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A more precise, repeatable and diagnostic alternative to surface electromyography – an appraisal of the clinical utility of acoustic myography

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Summary

Acoustic myography (AMG) enables a detailed and accurate measurement of those muscles involved in a particular movement and is independent of electrical signals between the nerve and muscle, measuring solely muscle contractions, unlike surface electromyography (sEMG). With modern amplifiers and digital sound recording systems, measurements during physical activity both inside and outside a laboratory setting are now possible and accurate. Muscle sound gives a representation of the work of each muscle group during a complex movement, and under certain forms of movement even reveals both concentric and eccentric activity, something that sEMG is incapable of. Recent findings suggest that AMG has a number of advantages over sEMG, being simple to use, accurate and repeatable as well as being intuitive to interpret. The AMG signal comprises three physiological parameters, namely efficiency/coordination (E-score), spatial summation (S-score) and temporal summation (T-score). It is concluded that modern AMG units have the potential to accurately assess patients with neuromuscular and musculoskeletal complaints in hospital clinics, home monitoring situations as well as sports settings.

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Introduction

Surface electromyography (sEMG) recordings are frequently used to assess muscle function in a non-invasive way. Indeed, the technique has more or less become a gold standard (De Luca, 1979; Hermens *et al.*, 1999). Its strongest feature is that it is relatively easy to use, but as some have pointed out, this can also represent its greatest weakness (De Luca, 1997). To remove some of the typical errors associated with sEMG, the SENIAM project wrote a very detailed report, documenting how electrodes should be placed one to another, and relative to the muscle of interest (Hermens *et al.*, 1999). This report also addressed more complex issues of sampling rate, noise and interference and such specific issues as causative, intermediate and deterministic factors that can and do affect the recorded signal, making it at times difficult and complex to interpret (Hermens *et al.*, 1999). Yet, when each of these aspects is taken into account, a single problem with sEMG remains, that it is a combined signal of motor neurone and muscle fibre depolarization, making it difficult to discern whether changes in the sEMG signal arise from the motor neurone and/or the muscle fibres.

The application of sEMG appears to be further confounded by older and more recent investigations into muscle contractility and force production, which confirm the existence of other means, besides the motor neurone, of modulating processes ranging from development, to metabolism, to blood flow and contractile function in muscle (Bevington *et al.*, 1986; Reid, 2001; Harrison *et al.*, 2006). It is for these very reasons that scientists have sought to find an alternative to sEMG, one that accurately records muscle contractions.

Recently, technological advances in microphones and contact transducers (piezoelectric devices), as well as recording systems, have not only improved the size, but also the quality, of systems capable of detecting muscle contractions, enabling them to be applied to a normal daily setting as well as to hospital and sports clinics. These new possibilities have paved the way for a useable and accurate clinical tool in the form of acoustic myography (AMG). Indeed, such a wireless, stable and quick and easy to use technique lends itself to the assessment of patients with musculoskeletal complaints during daily activities, or assessment of athletes in terms of their efficiency of muscle use (Harrison *et al.*, 2013).

This review aims to: (i) assess the inherent faults and issues associated with sEMG in a clinical setting and examine the extent to which improvements in its diagnostic capabilities can be made, (ii) to evaluate to what extent an AMG signal

can be used to reliably determine coordination as compared with the 'gold-standard' sEMG, and (iii) to investigate the ability of AMG to accurately measure muscle functions, in physically active human subjects – presenting data from clinical cases, thus illustrating its application in clinical practice.

Illustrating examples

The occasional human data presented in this study were obtained from subjects that had given their informed written consent according to the principles outlined in the Declaration of Helsinki. All recordings were saved using a code that protected the individual's personal data and identity (e.g. name and date of birth).

Equipment and measurements applied in the examples

Acoustic myography

Specially made sensors (MyoDynamik ApS, Copenhagen Denmark) were placed on the muscle of interest. These were then connected to an AMG unit (MyoDynamikApS – www.myodynamik.com – referred to as a CURO), capable of recording internally as well as transmitting to an iPad up to 100 m away from the subject. Recordings were made at a rate of 1000 Hz with 10 bit resolution, to dedicated iPad software (CURO Clinic App – App Store), where the signal was presented in real time as a muscle-sound signal and detailed balance and ESTi® Score. The unit was switched on, and recordings of muscle sounds were carried out transdermally.

The piezoelectric sensors have a resonant frequency range of 0·5–20 ± 0·5 kHz and were moulded together with an amplifier, A-D converter and signal filter (0–500 Hz) (MyoDynamikApS – www.myodynamik.com). Each sensor was covered with Acoustic Gel (MyoDynamikApS – www.myodynamik.com) to ensure a good connection with the skin above the muscle of interest. Sensors were attached with the aid of a self-adhesive bandage (Co-Flex, Andover – Salisbury MA, USA).

The recorded data were analysed for its efficiency/coordination (E-score), amplitude (S-score; spatial summation) and frequency (T-score; temporal summation) parameters as represented by an integrated ESTi® Score using the CURO System Software (MyoDynamik ApS). Recorded signals were also analysed using Chart software (ADInstruments, Chalgrove, Oxfordshire, UK), after being sampled as a sound file (WAV). The recorded signal is derived from the actual contractions of the muscle fibres, which results in mechano- or resonance waves transmitted through the tissue to the skin surface (Stokes & Blythe, 2001), where they were accurately detected by sensors. Coordination (E-score) of the muscle in terms of physical activity was assessed as periods of active/inactive function relative to the duration of each activity period (Harrison *et al.*, 2006). The recruitment (S-score) of motor units equates to sound signal amplitude, and the frequency (T-score) with which active motor units fire equates to sound signal frequency. The combined E-, S- and T-scores were then used to derive a mean ESTi® Score.

Whilst AMG implies the detection of sound, the AMG system presented and discussed in this manuscript strictly records the vibrations created by contracting muscles, subsequently converting them to a sound file (WAV format) for analysis and storage.

Surface electromyography

The sEMG recordings were obtained following the guidelines laid out in the *European Recommendations for Surface ElectroMyoGraphy* (Hermens *et al.*, 1999). The recorded surface EMG signal was assessed in terms of signal frequency (Hz) and peak-to-peak amplitude (mV), using Chart analysis software (AD Instruments) (Harrison *et al.*, 2006).

A double differential electrode configuration, with electrodes (N-00-S & R-00-S; Blue Sensor, Ambu, Ølstykke, Denmark), was adopted (Harrison *et al.*, 2006). sEMG recordings were taken *via* an ML 132 amplifier connected to a ML780 PowerLab/8s A/D converter (ADInstruments) with a further connection to a MacBook Air with Chart v. 5.5.6/s Software. Input impedance was 200 MΩ differential, and a high and a low pass filter of 0·3 Hz and 500 Hz, respectively, were used. Sampling speed was set to 100 000 s^{-1}, which is way above what is needed in terms of the Nyquist frequency (Diniz *et al.*, 2002). Measurements were *via* two electrodes placed on the body of the muscle of interest, with a reference electrode placed on a non-muscular site close by to the muscle of interest.

Statistical analysis applied in the examples

Data are presented as mean ± SD. Differences between means were tested for statistical significance with the use of GraphPadInstat 3 for Mac (Version 3.0b, 2003; GraphPad Inc., La Jolla, CA), with an additional test for Gaussian normal distribution, to justify the use of the mean. Differences between means showing a P value >0·05 were considered non-significant.

Background for muscle assessment

What initiates a muscle contraction

Motor nerves serve to relay signals from the CNS to the muscle fibres, crossing the neuromuscular junction as a chemical signal and instigating a muscle contraction if the end plate potential is sufficient enough to trigger a wave of depolarization in the muscle fibre (for further details, see Katz, 1966).

Beyond the neuromuscular junction

One of the myths that seems to persist in the field of skeletal muscle research is the belief that muscle contractions are

solely controlled through the neuromuscular junction *via* a motor neurone. It is such a belief that has reinforced the use of sEMG, as under such a misguided understanding one can clearly correlate nerve ending and muscle depolarization with muscle activation. However, for a number of years, it has been known and proven that other factors than neural stimulation can effect the contractile performance of skeletal muscle. For example, force production is inhibited by a build-up in both P_i and H^+, two products that are known to change with a period of intense exercise with P_i increasing from 5 to 30 or 40 mM, and intracellular pH declining from 7·0 to 6·2 (Thompson & Fitts, 1992; Fitts, 1994). It is also known that alterations in sarcolemma function induce muscle fatigue by preventing cell activation (Sjøgaard, 1990). Indeed, it has been shown that exposure of muscles to a high extracellular K^+ concentration gives rise to depolarization of muscle fibres and results in a loss of contractility (Fitts, 1994), particularly when this is associated with a simultaneous reduction in extracellular Na^+ concentration (Nielsen & Overgaard, 1996). Elevated Mg^{++} concentrations in plasma also affect muscle function with such symptoms as muscle weakness, fatigue and tremor (Yu-Yahiro, 1994). Thus, it is clear that the composition of the extracellular fluid bathing muscle cells can have a dramatic effect on their excitability and force production. As the sEMG signal is a combination of both the neuro-muscular junction and the muscle fibres themselves as they depolarize, it is difficult to ascertain whether a weak sEMG signal represents activation of fewer motor units or simply changes in the extracellular fluid affecting the excitability of the muscle fibres alone. Whilst in general, the neural and neuromuscular component of the recorded sEMG signal is relatively minor, having an amplitude in the order of microvolts compared with a millivolt sEMG signal, it may on occasions be of importance. In small muscles, where the sEMG signal is in the order of a few hundred microvolts (Fig. 2), the neural and neuromuscular signal can be expected to have a proportionally greater influence on the overall analysis of signal parameters. Whilst in large muscles, where individual neurones typically innervate several hundred muscle fibres, one could equally expect the spatial effect of neural and neuromuscular depolarization to have an adverse impact on the overall recorded signal, particularly in cases of more superficial muscle fibre recordings.

One instance in which muscle weakness occurs is with renal failure (Kouidi *et al.*, 1998). Whilst there are many factors that play a role in the fatigue that patients complain of Fahal *et al.* (1997), it is known that inorganic phosphate plays its part. Typically, dialysis patients have a plasma phosphate level of 1·85 mmol l^{-1} pretreatment as opposed to 0·96 mmol l^{-1} post-treatment (Harrison *et al.*, 2006). This is of interest as Bevington and colleagues showed that the inorganic phosphate concentration of skeletal muscle fibres increased in a linear fashion with that of plasma inorganic phosphate (Bevington *et al.*, 1986). It has, furthermore, been shown that dialysis has a considerable restorative effect on plasma inorganic phosphate levels and that addition of P_i to isolated muscles results in a significant reduction in maximal isometric force production in predominately fast-twitch muscles compared with controls (Harrison *et al.*, 2006). Indeed, a study involving genetically modified mice ($CK^{-/-}$) showed not only that fast-twitch skeletal muscles from such mice had elevated concentrations of myoplasmic P_i at rest, but were also markedly weaker in terms of force production compared with the same fast-twitch muscles of wild-type mice (Westerblad *et al.*, 2002).

Surface electromyography and AMG for muscle assessment

What is electromyography

Electromyography, as a technique, started out as an invasive method for measuring a few motor units within a muscle using an electrode that was inserted through the skin and fascia (Pullman *et al.*, 2000). This technique, often referred to as needle EMG, ultimately causes damage to those fibres in the vicinity of the recording electrode and cannot be sensibly used during periods of physical activity. Later, the technique of sEMG was developed, recording from much larger areas of the muscle of interest, but doing so in a non-invasive and non-destructive fashion (Fig. 1).

Application

In a recent clinical trial using sEMG to assess physical function in 21 peritoneal dialysis patients and 11 healthy controls, the sEMG signal analysis of m. *Vastus lateralis* was only capable of revealing such simple conclusions as: (i) a high sEMG frequency and RMS score serves as a marker of good muscle function, and (ii) a short time interval from sEMG signal initiation to maximum frequency is a valid measure of a healthy muscle (Heaf *et al.*, 2010). These authors further concluded that uraemic patients exhibited a sEMG signal with a lower frequency and RMS score than healthy controls.

Considerations

The sEMG signal is well documented as being influenced by a number of variables: *technical*: temperature, humidity, electromagnetic fields, electrode construction, electrode-skin interface properties, amplifiers and filters; *experimental*: skin preparation, electrode configuration, contraction type, muscle length, contraction level, exercise duration; *descriptive*: signal processing, signal characteristics, chosen parameters, parameter estimates: and *physiological*: the physiological characteristics of the neuromuscular system, diameter of active fibres, spatial organization of the active fibres, motor unit spatial organization in the muscle, filtering properties of the tissue, fibre typing, motor unit recruitment, fatigue and muscular coordination (De Luca, 1979, 1992; Hermens *et al.*, 1999; Hogrel, 2005). It is for these very reasons that a great deal of care should be taken

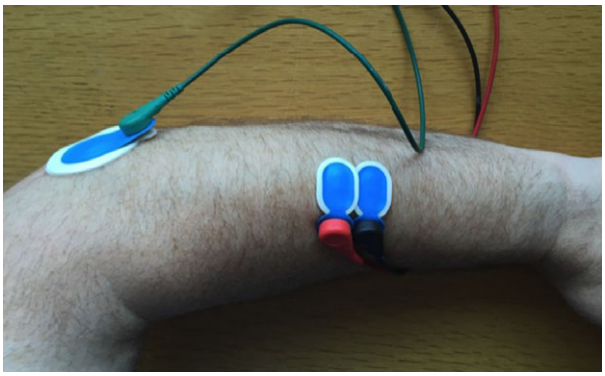

Figure 1 Typical surface electromyography (sEMG) recording electrode placement. The reference electrode (green cable) is placed close to the muscle of interest over a region with very few muscle fibres – elbow. The two recording electrodes (red and black cables) are then placed over the bulk of the muscle of interest with a set interelectrode distance (1·5 cm in this case). The sEMG signal is recorded as the difference between the two recording electrodes, minus the reference signal – a so-called double differential recording, using an amplifier and recording system.

when undertaking a sEMG measurement, especially if findings are to be reproducible and comparable. Therefore, the *European Recommendations for Surface ElectroMyoGraphy* were drafted (Hermens *et al.*, 1999).

One of the experimental issues that is repeatedly overlooked is that of electrode configuration (Merletti *et al.*, 2001). To illustrate this particular point, the author has recorded a sEMG signal from m. *Biceps brachii* during a period of physical activity – holding a weight in the palm of the hand with the forearm at 90° to the upper arm (Fig. 2). In this example, a sEMG recording was made from the upper, middle and lower regions of the muscle during the period of physical activity. It can clearly be seen that the amplitude of the recorded signal varies greatly with the location of the recording electrodes. It should be added that the reference electrode at the elbow remained constant for each recording. In the middle of the muscle, just above the innervation zone, the sEMG signal was the weakest, with a minimal amplitude. This has been reported many times before (Masuda *et al.*, 1985; Roy *et al.*, 1986; Mathiassen & Hägg, 1997; Rainoldi *et al.*, 2000). In a slightly more recent study, this very issue was made the focus of clinical and research applications of electromyography, and the authors concluded that '..electrodes should be positioned over the lower portion of the muscle and not the mid-point, which has been commonly used in previous studies..'' (Falla *et al.*, 2002). The reason for this phenomenon is of course due to the fact that a bipolar recording is being taken and that at the innervation zone, action potentials travel in both directions from the neuromuscular junctions. Thus, when differential recordings are made between adjacent electrodes positioned above the innervation zone, where the action potentials are travelling in both directions, the signals more or less cancel each other out, resulting in a very weak signal amplitude.

Surface electromyography and neuromuscular pathologies

Despite the detailed guidelines of the SENIAM project (Hermens *et al.*, 1999), eminent clinicians remain wary and doubtful as to the use of sEMG in clinical diagnosis and management of neural and muscular pathologies (Haig *et al.*, 1996; Pullman *et al.*, 2000).

In a recent review article, Hogrel raised the question as to the applicability of sEMG in a clinical setting (Hogrel, 2005). He stated that '..since its first description in 1984 {..}, surface electromyography is seldom used clinically in the evaluation of neuromuscular function..'. The main issues being the complex nature of the sEMG signal seen in the light of limited progress in terms of signal analysis, a lack of detailed correlation with underlying physiological processes and serious problems of reliability (Hogrel, 2005). Haig *et al.* (1996), in their assessment of sEMG in a clinical setting, went so far as to conclude that '..where correlation with disease is demonstrated, the clinical utility of the information gathered is not proven..'. The report by Pullman *et al.* (2000) is slightly more lenient, stating that '..surface electromyography may be used to classify movement disorders through measurement of frequency and amplitude of muscle activity..' serving as an acceptable tool for kinesiologic analysis of movement disorders, but based on Class II data, they conclude '..sEMG is considered unacceptable as a clinical tool in the diagnosis of neuromuscular disease at the present time..'.

In a more recent study of subjects with temporomandibular disorder (TMD), the authors likewise concluded that sEMG provides only a moderate sensitivity and specificity with regard to discriminating between healthy individuals and those with TMD, stating as their major reason of concern the variability of the sEMG data recorded (Santana-Mora *et al.*, 2014). Moreover, Manfredini and colleagues reached the same conclusions, stating that '..clinicians should not use sEMG and kinesiography devices as diagnostic tools for individual patients who might have myofascial pain in the jaw muscles..' (Manfredini *et al.*, 2011).

Surface electromyography and movement disorders

Returning to the application of sEMG in kinesiologic analysis of movement disorders, what evidence is there of accuracy and reproducibility with regard to 'fatigue' or 'training' for example?

Muscle fatigue, like the sEMG signal itself, is a complex physiological process involving metabolic, structural and energetic changes commonly grouped into three major topics: (i) central fatigue, (ii) neuromuscular junction fatigue, and (iii) muscle fatigue (Merletti *et al.*, 2004; Cifrek *et al.*, 2009). Indeed, it is often reported that sEMG lends itself to the continuous monitoring of myoelectric activity of specific muscles during periods of physical activity and that fatiguing

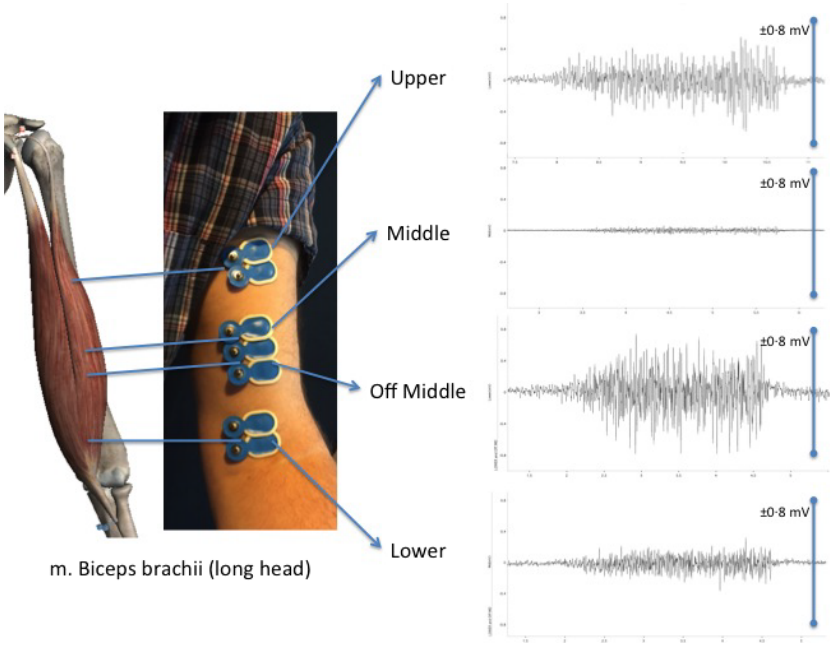

Figure 2 An example of the effects of electrode configuration on the surface electromyography signal recorded from m. *Biceps brachii* during a period of physical activity. A heavy weight was held in the palm of the hand whilst maintaining the forearm outstretched and at 90° to the upper arm. Inter-electrode distance was 20 mm (Ambu Blue Sensor N). The reference electrode (Ambu Blue Sensor R) was placed over the elbow. Note that the amplitude scale is identical for all four traces and that the best signal recording was obtained by placing the sensors over the region slightly lower than the middle of the muscle. Placement at the middle, above the innervation zone, results in the weakest recorded signal, and placement over the lower region where the muscle is interlaced with the tendon that attaches to the radial tuberosity, also gives a weak signal. Anatomical drawing source: Muscle Premium 5 App, Visible Body's – Argosy Publishing, Inc., 2007–2016.

contractions reflect properties of myoelectric signals recorded on the surface of active muscles (De Luca, 1984). A recent clinical study looked at the effects of a 16 week strength training programme in eight uraemic patients. Here, it was found that whilst the sEMG frequency over a 20-s period of sustained leg lift remained unaltered, a clear and significant ($P = 0{\cdot}017$) improvement in the amplitude of the recorded sEMG signal was noted when values taken pretraining were compared with those obtained post-training (Harrison *et al.*, 2012). Moreover, an isometric test (50% max) showed a significant decrease in peak frequency and mean frequency when expressed per kilo lifted (both $P = 0{\cdot}017$) for these same uraemic patients. These authors concluded that the strength training programme had resulted in enhanced spatial summation of the m. *Vastus lateralis* in these patients, enabling them to lift more weight (Harrison *et al.*, 2012).

Surface electromyography improvements

Clearly, there is a need for some improvement in the existing technique if sEMG is to be accepted as a clinical tool, and perhaps the work of Urbanek & van der Smagt (2015) represents just such an advance? These authors present the concept of imaging electromyography (iEMG) whereby the signal strength is related to muscle fibre distance using multiple sEMG electrodes, resulting in a reconstructed volumetric assessment of muscle activity (Urbanek & van der Smagt, 2015). With the aid of a 64 sEMG electrode array placed on a muscle of interest, a considerable degree of signal processing and some basic assumptions, these authors were able to demonstrate a 3D reconstruction of muscle activity in the forearm of six healthy male subjects (Urbanek & van der Smagt, 2015). Perhaps with improved mathematic models, smaller electrodes and more testing, iEMG may prove itself in the field of clinical diagnosis and management of neural and muscular diseases?

An alternative approach may be an improvement in the analysis of the complex recorded signal through some type of signal processing, making sEMG a valid, refined, accurate, useable and reproducible technique. Assuming that one takes a number of essential precautions with regard to *technical*, *experimental*, *descriptive* and *physiological* variables, how exactly should the raw sEMG signal be processed? In a recent paper, such signal processing approaches as time domain methods, spike analysis, frequency domains, Fourier transforms, time–frequency representations, wavelets, spectrum analyses and many other mathematical methods were reviewed with regard to sEMG analysis as a means of assessing muscle fatigue (Cifrek *et al.*, 2009). These authors were optimistic about the progress made to date in terms of arriving at a quantifiable sEMG analysis for what is a variable and complex state of skeletal muscle – namely that of muscle fatigue. However, a device capable of measuring 'muscle fatigue', which is based on the current sEMG method and many diverse mathematical methods

available, and which is capable of being applied to a clinical diagnostic context, both in sport and medical rehabilitation, has yet to be realized (Cifrek *et al.*, 2009).

What is acoustic myography

When muscle fibres contract, they generate vibrations. Perhaps the best known example of this is during cold exposure when skeletal muscles begin to shake visibly, creating warmth by expending energy in the process we know as shivering (Harrison *et al.*, 1994). Whilst, muscle fibre contractions are not always visible, they do vibrate in active muscles, and as such produce pressure waves, which can be recorded at the level of the skin above a muscle of interest.

In the past mechanomyography, sonomyography and other such techniques were tried and tested, but were found to suffer like sEMG from noise and interference, or simply prove to be insensitive to actual muscle frequencies, making them too imprecise to be of use as a diagnostic technique of muscle contractions (Hemmerling *et al.*, 2004; Shinohara & Søgaard, 2006; Beck *et al.*, 2010; Herda *et al.*, 2010; Tian *et al.*, 2010; Alves & Chau, 2011; Qi *et al.*, 2011). For example, early AMG recordings were often obtained using piezoelectric microphones with an air cavity between the skin and the sensor, a configuration that was subsequently shown with the aid of accelerometers to be incapable of detecting the lower frequency range of muscle contractions (Barry *et al.*, 1985).

Other techniques involving sensitive piezo-electric crystals proved too fragile and unsuited to the rigours of physical activity, limiting their application to very restricted movement rigs confined to laboratories that gave very little relevant information for the clinician or for sports trainers. For more detailed background, see the work of Stokes & Blythe (2001).

It is important to use an appropriate recording sensor when measuring such vibrations or pressure waves. Many studies have attempted to measure muscle contractions with the aid of accelerometers attached to the skin above the muscle of interest (Bajaj *et al.*, 2002; Hemmerling *et al.*, 2004; Beck *et al.*, 2010; Guo *et al.*, 2010; Alves & Chau, 2011), and whilst such a sensor can and does measure these pressure waves resulting from muscle fibre contraction, they also pick up the movements of the limb as it accelerates, decelerates, is lifted or lowered and particularly as it impacts a hard surface (e.g. the ground). In this way, accelerometers, as sensors of muscle contraction, are prone to a great deal of extraneous noise interference and have for this reason been largely abandoned as an accurate and repeatable means of measuring muscle contractions. It should be noted, however, that in cases involving evoked signals, accelerometers may prove to be more accurate than surface microphones, in terms of detecting muscle contractions, being free under such circumstances from movement artefact disturbances (Barry, 1992). Accelerometers also have the clear advantage of measuring data in units of m s^{-1}, which closely corresponds to actual muscle vibrations.

Muscle fibre vibrations, that is to say pressure waves, remain as such in the body. It is only when they reach the skin surface and are transmitted from tissue to air that they become sound waves (Stokes & Blythe, 2001). A number of studies have examined the possibility of recording such sound waves at the skin surface (Orizio *et al.*, 2003; Shinohara & Søgaard, 2006), and whilst very sensitive microphones can record these signals, they are often housed or mounted in a casing that receives extraneous noise interference, making them relatively inaccurate as a means of measuring muscle contractions.

If, however, one reduces the impedance at the skin/air interface with an acoustic gel, and adopt a very flat sensor that is devoid of casing, then accurate and sensitive measurements of muscle contractions, recorded using AMG, not only become possible, they also prove to be very repeatable (Harrison *et al.*, 2013).

Acoustic myography

With the improved accessibility of piezoelectric crystals, enabling accurate muscle-sound recordings transdermally, AMG has begun to be re-assessed in terms of its suitability and accuracy as a diagnostic tool for muscle function and performance (Harrison *et al.*, 2013; Fig. 3).

Many of the early AMG studies were undertaken with a great deal of care (Stokes & Blythe, 2001; Bajaj *et al.*, 2002; Hemmerling *et al.*, 2004; Guo *et al.*, 2010); however, a number of limiting factors still remain unresolved, namely the speed of sampling (on occasions too low), the size and weight of the equipment used (too big and heavy – preventing patients to move freely or wander outside of a laboratory environment), noise correction and, finally, the development of a better means of sensor/skin contact reducing sensor-air-tissue signal loss.

Recent advances have led to the development of a set-up for muscle-sound assessment which can be reliably applied without discomfort for the subject and which does not require specialist technical knowledge of the person carrying out the recordings (www.myodynamik.com; Harrison *et al.*, 2013). The CURO (MyoDynamik ApS) uses thin piezoelectric sensors with an acoustic gel, so extraneous noise and interference are almost negligible and a full working muscle frequency range is recorded (2–500 Hz), and the raw analogue signal is rapidly converted to a digital signal by a built in A/D converter for subsequent processing by an iPad using a specially designed App. The signal analysis is kept as simple and as pure as possible; only three parameters are analysed; the degree of efficiency/coordination with which the muscle is used (E-score); the number of active fibres recruited (spatial summation; S-score); and the frequency with which those active fibres are contracted (temporal summation; T-score), all three of which are utilized by the CNS when developing force in an active muscle (Fig. 4).

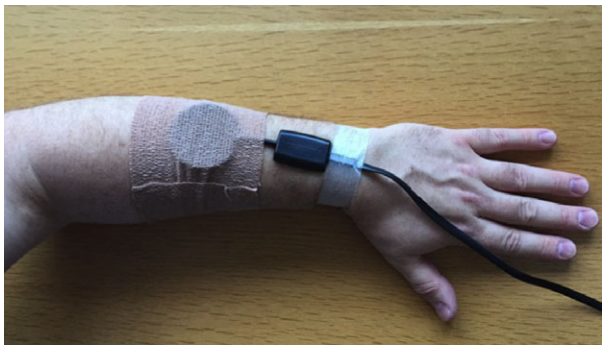

Figure 3 Typical acoustic myography recording set-up. This system only requires one sensor, unlike the three electrodes needed for surface electromyography. The sensor, which is flat, is covered on the skin side with an acoustic gel to reduce the impedance at the skin/sensor interface and then lightly held in place above the muscle of interest using a self-adhesive elastic bandage. An additional piece of tape can be used to secure the cable.

Acoustic myography and fatigue

Such an AMG signal, occurring in real time as it does, can also be used to assess the level of muscle fatigue. A stable amplitude and frequency being indicative of a non-fatigued muscle, and an irregular signal in terms of amplitude or frequency, or both parameters being a sign of early fatigue resulting in changes in the spatial or temporal summation (or both) parameters through CNS control (Fig. 5).

In addition, muscle performance and early signs of fatigue can be monitored in real time using this AMG set-up. Immediate changes in the S-score, which is a measure of spatial summation (Hunt & Kuffler, 1954), can inform the user as to whether more muscle fibres are being recruited with continuing physical performance. Likewise, a change in the T-score, which represents temporal summation (Hunt & Kuffler, 1954), can provide a minute-to-minute assessment of the frequency with which active fibres are being fired. Finally, the E-score, which represents muscle efficiency and coordination (Hunt & Kuffler, 1954), can be used to assess early fatigue signs. Typically, a fall in the E-score, representing relatively more fibre contraction time that relaxed time for a given physical activity, is an early sign of muscle fatigue.

Whilst on the subject of fatigue, it is important to point out that a number of muscle-related diseases, for example fibromyalgia, present with symptoms such as weakness, stiffness, exercise intolerance, tenderness and pain (Torgrimson-Ojerio *et al.*, 2014). It has been proposed that exercise-induced inflammatory responses in such patients originate from muscle microtrauma (Bruunsgaard *et al.*, 1997). Indeed, evidence in support of this proposal was reported much earlier by Danneskiold-Samsøe and colleagues, who found that an increase in myoglobin in the plasma of exercise intolerant patients following massage treatment was positively correlated with muscle tension (Danneskiold-Samsøe *et al.*, 1983). This group went on to discover that the degree of muscle tension in these subjects was correlated positively with pain, as well as an increase in plasma myoglobin concentration (Danneskiold-Samsøe *et al.*, 1986). In a more recent study, Graven-Nielsen and colleagues published results that showed that ketamine reduces muscle pain and also reduces temporal summation in fibromyalgia patients (Graven-Nielsen *et al.*, 2000). These authors were able to reveal a link between central hyperexcitability of muscles in subjects experiencing pain and the effects of pain relieving drugs, primarily a reduction in muscle temporal summation. This in noteworthy, as the AMG set-up reported in this manuscript appears to be able to accurately detect and monitor changes in temporal summation in a muscle, thereby providing an insight into not only muscle pain, but also the efficacy of various treatments.

AMG and patient monitoring/diagnosis

The AMG technique also lends itself to clinical assessment of a patient's muscle function and coordination. It is envisaged that

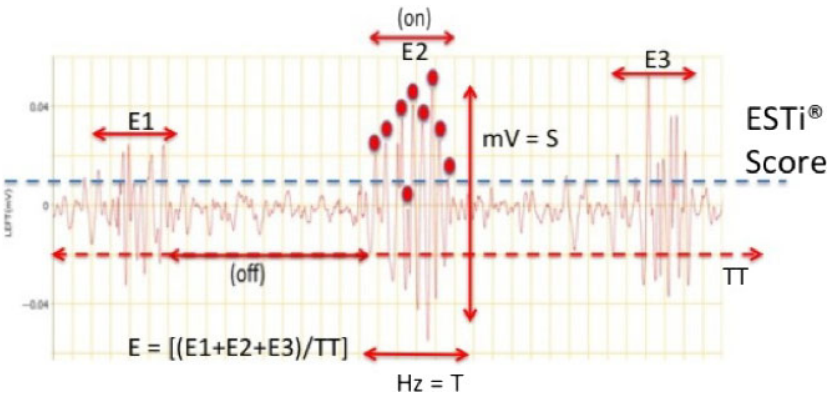

Figure 4 Acoustic myography (AMG) signals are analysed in terms of their spatial summation (S-score) and temporal summation (T-score) as well as their degree of efficiency/coordination – as measured by the period of activity 'on' (E1 + E2 + E3) as a proportion of the total activity time (TT) (E-score). To analyse the AMG signal, a threshold is determined (blue-dotted line) above which individual spikes are considered as being derived from muscle contractions (red circles). The three parameters E, S and T are also combined to provide an overall assessment of muscle function – known as the ESTi® Score.

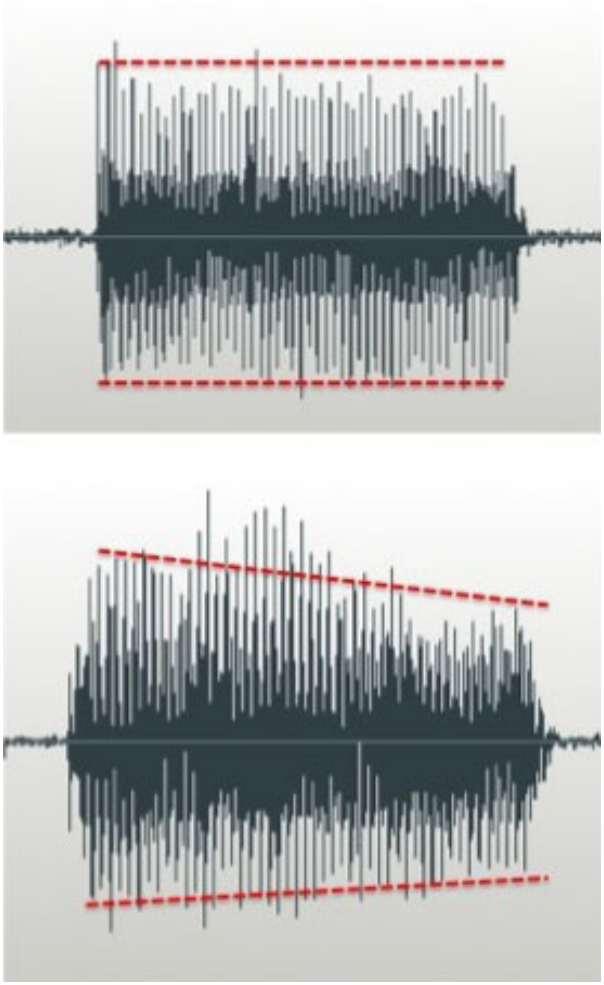

Figure 5 Acoustic myography signals can also be used to detect early signs of muscle fatigue as characterized by irregular muscle contractions, varying in intensity and amplitude. In the Upper Panel, a period of sustained contraction in a non-fatigued muscle has not only a similar frequency but also a very similar and stable amplitude. In the Lower Panel, this fatigued muscle shows signs of irregular amplitude – resulting in a decline in the signal during an identical period of contraction to that of the Upper Panel.

AMG could readily be applied to the clinical diagnosis and monitoring of such patient groups as Parkinson's disease, rheumatic diseases, Huntington's disease, myopathy, cerebral palsy, fibromyalgia, neuromuscular disease including amyotrophic lateral sclerosis, muscular dystrophy and radiculopathy, as well as such situations as sarcopenia assessment in the elderly and postsurgery/trauma monitoring (distance measurement) or retraining.

The AMG technique lends itself to such tests as diadochokinesis, which is often used as a means of assessing deficits in bimanual coordination in such patients as those with Parkinson's disease or Huntington's disease (Daneault *et al.*, 2015) as well as Multiple Sclerosis cases (Tjaden & Watling, 2003). Take, for example, a measurement of diadochokinesis involving supination and pronation of the right forearm, where measurements of the AMG signal from m. *Biceps brachii* were taken (Fig. 6). In this particular case, it is clear that supination results in a more powerful contraction than pronation. Note too, the very clean signal-to-noise ratio that is achievable with this technique.

Acoustic myography is also well suited to monitoring muscle changes in ALS patients. A baseline measurement of an ALS patient, in which the muscle function of m. *Flexor carpi radialis* was assessed for the right and left forearms by means of repeated voluntary movements, recorded an ESTi® Score of 4·9 Left and 3·2 Right. After a period of regular daily training covering a period of 21 days, the ESTi® Score was found to be 5·2 Left and 5·9 Right. The slight improvement in the left forearm was due to a slightly higher S-score and improved T-score, indicative of recruitment of fewer fibres and a lower firing rate, findings that not only support, but enhance those of Handa *et al.* (1995). In the right forearm, which was more affected by the disease than the left, the training period had not only improved both the S- and T-scores, but also improved the E-score, indicative of better coordination (Harrison, unpublished data).

In the case of recovery, post-trauma, AMG can be used to direct and follow muscle retraining in a safe and responsible way. In the example of an individual who partially ruptured the Achilles tendon of their right leg, AMG was used to monitor and direct a retraining programme (Fig. 7). The AMG signal not only increases in a linear fashion with increasing physical activity, speed or power, it also remains stable throughout a period of constant physical exertion and is not affected by sweat production.

Surface electromyography versus acoustic myography

It has previously been shown that the sEMG and AMG signal, recorded from the same muscle, have a very comparable initiation and completion time (Fig. 8; Harrison *et al.*, 2013). Furthermore, there is some evidence that a combination of AMG and sEMG signal amplitudes can reveal useful diagnostic information. In a study of 16 children with muscle disease and 11 age matched healthy controls, the AMG to sEMG ratio was found to be significantly different between the two groups (Barry *et al.*, 1990).

The AMG signal is, however, more informative than that obtained using sEMG in that it shows an initial low-amplitude phase followed by a final high-amplitude phase, indicative of the initial concentric contraction and final eccentric contraction phases associated with this particular muscle movement. Such details are not possible using sEMG as a diagnostic tool.

It is also important to mention that the AMG signal is not affected by the experimental issue of electrode configuration, to which sEMG is so sensitive, as shown in Fig 2. If one moves the AMG sensor to a different region of an active muscle, then a comparable signal amplitude is measured (Fig. 9). Indeed, the E-, S- and T-scores for these three AMG measurements are very similar, as is the integrated ESTi® Score.

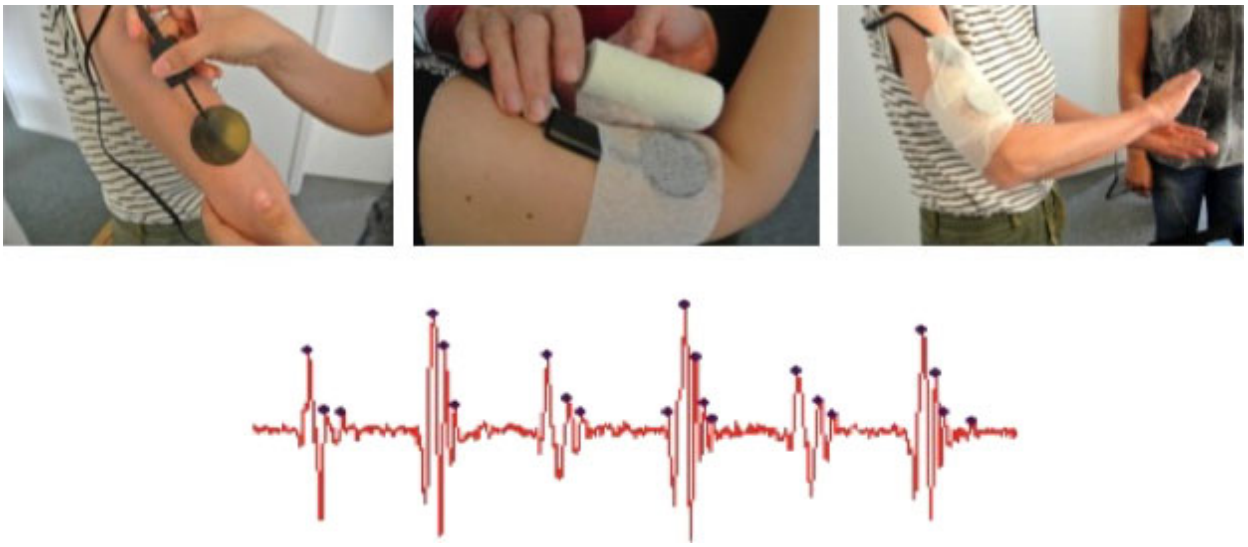

Figure 6 Acoustic myography (AMG) signals can be used for a number of clinical diagnostic tests – diadochokinesis for example. Here the ability to alternately bring a limb into opposite positions, for example flexion and extension or pronation and supination, can be assessed in real time, as well as saved for a more detailed analysis. Left Upper: a flat AMG sensor is wiped with acoustic gel and placed on the skin above the muscle of interest (m. *Biceps brachii* – long head). Middle Upper: the sensor is lightly held in place using an elastic self-adhesive bandage. Right Upper: the subject is then asked to alternate between placing the palm or the back of their right hand onto the open palm of their left hand. Lower: the AMG signal from this subject can be seen – it clearly shows period of muscle contraction interspersed with periods of inactivity in m. *Biceps brachii*. Note too that in this case supination results in a more powerful contraction than pronation. The small dark dots have been added to identify those spikes measured as being above threshold – these were recorded as being muscle contractions.

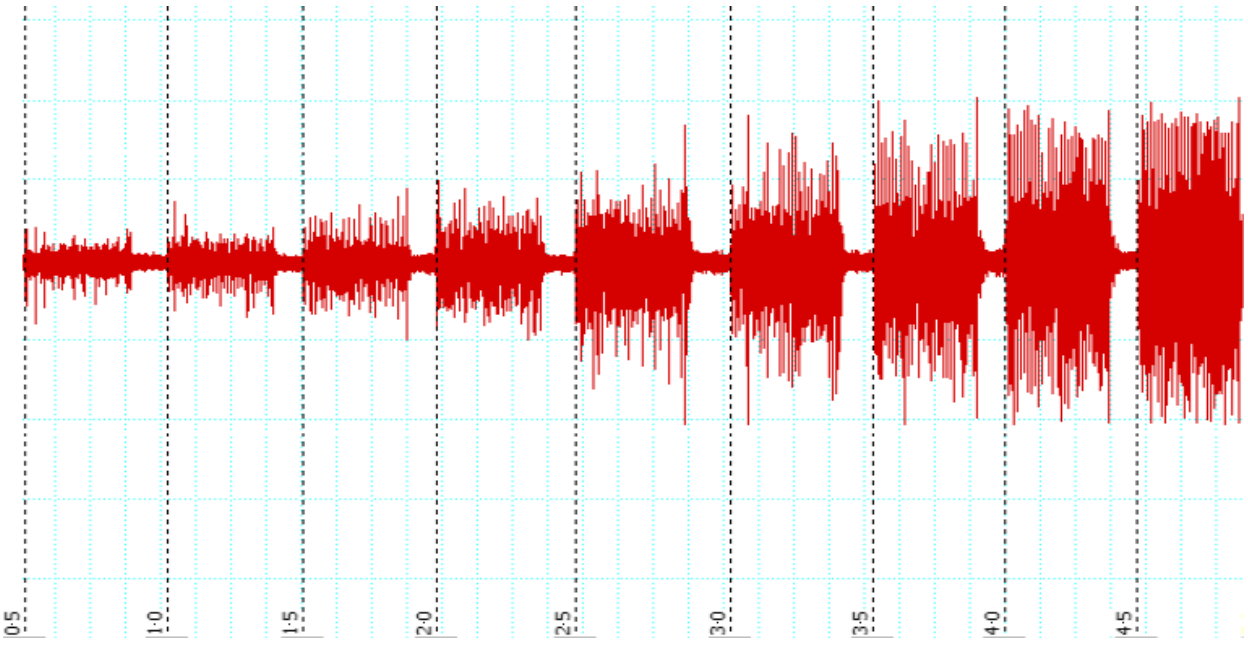

Figure 7 Acoustic myography (AMG) signals can also be correlated in a linear fashion with muscle work or the speed of movement. In the example below, AMG recordings were made from a patient that had suffered a partial rupture of their Achilles tendon, and after a period of rest, the AMG technique was used to assess the benefits of training in m. *Gastrocnemius*. This technique has the advantage of allowing the user to follow in real time and not only adjust the training programme to an individual needs, but also provide them with an overview of how long they should train safely. The AMG signals represent 30-s periods of walking/jogging on a treadmill with increasing speed from 0·5 to 4·5 km h^{-1} at 0·5 km h^{-1} increments. Note how stable the AMG signal is throughout the period of physical activity. Initially, this subject increased the number of active fibres in the muscle before finally increasing the firing rate of those active fibres to achieve the force of contraction required.

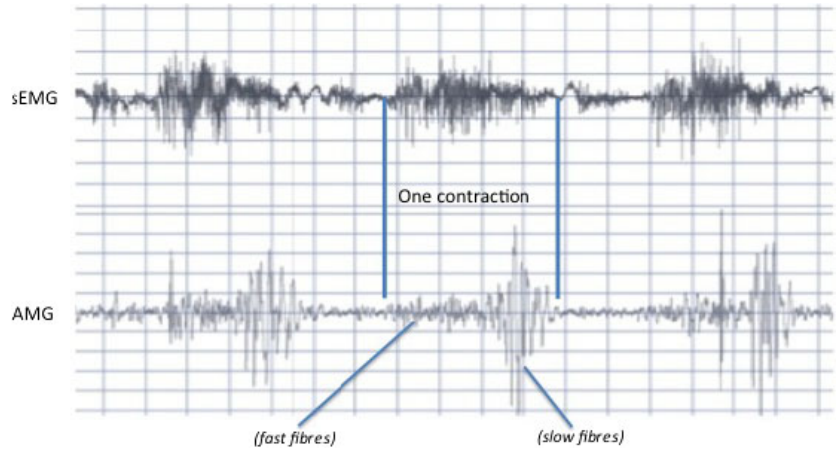

Figure 8 A simultaneous surface electromyography (sEMG) (upper trace) and AMG (lower trace) recording from m. *Gastrocnemius* of a healthy human control subject during a period of stair descent. Note: (i) the same time frame for the start and finish of the sEMG and AMG signals, and (ii) the clear fast-fibre (low amplitude – concentric contraction) phase and the slow-fibre (high amplitude – eccentric contraction) phase, only detectable using the AMG technique.

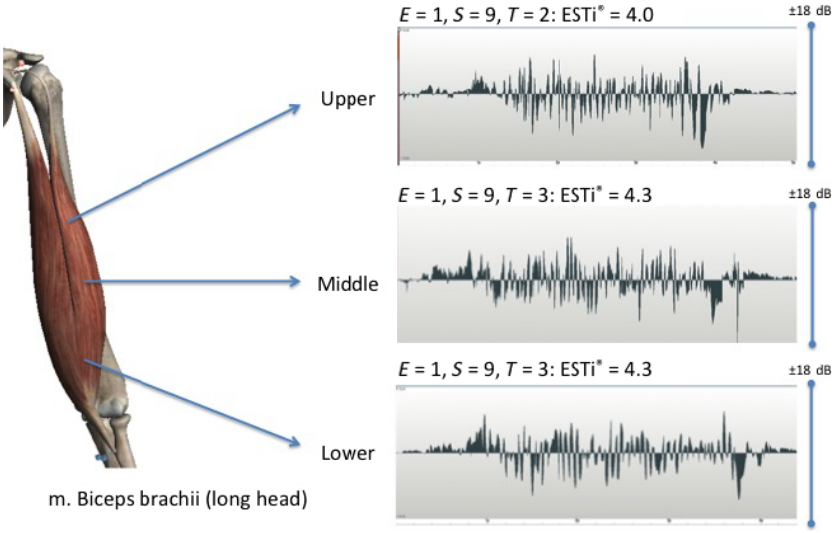

Figure 9 The acoustic myography signal from the upper, middle and lower regions of m. *Biceps brachii*, recorded during a period of physical activity. A heavy weight was held in the palm of the hand whilst maintaining the forearm outstretched and at 90° to the upper arm. Note that the amplitude scale is identical for all three traces, and that the E-, S- and T-scores, as well as the integrated ESTi® Score are all very comparable. Note too that for this type of contraction the E-score is very low, indicating almost constant muscle activation with very few inactive periods, that the S-score is high indicative of very few active muscle fibres, but that the T-score is low indicating a relatively high firing frequency of those active muscle fibres. Anatomical drawing source: Muscle Premium 5 App, Visible Body's – Argosy Publishing, Inc., 2007–2016.

A more detailed comparison of the advantages of AMG compared with sEMG can be found in Table 1.

Discussion

Whilst muscle monitoring using sEMG has a number of advantages and is a well-known technique, it also poses a number of problems, not least signal distortion during sweating, background noise disturbances, a combined neuro-muscular signal and interpretation difficulties in relation to physiological processes that limit its potential as a diagnostic tool (Haig *et al.*, 1996; Hermens *et al.*, 1999; Pullman *et al.*, 2000). It is, furthermore, confounded by issues relating to the variability of the recorded data (Santana-Mora *et al.*, 2014), some of which arise from incorrect placement of the sensors, as illustrated by Fig. 2. It is therefore important that an improved technique, capable of accurate, reproducible and understandable monitoring of muscle contractions is developed.

Perhaps the greatest drawback with regard to sEMG is related to the cases in which a failure of muscle contraction occurs. Muscle contraction failure or loss is categorized as 'central' when there is volitional or non-volitional failure of neural drive to muscles, or 'peripheral' when there is failure in force generation by mechanisms at or beyond the neuromuscular junction (Katz, 1966). sEMG measurements are not capable of discerning whether the exhibited changes in the

Table 1 The Pros and Cons of acoustic myography versus surface electromyography as a means of measuring muscle contractions in active subjects non-invasively.

	AMG	sEMG
Signal	A pure muscle contraction signal	A combined signal of nerve and muscle fibre depolarization
Accuracy	An accurate measurement of muscle contraction	Not an accurate measurement of muscle contraction – more of muscle depolarization
Stability	A stable signal during movement unaffected by sweating	An unstable signal – affected by movement, and distorted or lost during sweating
Lead artefacts	The signal recorded is not affected by lead movements	Very sensitive to lead movements – resulting in baseline shift
Interpretation	The signal recorded can be analysed into its concentric and eccentric phases	No clear concentric or eccentric phases can be discerned
Noise	The signal is not prone to extraneous noise from electromagnetic fields	Often affected by electric motors, treadmills or electromagnetic fields
Correlation	ESTi® Score signals (amplitude, frequency and efficiency) have been found to correlate in a linear fashion with muscle power	Less accurate correlation – usually a root mean square (RMS) of the signal has to be performed before muscle force correlations can be made
Preparation	There is no need to prepare the recording site, neither shaving nor alcohol wash is necessary	Typically, one would shave and clean the contact site prior to attaching an electrode
M-wave & H-wave	AMG recordings lend themselves to simple and accurate M-wave and H-wave recordings	sEMG recordings of M- and H-waves are technically more difficult
Placement	Only one sensor is needed and placement is less crucial with regard to the recorded signal	Three electrodes are required and their configuration is important for signal quality
Inactivity	The signal is noise-free during periods of inactivity	Background noise can often interfere with the signal during inactivity or slight movements – often requiring filtering
Repeatability	The same sensors can be used again for the same muscle or a subsequent measurement – improving repeatability	Electrodes have to be discarded after a single use and can be affected by storage/age

interference sEMG signal are due to factors affecting muscle contraction centrally or peripherally as they combine both neural depolarization and muscle depolarization signals. It is for this reason that any factor affecting a muscle in a direct way (e.g. postneuromuscular junction) cannot be accurately assessed using sEMG. Such factors include H^+ build-up, the ratio of intracellular to extracellular K^+ at the fibre membrane, elevated plasma Mg^{++} and plasma P_i concentration (Bevington *et al.*, 1986; Thompson & Fitts, 1992; Fitts, 1994; Yu-Yahiro, 1994; Nielsen & Overgaard, 1996; Westerblad *et al.*, 2002). However, any number of factors that effect changes in the sarcolemma of muscle fibres can induce fatigue by preventing cell activation (Sjøgaard, 1990) and these will in turn add to the inaccuracy of sEMG as a diagnostic tool.

The situation is further complicated by the fact that there is now considerable evidence that reactive oxygen species (ROS) and nitric oxide (NO) derivatives play a role in skeletal muscle contractile function (Reid, 2001). It is known, for example, that ROS and NO are continually generated in the muscles of healthy individuals (Reid *et al.*, 1993; Reid, 2001). At rest, skeletal muscles produce ROS and NO at a low rate, but these levels can be dramatically accelerated during periods of contractile activity (Reid, 2001). The low ROS levels present under basal conditions are essential for normal force production, and studies show that depletion of ROS in non-fatigued muscles results in a fall in muscle force upon activation (cited in Reid, 2001; source: Andrade *et al.*, 1998; Reid, 1998; Reid *et al.*, 1993).

Current research involving skinned fibres suggests that the effects of ROS and NO are at the level of the ryanodine sensitive calcium release channel of the sarcoplasmic reticulum (SR) and also at the level of the SR calcium-dependent ATPase, although myosin heavy chains and troponin are known to be redox sensitive (Scherer & Deamer, 1986; Viner *et al.*, 1996; Anzai *et al.*, 2000).

It has also been shown that nNOS appears to mediate changes in muscle gene expression in response to mechanical stimuli, to modulate glucose transport and neuromuscular transmission (Balon, 1998; Grozdanovic & Baumgarten, 1999). Indeed, evidence suggests that NO mediates the expression of cytoskeletal proteins in response to mechanical stimuli and is essential for the addition of sarcomeres when working length is chronically increased (Koh & Tidball, 1999; Tidball *et al.*, 1999).

None of these regulatory effects would be detected using sEMG, supporting the comments in the literature that '..where correlation with disease is demonstrated, the clinical utility of the [sEMG] information gathered is not proven..' (Haig *et al.*, 1996), and '..sEMG is considered unacceptable as a clinical tool in the diagnosis of neuromuscular disease at the present time..' (Pullman *et al.*, 2000).

In contrast, AMG, which solely records muscle contractions, detected as pressure waves that are transmitted through the

body tissues to the skin and *via* an acoustic gel at the skin/air interface to a thin yet sensitive sensor are capable of monitoring and measuring failure in force generation by mechanisms at or beyond the neuromuscular junction. In this way, an elevated plasma P_i or Mg^{++}, an elevated extracellular K^+ concentration or elevated H^+ levels resulting in a loss of muscle fibre excitability and force production, would be detected as a weak AMG signal. Likewise, depletion of ROS in non-fatigued muscles resulting in impaired force production would also be detected using AMG.

In the face of repeated evidence that demonstrates that the sEMG technique, which cannot detect whether changes in the recorded signal are the result of a change in innervation or a change in the muscle fibres, is unsuitable in terms of confounding experimental issues (Haig *et al.*, 1996; Falla *et al.*, 2002; Santana-Mora *et al.*, 2014), the variability of the recorded signals (Santana-Mora *et al.*, 2014) as well as inaccuracies arising during signal analysis (Cifrek *et al.*, 2009), is it not time that an alternative technique be explored? Indeed, just such a technique, which appears capable of detecting muscle contractions in an accurate, reproducibly and explanatory fashion, appears to exist in the form of AMG. Should this not now be assessed in terms of its potential as a diagnostic tool in both clinical and sports settings?

The CURO system and ESTi® Score presented in this work adds to the knowledge obtained from previous attempts to record muscle sounds during contractions in human subjects (Stokes & Blythe, 2001; Bajaj *et al.*, 2002; Guo *et al.*, 2010). Through recent technological advances, it has been possible to demonstrate the strength and potential of the AMG technique, which has been validated against the more established sEMG method (Harrison *et al.*, 2013). Indeed, it has been shown that when measured together with sEMG (Fig. 8), the AMG signal clearly follows the sEMG pattern. It is also clear that high-frequency muscle sounds can be recorded using AMG, they just have small amplitudes, making an adequate sampling speed and signal-to-noise ratio essential for accuracy. To better understand the acoustic signal in terms of the signal amplitude (S-score) for a given type of physical activity, one needs first to consider the physics of structures or materials that have a tendency to oscillate. In such structures or materials, one finds that a low-frequency oscillation results in a relatively high amplitude signal (dB magnitude) compared to a high-frequency oscillation, where much smaller amplitude (dB magnitude) arises (Holm & Toiviainen, 2004). AMG recordings clearly reveal both the concentric and eccentric phase of contraction (Fig. 8), demonstrated in the presented case by the complex movement of stair descent.

This inherent property of muscle fibres can now be accurately detected and used as a diagnostic tool in the clinics. Moreover, the fact that the AMG sensors used are thin and that they have no housing or casing means that such small amplitude signals can be detected and recorded accurately without interference from background noise. It is therefore proposed that this new AMG technique provides an exciting insight into coordination and movement that can be of benefit to a number of fields and disciplines.

Conclusions

Surface EMG is a safe, quick, pain-free, non-invasive and repeatable technique that is often used for assessing physiological processes that cause muscles to generate force and produce movement. However, as a diagnostic technique, it has a number of limitations, which seriously restrict its use as a clinical tool. In contrast, the relatively new and portable technique of AMG shows considerable promise as a non-invasive method for assessing movement, movement type, muscle power and early fatigue status in most settings.

Is it not time for muscle scientists, whether their focus be clinical, research, physiotherapy or sports related, to begin to use techniques that accurately measure muscle contractions? Moreover, is it also not time to dispel the myth that muscle contractions are solely regulated by neural stimuli?

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Conflict of interest

AH is currently trying to commercialize the AMG recording system and is establishing a company to cover the costs of future development.

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