,12]. Thus, algorithms have been developed in order to automatically evaluate aberrant patterns in muscle activity [13], or to provide an in-depth characterization of motor-unit alterations in post-stroke patients [14]. A comprehensive literature of EMG applications to clinical purposes can be found, spanning through a variety of investigated muscles and pathologies, in order to detect abnormal patterns with evaluation, diagnosis, and rehabilitation aims. We report on a subset of paradigmatic applications that include, but are not limited to, the assessment of lower-back pain [15,16]; the investigation of patterns for motor recruitment [17]; the analysis of walking patterns in Parkinson's [18]; gait pattern abnormality detection in multiple sclerosis [19]; applications to stroke hand rehabilitation [20]; and many others.

On the other hand, NIRS techniques are based on the use of light to monitor, in a non-invasive way, the hemodynamics of a muscle, with the aim of extrapolating information about the mechanism of local muscle oxidative metabolism during exercises. In the clinical setting, NIRS allows clinicians to follow-up the impairments over time, to identify possible correlations with other symptoms, and to evaluate the effects of particular rehabilitative interventions [5]. In fact, through the estimation of the oxy (O_2Hb)- and deoxy (HHb)-hemoglobin content, or through the derived parameters of total hemoglobin content (tHb) and oxygen saturation (SO_2), it is possible to understand the dynamic balance between oxygen delivery and oxygen consumption in muscle [21]. This assessment has been shown to be a valid and sensitive tool for monitoring changes in muscle oxygenation and blood volume in human tissues [22]. For further details, in a recent review from Barstow [23], a very deep explanation of the NIRS technique and its application to skeletal muscle has been presented. For what concerns clinical applications, where NIRS can be applied for muscle monitoring, we cite some important examples, selected from a seemingly boundless literature. In patients with chronic heart failure, it is possible to test the tolerance to exercise and training [24,25] and to monitor the effects of therapeutic interventions in subjects with diabetes or peripheral arterial diseases [26,27]. NIRS can also be employed on patients with muscular impairments, such as dystrophies [28] or spinal cord injuries [29]. Finally, we mention the monitoring of patients during the rehabilitation process (e.g., lower back pain [30] and stroke [31]).

Several studies are available in literature where EMG and NIRS techniques have been combined together on healthy subjects. This includes a variety of applications, which range from the monitoring of personal health and sports performance in athletes [32] to the detection of muscular fatigue [33], or to their combination, in smart sensors, for sports and brain computer interface (BCI) applications [34].

On the contrary, the literature which has reported results where EMG and NIRS were used for combined targeting muscle analysis in a clinical setting (i.e., on patients) is more limited, and a systematic review is still missing. Following this need, after a brief introduction of the two techniques in Sections 2 and 3, we present the results of a literature review, including the works which combined EMG and NIRS for clinical purposes, in Section 4. Finally, in Section 5, a list of discussions is presented.

2. Electromyography

The surface electromyogram (EMG) is comprised of the sum of the electrical contributions made by the active motor units (MUs), as detected by electrodes placed on the skin overlying the muscle [10]. Thus, an EMG record includes the spatio-temporal summations of the action potentials originating from many motor units (MUAPs) located in the neighborhood of the recording electrode site. The recorded signal is influenced by some main factors, including the entity of the contraction, the number and type of involved fibers, and the distance of each MUAP from the site of signal detection. However, these aspects are only a relevant subset of the factors and sources of variability that impact on the temporal and frequency features of the EMG signal and may affect its interpretation. In previous studies, such factors have been sub-divided into three categories: causative, intermediate, and deterministic [35]. Causative factors include geometrical features of the muscle tissue, as well as the number of active motor unit potentials; intermediate factors include cross-talk, amplitude of the detection volume, and skin conductance, among others; deterministic factors include the measure MUAP firing rate, along with others. For an in-depth explanation, previous works have described these aspects in detail [35,36].

Despite the presence of the limitations and confounding factors previously discussed, the shapes and firing rates of MUAPs in EMG signals provide an important source of information for the diagnosis and evaluation of neuromuscular disorders [36]. For this reason, a wide range of algorithms and applications have been developed and applied in a wide variety of contexts, including, in particular, those related to clinical practice. More specifically, an EMG signal can be used with the aims briefly discussed as follows.

2.1. Detection of the Activation Timing (On/OFF)

Precise detection of onset and offset events in the EMG signal is a key feature in the analysis of the motor system under investigation. Differing from other measures, the activation timing can be estimated in isometric or anisometric conditions. However, several confounding factors may affect the detection, including a physiological limit for accuracy (about a 10 ms interval) due to fiber nervous transmission velocity and the delay with force production, with respect to the EMG signal, which depends on muscle fiber composition. Apart from recording recommendations, such as placing the electrodes in the midline of the muscle belly [35], the detection accuracy depends on the employed detection algorithm. Several methods have been proposed for detecting the on and off timing of the muscle; they can be divided into categories, depending on the application. Some algorithms are suitable for online detection [37], or are designed for offline analysis [38]. Algorithms may follow different computational approaches: The single threshold technique is based on the comparison of the rectified raw signals and an amplitude threshold whose value depends on the mean power of the background noise [37]. Alternatively, the double threshold algorithm [39] follows a probabilistic approach, selecting the thresholds such that their values minimize the false-alarm probability and maximize the probability of correct detection for each specific signal-to-noise ratio.

2.2. Force/EMG Signal Relationship

It is known that, in general, a larger EMG signal (envelope) originates from a higher recruitment (number and strength) of the muscle fibers and, thus, a higher produced force. Several works propose approaches to detect a closed form relationship for EMG and force, in order to estimate force from EMG recordings; however, it is not possible to determine it with general rules. In fact, apart from issues related to investigation of non-isometric contractions (which alter the properties of the muscle

during the recording, as well as the force–length relationship), the intrinsic EMG–Force relationship is potentially non-linear, is muscle and subject-dependent, and, because of the many factors that can influence this relation, an EMG amplitude–force relationship has not shown general validity [10,35,40]. Furthermore, the recruitment of the motor units is differently weighted, depending on their distance from the electrodes. While filtering methods may attenuate these two effects, their use may alter the instantaneous and intimate link between force and EMG [35]. The measure of the Force/EMG relationship is usually performed by comparing the Root Mean Square (RMS) of the EMG to a reference value, represented by the Maximum Voluntary Contraction (MVC) which defines the maximum reference value for the RMS.

2.3. EMG for Measuring Fatigue

Fatigue should not be defined as a failure (e.g., in holding an isometric configuration), since fatigue onset should be detected before a macroscopic failure is achieved [35]. In the detection of fatigue, several confounding factors are, however, present, such as the facts that force might not be constant and could be addressed to other muscles, and that biochemical and physiological factors may alter the nature of the contraction. Common methods used for fatigue detection are related to frequency-domain analysis: Metrics that are usually employed are the decrease of the Median Frequency (MF), and/or of the Mean Power Frequency (MPF) [41]. A decrease in MF or MPF in the estimation of the power spectrum, calculated over consecutive time windows, is considered to be a biomarker for fatigue. In some studies, even an increase of the RMS has been considered as a biomarker for fatigue, but this relationship is not always observed. During fatigue, the power spectrum decreases due to two main phenomena: The decrease in the firing behavior of motor units, and the shape of MUAPs [35]. These factors cause a compression of the spectrum of the EMG signal during fatigue [35].

2.4. EMG in Motor Control

Several algorithms for EMG decomposition have been used in the literature, with the aim of extracting relevant features for clinical practice. For a detailed analysis, several works can be consulted [36]. In this paragraph, a specific valuable approach to EMG analysis for clinical purposes is briefly reviewed: The muscle synergy framework.

Time-domain multi-channel EMG measurements can be used for coupling with algorithms that find coherent co-activation patterns shared by different muscles. Such approaches have found recent application in the study of motor control and medical practice, in the framework of muscle synergies [42]. Starting from the rectified and filtered EMG signal (time-domain), the decomposition approach attempts to identify the invariant muscle co-activations underlying neuromotor organization under the conditions of variability of movement. The invariant elements are the motor synergies, which are a model of the implementation of the modular neuromotor organization at a neural level. Muscle synergies have been employed in several fields and include, among others, comparison of algorithm performance and interpretation for synergy extraction [43], investigation of muscles synergies in upper-limb physiological motor control [44,45] or after neurological lesions [46–49], applications to locomotion [50], and postural perturbations [51].

3. Near Infrared Spectroscopy

Near Infrared Spectroscopy (NIRS) is an optical technique that exploits the fact that light in the spectral range between 600–1000 nm (the "therapeutic window") can penetrate biological tissues, up to a few centimeters, in a complete non-invasive way [52]. When light propagates into a turbid medium, such as into a biological tissue, photons undergo many absorption and scattering events, which affects the signal exiting from the medium. This absorption is related to the presence of chromophores, which absorb the radiation at specific wavelengths. By measuring the absorption coefficient (μ_a) of a biological tissue at different wavelengths, it is possible to retrieve the concentrations of the main absorbing chromophores. The main absorbers which NIRS aims to investigate are HHb and O_2HB,

which absorb light both in the visible and NIR regions and play a central role in representing muscle oxidative metabolism functions [53]. Scattering events are related to changes in direction of the photons inside the medium, and are mainly caused by refractive index mismatches due to the presence of different morphological structures. From the knowledge of the reduced scattering coefficient ($\mu_s{}'$), it is possible to calculate the Differential Pathlength Factor (DPF), a factor that relates the geometrical distance between source and detector and the photon path-length in the biological tissue. In order to accomplish a NIRS measurement, we should be able to discriminate the contribution of both μ_a and $\mu_s{}'$ with an acquisition, such that it is possible to calculate the absolute values of O_2Hb and HHb.

Not all the NIRS techniques exploited in research studies or present in the market allow for the discrimination of the two coefficients. For this reason, in the next sub-section (Section 3.1) we will briefly present the three main modalities of the NIRS technique. In Section 3.2, the muscle parameters which can be obtained from NIRS measurements are, then, presented.

3.1. Different NIRS Techniques

In this section, we would like to give the reader a brief introduction to the different NIRS techniques available. They are based on different hardware configurations and the different kinds of parameters that can be extrapolated [23].

Continuous Wave NIRS (CW-NIRS) employs LEDs or lasers with constant intensity as light sources, and the main parameter acquired is the light attenuation caused by biological tissues. Its simple approach allows CW-NIRS based systems to be user-friendly, low cost, and, in many cases, portable, wearable, and wireless [54]. These characteristics make them the most widespread devices on the market for monitoring muscle oxygenation and metabolism in both sport and medical applications. However, this technique presents a limited depth sensitivity and an inability to decouple the absorption from the scattering contribution. This means that we can retrieve just the variations of O_2Hb and HHb with respect to a baseline (arbitrarily set to zero) and not an absolute value [55]. Since, in CW measurements, it is not possible to retrieve the absolute value of the reduced scattering coefficient, a constant a priori DPF has to be taken from literature. However, the DPF depends on many factors, such as the wavelength, the source–detector distance, and the inter-subject variability [23]. Another limitation is that it is not possible to calculate SO_2 with this method. In order to overcome these limitations, it is necessary to perform measurements at different source-detector distances (Spatially Resolved NIRS, SR-NIRS) which allows to obtain, by doing some approximations (i.e., scattering linearly dependent on wavelength), a parameter called the Tissue Oxygenation Index (TOI) or Tissue Saturation Index (TSI) [56]. Furthermore, in the CW measurements, the acquired signal is contaminated by the more superficial layers: The contributions of the skin, superficial capillary bed, and fat layer cannot be decoupled with a single measurement. In order to overcome this issue, it is necessary to perform more measurements—for example, at different wavelengths or different inter-fiber distances [57]—making the hardware more complex or increasing the total measurement time. A comprehensive list of CW-NIRS devices can be found in the review from Grassi and Quaresima [5].

Some approaches, such as Frequency Domain (FD)- or Time Domain (TD)-NIRS, overcome the disadvantages of the CW-NIRS measurements. In particular, these approaches can be exploited to retrieve absorption and scattering coefficients independently, allowing the calculation of the absolute values of O_2Hb, HHb, and DPF.

FD-NIRS is based on amplitude-modulated light sources, with modulation frequencies ranging from 100 MHz up to 1 GHz. The signal exiting the tissue is demodulated, in order to obtain amplitude and phase as a function of the frequency. In fact, while travelling into the tissue, light amplitude and phase, at different modulation frequencies, depend on the absorption and scattering properties [58]. These instruments are quite complex and not widespread, both in research laboratories and on the market. To our knowledge, the only available FD devices specifically developed for muscle applications are the OxiplexTS^{TM} [5] and its clinical version OxiplexTS200^{TM}, made by the ISS company [59].

TR-NIRS instruments typically employ short laser pulses with duration of tens of picoseconds as light sources. The injected pulses are delayed and broadened in time, since scattering causes photons to follow different randomized paths inside the tissue [60]. Furthermore, the pulses are attenuated due to tissue absorption. Overall, the signal collected at a certain source-detector distance is given by the photon Distribution of Time Of Flight (DTOF) during their travel inside the diffusive medium. The information about the depth reached by photons into the tissue is, straightforwardly, linked to their arrival time: Photons which arrive early ("early photons") travelled shorter paths through the tissue and, thus, they explored only the surface layer. Hence, they are related with physiological changes occurring in the superficial capillary bed and are strongly influenced by the fat layer. Photons which arrive later ("late photons") travelled through longer paths inside the tissue and, thus, they investigated deeper layers where the muscular tissue is located. By exploiting these peculiar characteristic of time-resolved measurements, it is possible to remove the more superficial physiological and confounding contributions from the detected signal [61,62]. Up to now, due to the high cost of components and the complexity of the technique, there are few commercially available instruments which exploit the TD-NIRS approach for muscle monitoring. The Hamamatsu Photonics K.K. company has developed three devices: The tNIRS-1, originally designed for cerebral measurements, but which has been used also in muscle studies, and the TRS-10 and TRS-20 systems [63]. A high-power version, the TRS-20SD, has been used by Koga et al. [64] to probe deep into quadricep muscles. Moreover, a research-oriented TD-NIRS device dedicated to muscle metabolism monitoring has been recently developed by Re et al. [65].

3.2. NIRS Parameters

As previously stated, NIRS techniques allow for the monitoring of the oxidative metabolism and O_2 consumption rate of skeletal muscle. In particular, the parameters that can be directly extrapolated are O_2Hb and HHb hemoglobin. The sum of these two represent the total content of hemoglobin (tHb), which is relative to the blood volume under the probe. The ratio between O_2Hb and tHb represents the oxygen tissue saturation (SO_2 or $SO_2\%$). Moreover, there is a lack of standardization in NIRS parameter nomenclature in the literature and different acronyms can be found to indicate the same quantities. Hence, besides the one already reported, it is also possible to find the terms StO_2 or SO_{2m} for muscle oxygen saturation or TOI and TSI, especially in studies that have employed CW-NIRS devices. Furthermore, to highlight the fact that, with NIRS, it is not possible to discriminate the contributions of hemoglobin and myoglobin species, the terms oxy[Hb + Mb], deoxy[Hb + Mb], and total[Hb + Mb] are frequently reported in muscle studies. In this review, the shorter acronyms will be used.

When TD or FD instruments are used, besides these physiological parameters, it is also possible to investigate the absolute values of μ_a, $\mu_s{}'$, and DPF.

Overall, the NIRS derived parameter that seems to be more representative of muscle oxygenation metabolism (and the more studied, to present) is HHb [5,66], which reflects the balance between O_2 delivered and O_2 consumption and, thus, can be indicator of the physiological status and performance of a muscle.

4. NIRS-EMG: Review of Studies in Clinical Practice

The aim of this literature analysis is to review all available studies which have combined EMG and NIRS for clinical practice, targeting applications of the techniques for patients with motor impairment or oxygen metabolism diseases. The design of this research attempts to answer the question: "Have NIRS and EMG been effectively combined, on muscle, in clinical practice?". With this aim, the following procedure was employed for the literature screening. A collection of articles were obtained by screening PubMed, PubMed Central, and Google Scholar, using the following keyword combinations: (1) "EMG" and "NIRS" and "Rehabilitation": 225 papers; (2) "EMG" and "NIRS" and "Clinical": 354 papers; (3) "EMG" and "NIRS" and "Patient": 369 papers; (4) "EMG" and "NIRS" and "Instrument": 48 papers; and (5) "EMG" and "NIRS" and "Device": 140 papers. The papers found in the literature research were

screened, one by one, for inclusion. The further inclusion criteria were that papers had to be published in journals with impact factor; include measures on EMG and NIRS; the measurements had to be done not only on healthy volunteers, but performed also on people with orthopedic or neurological diseases ("patients", not "subjects"); and, in case of NIRS, the measurements had to refer to muscles (not the brain).

According to the proposed inclusion criteria, only 25 studies were eligible for inclusion in this paper. They were further classified into three subgroups. In the first subgroup, we included all the works (n = 9) where both EMG and NIRS signals were acquired, interpreted, and correlated to each other, in order to represent the physiological muscular status. In these studies, both EMG and NIRS were outcome measures (see Section 4.1, NIRS and EMG). In the second subgroup, we gathered studies (n = 8) where only the EMG signal was used to verify that a movement had effectively occurred, or to understand whether a certain muscular work threshold was reached. In these studies, the EMG signal was employed as a feedback (or as a methodological measure) to support NIRS-based findings (see Section 4.2, NIRS > EMG). Finally, the third subgroup regards the works (n = 7 + 1 review) in which integrated NIRS-EMG hardware systems were developed or employed (see Section 4.3, NIRS and EMG HW).

4.1. NIRS and EMG

In this section, we only present the works in which both NIRS and EMG signals were acquired at the same time and where an interpretation, from a physiological point of view, was given to both the signals. In Table 1, a list of the nine works found is reported. In this table, for each work, we have summarized: The number of patients and controls involved, the aim of the study, the target muscles, the experimental protocol, and the NIRS and EMG parameters extrapolated. Most of them focused on the understanding of the metabolic and fatigue mechanisms in patients with muscular pain. Furthermore, we added (in squared brackets) a classification label for these works, based on their field of application.

Table 1. List of the works founds for the "NIRS and EMG" group.

Reference	Subjects	Aim	Target Muscle	Protocol	NIRS-EMG Parameters
Kankaanpää 2005 [67]	17 patients with chronic low back pain, 12 control.	[CLINICAL RESEARCH] To assess if chronic low back pain patients have impaired paraspinal muscle O_2 turnover and endurance capacity	L4, L5 level paraspinal muscle.	90 s dynamic back endurance test (fatigue).	NIRS: O_2Hb EMG: MPF, amplitude
Sakai 2017 [68]	234 lower back pain patients.	[CLINICAL RESEARCH] To identify the features of motion-induced and walking-induced low back pain in patients with lumbar spinal stenosis.	Left and right posterior aspect of the lumbar multifidus muscle.	The lumbar spine was extended gradually 30° backward and forward for 15 s each.	NIRS: O_2Hb EMG: RMS, MPF
Elcadi 2013 [69]	18 patients with neck-shoulder-arm pain, 17 controls.	[RESEARCH] To test hypotheses of (a) reduced oxygen usage, oxygen recovery, blood flow, and oxygen consumption; (b) increased muscle activity for patients diagnosed with work-related muscle pain.	Extensor carpi radialis and trapezius descendes.	20 s isometric contractions at 10%, 30%, 50% and 70% MVC.	NIRS: tHb, SO_2%. From occlusion: also HHb slope EMG: RSM, MPF
Elcadi 2014 [70]	18 patients with work related muscle pain, 17 control.	[RESEARCH] To test if oxygenation and hemodynamics are associated with early fatigue in muscles of patients suffering from work-related muscle pain.	Extensor carpi radialis and trapezius.	A low-level contraction of 15% maximal voluntary contraction sustained for 12–13 min.	NIRS: HHb, O_2Hb, tHb EMG: RMS, MPF

Table 1. *Cont.*

Reference	Subjects	Aim	Target Muscle	Protocol	NIRS-EMG Parameters
Sjøgaard 2010 [71]	43 females with trapezius myalgia, 19 controls.	[DIAGNOSTIC] To study females for differences between those with trapezius myalgia and without.	Descending part of trapezius muscle.	40-min repetitive, low-force exercise: PEG task + 10 min Stroop test.	NIRS: O$_2$Hb, HHb, tHb EMG: RMS, MPF
Søgaard 2012 [72]	39 females with trapezius myalgia.	[DIAGNOSTIC] To assess changes in myalgic trapezius activation, muscle oxygenation, and pain intensity during repetitive and stressful work tasks in response to 10 weeks of training.	Descending part of trapezius muscle.	40-min repetitive, low-force exercise: PEG task + 10 min Stroop test.	NIRS: O$_2$Hb, HHb, tHb EMG: RMS, MPF
Kawashima 2005 [73] and Jigjid 2008 [74]	15 chronic stroke patients.	[REHABILITATION] To evaluate the effects of passive leg movements in the lower limbs in chronic stroke patients.	Medial side of gastrocnemius muscle. EMG also on the soleus.	10 min passive leg movement on a gait apparatus.	NIRS: O$_2$Hb, HHb, tHB EMG: Mean Amplitude, RMS
Žargi 2018 [75]	20 patients scheduled for an arthroscopic anterior cruciate ligament (ACL) reconstruction.	[TREATMENT ASSESSMENT] To test if short-term pre-conditioning with low-load blood flow restricted exercise can attenuate quadriceps femoris muscle endurance deterioration in the post-operative period.	Vastus medialis and lateralis muscle.	Sustained isometric contraction at 30% of maximal voluntary isometric contraction (MVIC) performed to volitional failure.	NIRS: Blood Flow EMG: RMS, Median Frequency

The first work on patients with chronic lower back pain (CLBP) was that of Kankaanpää et al., dated 2005 [67]. Their aim was to compare the paraspinal muscle oxygenation and muscle function characteristics (activation level and fatigue) between CLBP patients (n = 17) and healthy controls (n = 12). Furthermore, they studied the effects of subcutaneous tissue thickness on NIRS and EMG measurements. The paraspinal muscle NIRS oxygenation and EMG fatigability results, during a dynamic back endurance test, did not differ between the groups. This indicates that the oxygen consumption and endurance capacity was similar in the CLBP and healthy control groups. It was shown that the subcutaneous tissue thickness over the lumbar paraspinal muscles strongly influenced the NIRS and EMG amplitude measurements; for this reason, it should be incorporated in the statistical analysis as confounding factor. More recently, in 2017, Sakai et al. investigated patients with LBP (n = 273), after a decompression surgery, for lower extremity symptoms in lumbar spinal stenosis (LSS) [68]. The patients were, then, divided into three groups: Walking-induced, LBP that was aggravated during walking (W group); motion-induced, LBP that was aggravated during sitting (M group); and no LBP (N group). In particular, they wanted to identify the features of motion-induced and walking-induced LBP in patients with LSS and to assess whether neuropathic LBP had developed. The electrodes and optodes were placed on the lumbar multifidus muscle during extension of the lumbar spine. In the hemodynamic evaluation, the oxygenated hemoglobin level was significantly lower in the W group than in the M and N groups. In an electrophysiological evaluation of lumbar multifidus, the mean power frequency from the EMG signal was significantly higher in the W group than in the N group. These results suggest that neurologic disturbance in patients with LSS may be attributed to "neuropathic LBP". They concluded that neuropathic multifidus disorder could play a role in walking-induced LBP.

When considering muscular pain, we cite two works from Elcadi et al., one published in 2013 [69] and one in 2014 [70], where patients with neck–shoulder–arm pain (n = 18) were considered together with control subjects (n = 17). Extensor carpi radialis (ECR) and trapezius descendens (TD) were both

investigated. In the first work, subjects had to perform randomized isometric contractions (lasting 20 s) at 10%, 30%, 50%, and 70% of the maximum voluntary contraction (MVC); in the second one, they performed a low-level contraction of 15% MVC, sustained for 12–13 min. From a combined NIRS-EMG analysis, as $\Delta StO_2\%$, $StO_2\%$ recovery for either muscle, and ECR arm venous and arterial occlusion-generated slopes of total hemoglobin were not different between groups, the researchers could affirm that there was no reduction of oxygen use, recovery, and blood flow for patients. However, patients had a significantly lower ECR slope for HHb after occlusion, which underlined a reduced consumption, as compared to the healthy subjects. Further, there was no difference in RMS%max during contractions, meaning that there was no increased activity for patients. From the low-level contractions of the 15% MVC experiment, they could affirm that the early fatigue for the patients suffering from work-related muscle pain was not associated with muscle oxygenation and hemodynamics.

The descending part of the trapezius muscle was also investigated by Sjøgaard et al., in 2010, on 43 female workers with trapezius myalgia and 19 controls [71]. They performed a 40-min repetitive low-force exercise, a PEG task during micro-dialysis delivery, and a 10 min of Stroop test (i.e., stress and repetitive work). RMS was higher in patients, with respect to the controls. From the NIRS signal, it was shown that the females with work-related neck-shoulder complaints had muscle metabolic insufficiencies at rest and during standardized repetitive and stress tasks, similar to those among chronic neck-shoulder pain patients. Søgaard et al. published a work, in 2012, presenting the results during the same protocols and on the same subjects, after 10 weeks of training [72]. The subjects underwent general fitness training, performed by leg-bicycling (GFT) or specific strength training for the neck/shoulder muscles (SST). GFT improved trapezius oxygenation, decreasing pain development during repetitive work tasks. SST lowered the relative EMG amplitude (i.e., the overall level of pain) both during rest and work. These results show a differential adaptive mechanism of contrasting physical exercise interventions on chronic muscle pain at rest and during repetitive work tasks.

A completely different NIRS-EMG application was presented by Kawashima et al. [73] and Jigjid et al. [74]. They evaluated the effects of passive leg movements on muscle oxygenation levels and electromyographic activity in the lower limbs of 15 chronic stroke patients. Passive leg movement was achieved by means of a gait apparatus, where patients trained on for 10 min. EMG and NIRS probes were placed distally and proximally on the medial side of gastrocnemius muscle; EMG probes were also placed on the soleus muscle. The EMG signal was evaluated only in terms of amplitude and was useful in the comparison of muscular activity between the two muscle types and between paretic and non-paretic muscles. In particular, in patients with good motor recovery, the MVC level of the paretic calf muscle was higher than in the poor recovery subgroup, but there was no difference in the EMG activity induced by passive movement. These results, therefore, suggest that passive movement could induce EMG activity in the paretic muscle, regardless of its voluntary contraction capacity. Concerning the NIRS findings, they affirmed that the muscle oxygenation levels of both paretic and non-paretic calf muscles could be enhanced by imposing passive leg motion. The effects of passive movements varied in accordance with the motor recovery level. This type of exercise may be a useful and efficient method for prevention of muscle metabolic deterioration and bring forth new perspectives in clinical rehabilitation settings.

The most recent work which employed both NIRS and EMG on patients was from Žargi et al., published in 2018 [75]. They focused on 20 patients scheduled for an arthroscopic anterior cruciate ligament (ACL) reconstruction with ipsilateral hamstring autograph ACL reconstruction. They investigated the vastus medialis and lateralis muscle, respectively, with NIRS and EMG techniques during sustained isometric contraction at 30% of maximal voluntary isometric contraction (MVIC) performed to volitional failure. Patients were assigned into either a blood flow restricted (BFR) group, performing a low-load BFR knee-extension exercise, or a SHAM-BFR group, replicating equal training volume during a sham occlusion. Measurements were carried out prior to the intervention and again 4 and 12 weeks after surgery. From the analysis of the RMS, amplitude, and median frequency of the EMG and blood flow consideration coming from the NIRS signal, they could affirm that patients

treated with the low-load BFR exercise protocol did not display deterioration in quadricep muscle endurance in the first 4 weeks after surgery; whereas patients who had performed the same exercise protocol with sham occlusion demonstrated an approximate 50% reduction in muscle endurance. This difference in endurance between groups was no longer evident at 12 weeks post-surgery and, thus, the main hypothesis was only partially confirmed.

Finally, we found also a recent work about the evaluation of the skeletal muscle function during rehabilitation after acute heart failure, which was only a design study; namely, no data from patients has yet been acquired [76].

4.2. NIRS > EMG

In this section, we briefly present the works which considered both NIRS and EMG signal acquisition on patients, but where EMG was used only as a feedback and was not analyzed in order to obtain parameters useful for understanding the muscle function. In a study by Ivany et al., 11 women affected by myalgia underwent a therapeutic massage [77]. EMG sensors placed on the trapezius muscle were used to determine if the observed changes in muscle parameters were due to the effect of the treatment, rather than the engagement of the muscles themselves. Van Ginderdeuren et al. investigated the hemodynamics of the biceps brachii during submaximal contraction in children with Duchenne muscular dystrophy [78], where the EMG was used only to control if any muscular activity was present. With the same aim, the EMG sensors were applied, in Stavres et al. [79], between the anterior spina iliaca and (lateral to) the patella on the vastus lateralis of 9 individuals with complete spinal cord injuries and, in Molinari et al. [80], on the tibialis anterior muscle during the monitoring of 40 diabetes type II patients. Additionally, Kawashima et al. presented a study on 8 patients with spinal cord injuries, where EMG was only mentioned and no particular analysis was carried out on the signal, as the principal aim of the paper was to present a rehabilitation device for producing passive movement in paralyzed ankles [81]. Farag et al. [82] and Macnab et al. [83] monitored the abdominal wall muscles of patients with bladder problems (i.e., detrusor over-activity) in 41 adults and lower urinary tract dysfunction in 6 children, respectively. In the first work, EMG was used to rule out motion artifacts and, in the second one, was just cited as a regular urologic study planned in the clinical practice. Finally, EMG sensors were used to control the quality of the MVC in a study by Waltz et al., where they studied the flexor digitorum superficialis muscle metabolism in 20 sickle cell-hemoglobin C disease patients and 16 sickle cell anemia patients [84].

4.3. NIRS and EMG HW

For the interested reader, a comprehensive review describing NIRS instruments for monitoring muscles can be found in a recent review by Grassi et al. [5]. Furthermore, in Section 3.1, a list of the devices and sensors for the different NIRS modalities was presented. In the same line, we do not provide an overview of the countless commercial and prototype EMG sensors available, as well as the possible technical set-ups and aspects of the recording, for which relevant works are already available in the field [85]. Instead, according with the purpose of this review, we present, in chronological order, the works we found where integrated NIRS-EMG systems were presented or employed. In 2008, a rehabilitation strategy which presented the idea of the integration of sensors for upper limb rehabilitation after stroke was outlined [86]. The first paper where a physical prototype was presented supporting this concept was very recent and only dates back to 2010, when Herrmann et al. proposed a novel sensor in which the two techniques were combined [87]. As a main application, they specified the detection of muscle exertion for the real-time control of assistive devices. In 2015, Kimoto et al. proposed a new layered sensor for simultaneous measurements of EMG, mechanomyography (MMG), and CW-NIRS, which was tested during a cuff occlusion [88]. In 2016, Hu et al. developed an integrated 64-channel portable CW-NIRS instrument with physiological sensors [89]. These sensors were: High-resolution EMG, electrocardiography (ECG), electrooculography (EOG), and electroencephalography (EEG) sensors. The device was tested electronically, on phantoms

and during in-vivo measurements, on muscle. Guo et al. presented a multi-channel and wireless EMG-NIRS (CW) sensor system [90]. It was suggested in the context of prosthetic manipulation, even if, in the paper, it was characterized from an electronic point of view on a healthy subject performing incremental isometric exercises. The same device was, then, applied on 13 able-bodied male subjects and 3 transradial amputees for improving the control of upper-limb prostheses [91]. The most recent example was that from Dziuda et al., in 2018 [92]. The main focus of their work was to create a prototype system, comprised of a tilt table and a lower body negative pressure (LBNP) chamber, for space medicine application. Inside the chamber, they integrated a sub-system for monitoring the physiological parameters of subjects undergoing tilt and pressure tests. The monitored parameters included ECG, pulse oximetry, EMG, skin conductance, blood pressure, body temperature, impedance reography, EEG, capnography, NIRS, and arterial pressure.

In a review by Peake et al., an overview of the wearable equipment for giving biofeedback in the physically active population has been provided [6]. In their Table 5, we find a list of portable NIRS device with the addition of physiological sensors. They cited two commercial instruments in which EMG sensors were integrated: the NIRSPORT from NIRx and Mobita from TMSi, both based on CW-NIRS.

5. Discussion and Conclusions

Performing a search on PubMed Central by employing "NIRS and EMG" as keyword combinations, a list of 491 studies, from the year 2000 onwards, was found. This number indicates that the combined use of the two techniques has been an explored field over the last 20 years. However, from the critical analysis of the results of this review, as shown in Section 4, it has emerged that the combined use of EMG and NIRS has been only partially exploited in clinical practice for the assessment and evaluation of patients with muscular dysfunction. In fact, only 17 studies matched the research criteria. The first one was dated 2005, but only in the last 7–8 years, the number of papers combining the two techniques started to increase, as is shown in the road-map in Figure 1. This is due, in our opinion, to the fact that NIRS is a relatively recent technique and it is difficult to find, in the clinic, both NIRS and EMG instruments.
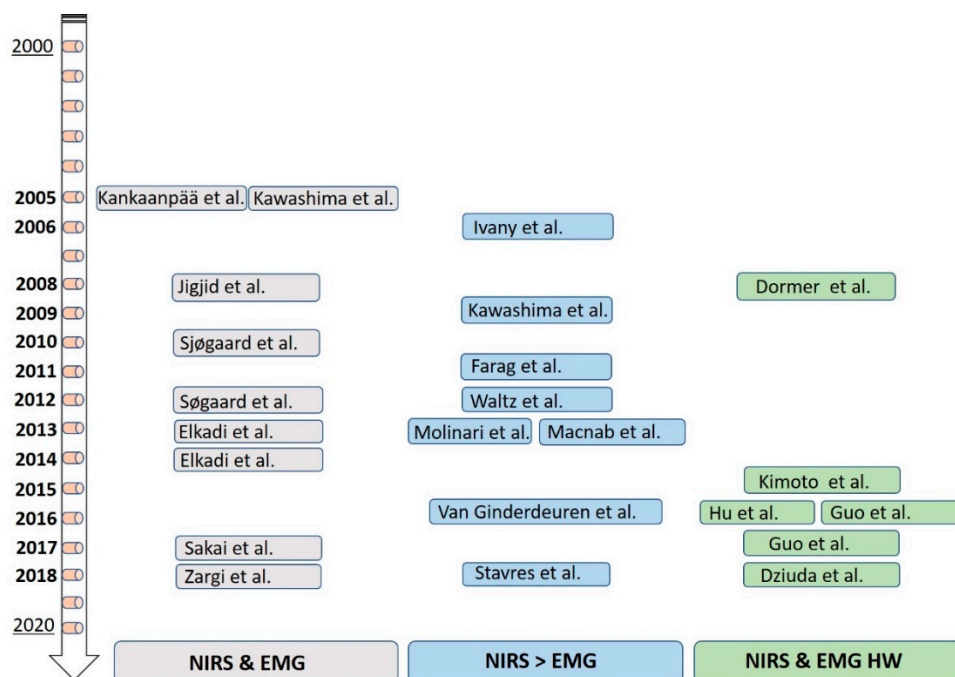

Figure 1. Road map of the papers found for the NIRS and EMG, NIRS > EMG and NIRS and EMG HW research.

Furthermore, the use and interpretation of data coming from both techniques requires the employment of technical staff, which is often not available in the clinical environment. In this perspective, groups of specialized personnel have to be recruited and employed with a consequent investment, which is not always bearable; especially within public structures. The development of instruments embedding both type of sensor has started only recently (the first instrument was released in 2015) and, if the research and the market go ahead in this direction, we expect the number of studies to increase remarkably. The fact that dedicated hardware has been released indicates that the joint use of NIRS and EMG will be probably exploited in the near future, in research and in clinical practice. Nevertheless, from a hardware point of view, the combined used of EMG and NIRS has been well-assessed and the integration of the two techniques is not compromised by issues related to signal interference, considering the differences in the signal nature; electrical and optical, respectively.

The same level of integration has not been found in the data analysis so far. In fact, according to the studies screened in this review, while many parameters have been separately extrapolated from both techniques, no merged outcome measures have been proposed. In the literature, we can find very few examples such as that of Herrmann et al., who proposed a feature, named NIRSRMS, which combines a weighted NIRS signal with the RMS value of EMG signals [87,93]. In our opinion, the biggest challenge for the future of the clinical application of combined NIRS-EMG sensors will be the interpretation of the combination of these two signals, in order to provide a clear picture of the oxidative and electrical status of the muscle to medical professionals. This process will take place in two main lines: First, evaluating how to merge the parameters extracted by the two techniques; or, secondly, by establishing evidence of the relationships between NIRS- and EMG-based measures.

The combination of these two techniques provides some issues. First, there is still a numerical decoupling, in terms of number of employed sensors. The EMG electrodes are smaller than the actual NIRS optodes. Furthermore, both techniques are based on "integral" measures, which do not guarantee that the same volume of tissue is mapped, even if effort is dedicated to the careful placement of sensors. This means that, in general, the mapping of the muscle with a certain number of EMG probes might not be completely consistent with same number and positioning of NIRS probes. Recently, with the advent of the 3D-print technologies, it is possible to create custom probes for the measurements allowing for a better organization of the optodes, but the physical dimensions of the optical fibers still limit the number of NIRS probes which can be used at the same time. The encumbrance of the sensors also limits the possibility to take both measurements exactly at the same point. For the NIRS signal, this is not a big issue, as the investigated muscle is the whole volume under the probe, while the recorded EMG is strongly affected by electrode positioning and should be placed consistently with anatomical positioning sites. Another limitation may be the fact that, with the combination of NIRS and EMG, it is possible to have only a muscular evaluation of the patient and not a description of other related domains—such as the activity of the motor cortex—during movement. In order to overcome this limitation, it should be possible to employ multi-channel devices for the NIRS signal, positioning some optical channels also on the brain and then coupling them with traditional techniques, such as EEG. Of course, this configuration increases the cost of the device, which is, instead, limited for the muscle-only application. Furthermore, the use of multiple techniques increases the time for the subject preparation, which is compliant with clinical sessions only in the case of application of NIRS and EMG sensors on muscle.

The joint use of the two techniques might impact several fields of medicine and rehabilitation. In fact, while several neurological or orthopedical pathologies are commonly assessed only in the domain of one of the measures, the coupling of the two may strengthen the assessment and produce multi-factorial and reliable results. Looking at the applications, we have found, the main field where these two techniques are promising seems to be that of diagnostics and rehabilitation. In our opinion, joint NIRS-EMG assessment will provide insights into clinical cases where a muscle impairment needs to be assessed in order to plan a physiotherapeutic program, following the progress of the patient. The EMG can give information about the muscular fibers, whether they are recruited in a higher

number or in a different way during the rehabilitation process, while NIRS can contribute to the characterization of the muscle from a metabolic point of view, assessing the dynamic balance between O_2 utilization and O_2 delivery.

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