Neuromuscular Electrical Stimulation for Treatment of Muscle Impairment: Critical Review and Recommendations for Clinical Practice

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ABSTRACT

Purpose: In response to requests from physiotherapists for guidance on optimal stimulation of muscle using neuromuscular electrical stimulation (NMES), a review, synthesis, and extraction of key data from the literature was undertaken by six Canadian physical therapy (PT) educators, clinicians, and researchers in the field of electrophysical agents. The objective was to identify commonly treated conditions for which there was a substantial body of literature from which to draw conclusions regarding the effectiveness of NMES. Included studies had to apply NMES with visible and tetanic muscle contractions. ***Method:*** Four electronic databases (CINAHL, Embase, PUBMED, and SCOPUS) were searched for relevant literature published between database inceptions until May 2015. Additional articles were identified from bibliographies of the systematic reviews and from personal collections. ***Results:*** The extracted data were synthesized using a consensus process among the authors to provide recommendations for optimal stimulation parameters and application techniques to address muscle impairments associated with the following conditions: stroke (upper or lower extremity; both acute and chronic), anterior cruciate ligament reconstruction, patellofemoral pain syndrome, knee osteoarthritis, and total knee arthroplasty as well as critical illness and advanced disease states. Summaries of key details from each study incorporated into the review were also developed. The final sections of the article outline the recommended terminology for describing practice using electrical currents and provide tips for safe and effective clinical practice using NMES. ***Conclusion:*** This article provides physiotherapists with a resource to enable evidence-informed, effective use of NMES for PT practice.

Key Words: critical care; orthopaedics; physical therapy modalities; rehabilitation; stroke; therapeutic electrical stimulation.

RÉSUMÉ

Objectif : en réponse à des demandes de conseils de physiothérapeutes pour optimiser la stimulation musculaire à l'aide de la stimulation électrique neuromusculaire (SENM), une revue, une synthèse et une extraction de données de la littérature ont été entreprises par six formateurs, cliniciens et chercheurs en physiothérapie dans le domaine des agents électrophysiques. L'objectif était de cibler des affections couramment traitées ayant fait l'objet d'une quantité suffisante d'études pour tirer des conclusions concernant l'efficacité de la SENM. Les études devaient porter sur la SENM produisant des contractions musculaires visibles et toniques. ***Méthodes :*** quatre bases de données électroniques (CINAHL, Embase, PubMed et Scopus) ont été parcourues à la recherche d'études pertinentes publiées entre la création des bases de données et mai 2015. D'autres articles ont été tirés de bibliographies de revues systématiques et de collections personnelles. ***Résultats :*** les données extraites ont été synthétisées par consensus des auteurs en vue de dresser des recommandations sur l'optimisation des paramètres et des techniques d'application de la stimulation dans le traitement de déficits musculaires associés aux affections suivantes: accident vasculaire cérébral (extrémité inférieure ou supérieure; aigu ou chronique), reconstruction du ligament croisé antérieur, syndrome fémoro-rotulien douloureux, arthrose du genou et arthroplastie totale du genou, ainsi que des maladies graves et en stade avancé. Les auteurs fournissent également un résumé des éléments clés de chaque étude incluse dans la revue. Enfin, ils recommandent une nomenclature de l'électrothérapie et présentent des conseils pour l'utilisation sécuritaire et efficace de la SENM. ***Conclusion :*** ce document constitue pour les physiothérapeutes une ressource permettant d'appuyer leur utilisation de la SENM sur des données probantes.

INTRODUCTION

This article was developed by six Canadian physical therapy (PT) educators, clinicians, and researchers dedicated to evidence-informed practice in the use of electrophysical agents (EPAs). Although a previous publication, "Electrophysical Agents—Contraindications and Precautions: An Evidence-Based Approach to Clinical Decision Making in Physical Therapy,"[1] has become a widely used reference, nationally and internationally, for informing safe application of EPAs, there is still no resource to guide the effective application of EPAs.

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Impetus

The project was initiated in response to requests from physical therapists across Canada for guidance on which EPA parameters to select to effectively facilitate and enhance their patients' recovery from injury, disease, or immobility. Specifically, they asked for a resource that would provide (1) summaries of the best evidence to support the use of EPAs and (2) recommendations for the effective parameters and application techniques required to achieve optimal results. Many of the therapists' questions concerned the plethora of parameter options associated with neuromuscular electrical stimulation (NMES) devices (low-frequency current, medium-frequency current, monopolar pulses, bipolar pulses, etc.); thus, we selected NMES as the first EPA to address.

Numerous systematic reviews, with or without meta-analysis, have been published regarding PT interventions that use EPAs. In some instances, the research has been synthesized into clinical practice guidelines. In a meta-analysis, results from several studies can be pooled, and if the overall effect favours the treatment, it is considered the highest level of evidence to support the use of that treatment in clinical practice. However, most systematic reviews give little appraisal of the appropriateness of protocols or parameters used in individual studies, and they provide very little direction regarding the optimal parameters and application techniques for specific treatment interventions. Furthermore, systematic reviews commonly incorporate a wide range of approaches that use the treatment of interest and then pool results, so the benefits of a particular treatment protocol or specific approach can be missed. In this article, we have used a critical synthesis of the evidence to recommend specific parameters and techniques that are most likely to optimize effectiveness.

Scope

In this article, the abbreviation *NMES* refers to forms of therapy that apply electrical currents over muscles and nerves in a manner that produces smooth tetanic muscle contractions that simulate an exercise therapy session. However, NMES is distinct from exercise in that although the muscle is contracting, it is not voluntarily contracting; NMES is also not a passive modality because the muscle is active. The possible mechanisms by which NMES strengthens muscle and retrains limb movements, as well as the differences between voluntarily recruited and NMES-activated muscle contractions, are much debated; views are often contradictory. This article does not focus on the physiological basis of NMES effects, for example metabolic changes, neural adaptations, and fatigue resistance; for discussion of these issues, the reader is referred to alternative sources.[2–5] Some physical therapists hold the view that NMES is useful only when combined with simultaneous voluntary contraction of the target muscle; however, the extensive literature that we reviewed for this project does not support this viewpoint. Rather, electrically stimulated muscle contractions may be appropriate therapy with or without patient participation and whether or not limb movement is produced. This article also includes a brief description of what some refer to as *functional electrical stimulation* (FES). However, we should note that there are differences between NMES and FES; these are explained in Section 5, "Terms and Definitions in NMES."

To provide in-depth analyses, we limited this review to the following clinical conditions: stroke rehabilitation, orthopaedic conditions (hip and knee arthroplasty, anterior cruciate ligament [ACL] repair, patellofemoral pain syndrome [PFPS], and osteoarthritis [OA]), advanced disease states (mainly chronic obstructive pulmonary disease [COPD] and congestive heart failure [CHF]), and critical illness weakness associated with a stay in an intensive care unit (ICU). We included these conditions because they span the main areas of PT practice (neurology, orthopaedics, cardiopulmonary), represent patient groups seen in a variety of health care settings, and were those specifically requested by clinicians. Specialized use of NMES in conditions such as spinal cord injury, incontinence, and pediatric neurology were excluded. In all the conditions included in this review, NMES has been used to activate, strengthen, or retrain muscles to improve outcomes or hasten the achievement of treatment goals.

Throughout this article, we provide details and analysis of clinical studies in which NMES was used in a manner that is relevant to PT practice. We focused on the details of the treatment interventions—in particular, the stimulus parameters, application techniques, and treatment schedules evaluated in each included study. We hope that by taking this approach, and by recommending treatment protocols that are most likely to produce improvements in their patients, this document will be useful to clinicians. The final sections of the article include a guide to safe practice and definitions of the terms that we recommend clinicians use when working in this field. Ultimately, we aim to promote effective and safe EPA practice among physical therapists that is based on best evidence.

Purpose

The purpose of this document is to provide physical therapists with an evidence-based resource that can guide clinical decision making, thereby enabling clinicians to make effective use of electrical stimulation to improve muscle function in patients with musculoskeletal, neuromuscular, and critical care illnesses.

The specific objectives of this review are to

1. Increase awareness of the range of applications for NMES;
2. Demonstrate how NMES protocols are specifically designed to meet different treatment goals (e.g., strengthening vs. endurance training) and are customized to match the unique circumstances of each clinical situation (e.g., stage of recovery, level of fatigue);

3. Appraise the research related to NMES in the included conditions;
4. Provide general recommendations that will promote best practices for applying NMES in a safe and effective manner; and
5. Suggest terminology that should be used to describe NMES parameters and device features to facilitate communication among physical therapists, equipment suppliers, and other members of the clinical community.

METHODS

Literature searches

We used a deliberate, collaborative, and consensual selection process that included all authors. Four electronic databases were used (CINAHL, Embase, PUBMED, and SCOPUS) to search for relevant literature that had been published between database inceptions through May 4, 2015. We worked in pairs to identify relevant citations, for which the full articles were then retrieved. Additional articles were identified by hand searching the bibliographies in the systematic reviews and searching our personal libraries. We reviewed the full text of selected articles to confirm that all included studies met predetermined criteria and fit the objectives of the review.

Selection of studies

Types of NMES interventions

Articles included in this review involved the application of NMES in such a way that visible and tetanic contractions of muscles were reported or could be expected to occur, even if not seen (e.g., some patients in ICU). We did not include studies in which only sensory-level electrical stimulation was applied (often called *transcutaneous electrical nerve stimulation,* or TENS) or in which electrical current was applied to muscle in experimental laboratory settings to elucidate underlying physiological effects. To ensure that clinicians could reasonably replicate the NMES protocols, we also eliminated studies that did not include at least three of the following parameters: frequency (measured in Hertz), ON:OFF duration (or use of a foot-pressure switch), amplitude, duration of application per session, and total number of NMES sessions or weeks of application.

Included in this review are studies that used NMES protocols that could be delivered within a typical PT treatment session and included patients who were at an acute or chronic stage of recovery. Treatment could be delivered in a variety of health care settings in which PT services would normally be provided, including outpatient clinics, community and home care, rehabilitation centres, acute care hospitals, and long-term care facilities. However, none of the included studies involved the use of NMES for denervated muscles (for an explanation of denervated muscles, see Section 4, ''Equipment and Application''). We also included studies that evaluated NMES protocols that were quite complex, such as those in which NMES was applied using multiple channels or in which current was activated by an external trigger (electromyography [EMG] or foot pressure). We did not include those using equipment that is either not available commercially or not feasible for use in PT practice; examples are computerized (robotic) devices that are preprogrammed to sequentially activate several different muscle groups, proprietary devices that have undisclosed NMES parameters, and equipment that requires very complicated set-up, usually found only in experimental laboratories. These types of studies are usually labelled as FES.

We excluded studies requiring procedures out of the scope of PT practice, such as placement of indwelling or implanted electrodes or requiring medication to be injected immediately before stimulation—for example, botulinum toxin (Botox) and lidocaine. Studies were included even if they were of dubious quality to provide a fair representation of the literature. We have highlighted some of the flaws pertaining to individual studies in the Comments column of the even-numbered tables (Tables 2–16). Readers who desire a complete quality appraisal can consult the systematic reviews, when available, which are also listed in these tables.

In most instances, NMES was not the sole therapy but was applied in combination with other interventions considered to be conventional care for that condition or setting. Conventional care included supervised strengthening programmes; home exercise programmes; slings; braces; gait aids and other supports used to prevent tissue damage; other commonly used, hands-on therapies—for example, neuro-developmental treatment (Bobath) and manual therapy; and therapies provided by other health care professions that are considered to be usual care.

Types of study design

We selected studies that included subjects with the clinical conditions of interest and that had been designed to determine the effect of NMES on muscle strength, limb function, or both (see Sections 1–3 on clinical conditions). The controlled studies, whether randomized or not, compared the effect of NMES administered either alone or in combination with conventional care (which could include PT) to an appropriate control group, who received the same conventional care. Seldom was NMES compared with sham or placebo NMES because the visible muscle contractions produced by NMES make the blinding of subjects and therapists impractical.

The included studies had to systematically evaluate the effect of NMES and control treatments on outcomes such as strength, range of motion (ROM), and spasticity as well as on other standardized outcome measures of limb or body function and global performance measures, such as activities of daily living and quality of life (QOL).

Because the primary objective of this article was to evaluate the effects of NMES on muscle function, we excluded studies that evaluated only outcomes such as QOL.

Within the three main clinical areas of interest, the literature search yielded studies clustered around certain common clinical conditions, giving us a body of literature to analyze in terms of parameters and effectiveness.

1. *Stroke rehabilitation:* NMES to promote muscle strengthening and recovery of limb function in adults (aged > 18 y) with hemiplegia who had recently been affected by a stroke (acute) and in those several months and even years after sustaining a stroke (chronic). Section 1 focuses on the three most common physical impairments affecting patient mobility and function: muscle weakness, abnormal muscle tone, and impaired motor control. The conditions reviewed are
   a. shoulder subluxation (sublux);
   b. loss of hand and upper extremity (UE) function; and
   c. gait impairments resulting from foot drop and impaired control of leg muscles.
2. *Musculoskeletal conditions:* NMES treatment of orthopaedic conditions affecting muscles of the lower extremity (LE), including both acute injuries and chronic conditions. The conditions addressed in Section 2 are
   a. post-operative management of ACL reconstruction (could include meniscal injuries);
   b. pre- and post-surgical care after joint (hip and knee) replacement; and
   c. treatment of chronic diseases and conditions affecting the knee, including
      i. OA and
      ii. PFPS.
3. *Critical illness and advanced disease states:* NMES used to prevent muscle deconditioning, which occurs in severe illness or gradually over time in those with chronic progressive diseases. The conditions reviewed in Section 3 are
   a. those affecting patients admitted to an ICU and
   b. chronic progressive diseases that cause muscle weakness and reduced endurance, such as
      i. moderate to severe COPD and
      ii. CHF.

Consensus process and presentation of findings

Individual study data were summarized by two assigned reviewers and entered into tables (even-numbered Tables 2–16) and checked by at least one other reviewer. Working pairs conducted a critical review of each study and, using the data, developed protocol recommendations for each main clinical area (odd-numbered Tables 1–15). Key articles were shared among all authors, and multiple iterations of the table entries were discussed until 100% agreement was reached. More important, the rationale for selecting specific NMES stimulus parameters and treatment schedules has been provided to enable clinicians to customize the specific parameters to meet the needs of a particular patient or stage of recovery.

Organization

This review is divided into five sections. Some readers may benefit from first reading Section 5, ''Terms and Definitions in NMES,'' because it lays out the language and terms we used when writing this article. Unfortunately, the language used in the literature to describe EPAs generally, and NMES protocols in particular, can be confusing; this is evidenced in the NMES parameters provided in the summary tables that follow, which in each case have been taken directly from the source. We believe that an important first step in promoting good practice in this field is to gain a good understanding of what terms mean and ensure that terms are used consistently in and across professions.

The layout of Sections 1–3 is similar: Indications and the rationale for using NMES for the specific condition are discussed, followed by a table (odd-numbered Tables 1–15) summarizing NMES treatment recommendations, the rationale for the recommendations, and a critical review of related research. The outcome measures listed in these tables are those used by investigators that showed significant improvements compared with control conditions. Even-numbered tables (Tables 2–16) report on the NMES protocols, outcome measures, and results of each study. Where detail is missing, the omission was by the original authors—that is, it was not reported. These tables are provided for the benefit of readers who are interested in the specifics from which the recommendations were derived. In addition, the tables highlight some of the strengths and weaknesses of each study and provide clinicians with an opportunity to compare and contrast NMES protocols used in positive and negative studies and to interpret the research and establish its relevance to their patient populations.

Section 4 of this article, ''Equipment and Application,'' is intended to support clinical decision making and describes a generalized approach to the use of NMES for patients with muscle impairments or motor control deficits. The section describes device features and treatment parameters that a clinician must set when designing an NMES protocol and provides a background rationale to assist clinicians in making these important choices. Furthermore, this section includes a general approach for the safe and effective use of NMES, recommending or discouraging common practices in PT on the basis of the potential benefit or risk.

Section 5 of the article describes terms and definitions related to the application of electrical currents.

1. Stroke Rehabilitation

1A. HEMIPLEGIC SHOULDER SUBLUXATION

Indications and rationale for using NMES

Shoulder subluxation resulting from weak muscles of the shoulder girdle is one of the underlying causes of shoulder pain and arm dysfunction post-stroke.[6] Weakness can cause the joint and tendons to become stretched or torn and the joint surfaces to become abraded and inflamed; in addition, traction on nerves can alter sensory perception and interfere with muscle innervation. Susceptibility to shoulder problems is greatest immediately after stroke, when shoulder muscles are flaccid and unable to hold the humeral head in proper alignment. However, shoulder injury can also occur in later stages of recovery, when some shoulder muscles become spastic and produce muscle imbalance. NMES is applied to prevent disuse atrophy and increase muscle strength, thereby preventing or reducing subluxation and in turn improving active, pain-free ROM and promoting the recovery of UE function.

Table 1 Summary of the Literature and Recommendations for Use of NMES in Hemiplegic Shoulder Subluxation

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
Prevention or treatment of shoulder sublux resulting from UE flaccidity post-stroke	**Electrode placement:** over muscle belly of supraspinatus and posterior deltoid. Avoid upper trapezius fibres and excessive shoulder shrug. Applying a second channel to stimulate the long head of biceps can be beneficial in correcting humeral head alignment.[7] **Body and limb position:** patient sitting with arm support **NMES waveform:** symmetric or asymmetric biphasic PC **Frequency:** 30–35 Hz **Pulse duration:** 250–350 μs **Current amplitude:** sufficient to produce a smooth, sustained muscle contraction and reduction of shoulder sublux **Work–rest cycle:** ON:OFF 10–15 s ON time with progressively shorter rest time (30 s ON time, 2 s OFF time). Ramp-up time (1–4 s) is set to ensure patient comfort; longer ramp-down time may be required to prevent pain or tissue stretching when the arm sags due to gravity. **Treatment schedule:** progress to 2–4 h/d on the basis of muscle fatigue **Session frequency:** 7 d/wk for 4–6 wk or until voluntary control has been restored **Initiation of NMES:** as soon as shoulder flaccidity occurs and before pain has manifested; applied in conjunction with other rehab strategies. Can be safely and comfortably applied within 24–72 h post-stroke. NMES can reduce existing sublux even 6 mo post-stroke; however, the likelihood of improvement markedly reduces with time post-stroke. Concurrent arm support is needed when NMES is turned off to prevent further stretching of joint structures.	• Reduced sublux (X-ray)[8–15] • Increased muscle strength (shoulder abduction and external rotation)[12] • Increased ROM[9,10] • Increased EMG activity[10,12] • Reduced pain at rest and with shoulder movement with either passive or active ROM[9,10] • Improved arm function (e.g., F-M, ARAT, MAS)[9,15]

Table 1 *continued*

Rationale for recommended NMES protocol	Pulse frequency of 30–35 Hz is similar to the normal rate of discharge of motor units in these muscles.[16] Lower or higher frequencies than occur naturally have been shown to reduce muscle force generation and result in more rapid decline in force generation thought to be due to fatigue.[17] Lee and colleagues[18] showed that muscles affected by stroke require higher amplitude and longer pulse duration of NMES than the non-paretic contralateral muscles. Rest time (i.e., OFF time) is progressively shortened over several weeks as muscle endurance increases, and less OFF time is required to offset fatigue. Treatments are applied until the arm recovers, flaccid paralysis subsides, and the shoulder muscles are able to support the arm against gravity.
Physiological effect of NMES	Activation of supraspinatus and deltoid muscles produces an orthotic substitution that prevents stretching of the joint capsule and creates better alignment of the humeral head in the glenoid fossa, which protects connective tissues and nerves in the shoulder region. NMES-induced recruitment of motor units improves strength[19] and may change muscle fibre composition, which is known to be affected by stroke.[20] It is uncertain whether NMES improves movement by reducing muscle spasticity.
Critical review of research evidence	• All 8 of the RCTs included in Table 2 that measured shoulder sublux reported significantly less displacement after NMES compared with CON.[8–15] NMES-induced improvements in shoulder sublux were also confirmed in 3 SRs[21–23] and 2 meta-analyses.[24,25] • Shoulder pain is frequently measured in studies that examine NMES effects on hemiplegic shoulder sublux. Only 2[9,26] of 9 studies in Table 2 that evaluated shoulder pain detected greater improvements after NMES. Methods used to measure pain and the timing after NMES varied greatly across these studies. Chantraine and colleagues[9] reported significantly lower VAS scores in those patients who had received NMES treatment 6–7 wk earlier. Faghri and Rodgers[26] found less limitation in active shoulder abduction resulting from pain at the conclusion of 6 wk of NMES but no difference between NMES and control groups 12 wk later. A large, methodologically rigorous study performed by Church and colleagues[27] in 2006 did not find significant differences in pain rating scales (unspecified) after 4 wk of real or sham NMES or at 12 wk post-stroke. With such contradictory findings, it is not surprising that meta-analyses examining the pooled effect of NMES on pain[24,25,28] did not find a benefit. Inconsistency among findings is likely because there are many causes of shoulder pain post-stroke: Pain can occur secondarily to orthopaedic disorders (e.g., rotator cuff tears, adhesive capsulitis) and neurological conditions (e.g., cortico-somatosensory dysthesia and thoracic nerve injury).[6] It is not clear whether subjects are being adequately screened for underlying shoulder injuries that are not amenable to NMES before being included in studies on hemiplegic shoulder sublux. • Arm function is also commonly measured in NMES studies on hemiplegic shoulder sublux. 3 of the included studies showed that NMES improved arm use and function post-stroke,[9,15,26] and 3 studies[11,14,27] did not detect a benefit. All the studies used different measures of arm function. Faghri and Rodgers[26] detected improvements using the modified Bobath Assessment Chart after 6 wk of NMES; however, these gains were not sustained 6 wk after treatment ended. Interestingly, a study with an ON:OFF:ON design showed improvements in arm function (and reduction in sublux) after 6 wk of NMES, which regressed slightly when NMES was suspended for 6 wk; however, the improvements were regained when NMES was reapplied for a further 6 wk.[15] The implication is that NMES should be continued longer than 6 wk in patients with acute, post-stroke shoulder sublux. The importance of an adequate treatment period is reinforced by the finding that arm function, measured by several different functional scales, including the ARAT and MAS, was no different than CON after 2–4 wk of NMES;[11,14,27] these negative studies all applied NMES for very short periods. Also of note is that benefits were seen only when NMES was initiated early after sustaining a stroke and not in those who had their stroke at least a year earlier.[15] • Systematic reviews that evaluated the pooled effect of NMES on arm function also produced conflicting findings. Ada and colleagues[29] pooled results of 3 RCTs (82 subjects) and found that NMES applied early post-stroke resulted in better functional scores. However, Vafadar and colleagues[25] recently found no overall effect of NMES on shoulder pain and eventual arm function. Vafadar and colleagues'[25] results were likely strongly influenced by a large study by Church and colleagues,[27] which involved patients within 2 d of stroke: 46% of subjects reported shoulder pain, and NMES was applied to shoulder muscles for 4 wk with no benefit to arm function measured with the ARAT. Control subjects received sham NMES. Church and colleagues[27] concluded that NMES treatment may worsen arm function, especially in those with severe paresis; however, they did not describe any rehab interventions other than NMES that were provided either during or up to 12 wk post-stroke. A more comprehensive rehab programme is usual for managing the subluxed shoulder post-stroke; in particular, the programme should address arm function if arm function is an important outcome. Furthermore, short-term NMES has been shown in other studies not to produce long-term effects in arm and hand function.

NMES = neuromuscular electrical stimulation; UE = upper extremity; ROM = range of motion; PC = pulsed current; rehab = rehabilitation; EMG = electromyography; F-M = Fugl-Meyer Assessment; ARAT = Action Research Arm Test; MAS = Motor Assessment Scale; RCT = randomized controlled trial; CON = control; SR = systematic review; VAS = visual analog scale.

Table 2 Details of Individual Studies on Use of NMES in Hemiplegic Shoulder Subluxation

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Baker and Parker (1986)[8] RCT $N = 63$ enrolled; $N = 63$ analyzed Included in SR[23–25]	Stroke with $\geq$5 mm shoulder sublux (X-ray) NMES ($n = 31$) CON ($n = 32$): used hemi-sling or wheelchair support for arm when standing or sitting	4×8 cm 1 channel Electrodes: active (negative) on supraspinatus; 1 on posterior deltoid; positioned to minimize shoulder shrugging Standing and sitting with arm support, hemi-sling, or wheelchair	Compensated monophasic PC 12–25 Hz critical fusion frequency PD nr ON:OFF 1:3 ratio; gradually progressed to 24:2 ratio based on muscle fatigue (no longer able to normalize GH joint alignment) Amplitude set to produce tetanic contraction	30 min/d TID, progressed to a single 6 to 7 h session 5 d/wk 6 wk	Shoulder sublux by X-ray (blinded observers) Pain: subjective and use of analgesic drugs (20 subjects each group) @ 0, 6, and 18 wk	Sublux: less shoulder displacement @ 6 wk NMES = 8.6 mm; 10/31 patients with $<$5 mm CON = 13.3 mm; 3/32 patients with $<$5 mm Maintained shoulder position NMES 13/32 patients CON: 11/32 patients @ 18 wk No relationship between displacement amount and pain level No significant between-groups differences in all other outcomes	Very comprehensive description of NMES protocol. Compensated monophasic waveform is equivalent to asymmetric biphasic PC (personal communication, October 2015).[8] Complete resolution of shoulder sublux was not achieved by either NMES or CON Rx. Therefore, authors suggested starting NMES earlier post-stroke before sublux develops. Extended Rx times (6 h/d) make longer term use of NMES impractical.
Chantraine and colleagues (1999)[9] RCT $N = 120$ enrolled; $N = 115$ analyzed Included in SR[28]	Acute stroke (2–4 wk post-stroke) with sublux and painful shoulder NMES + PT ($n = 60$) CON ($n = 60$): PT, PT using Bobath techniques	Electrode size nr 4 electrodes Electrode placement and limb position nr	Biphasic PC Set 1: 8 Hz, 90 min Set 2: 40 Hz, 30 min Set 3: 1 Hz, 10 min PD 350 μs ON time nr ON:OFF 1:5 Amplitude nr	Wk 1, 130 min/d; wk 2–3, 140 min/d; wk 4–5, 150 min/d 5 wk	Sublux: % change—X-ray (de Bats scale) Pain: % patients with no pain (VAS) Motor function: Active shoulder ROM—% patients with at least 60° flex and 40° ABD @ 0 wk and 3, 6, 12, and 24 mo post-stroke	Greater % of patients with improved sublux @ 3, 6, 12, and 24 mo Greater % of patients with no pain @ 3, 6, 12, and 24 mo Greater % of patients able to actively move through ROM @ 6, 12, and 24 mo	Recruited non-stroke patients (19/120 with ABI); therefore, excluded from many SRs. NMES that produced tetanic muscle contraction was only 30–401 min of 130–150 min Rx (23%). Amplitude nr and unclear whether this NMES protocol reduced the sublux. Measurement times related to onset of stroke; therefore, post-Rx measures were not taken until 7–9 wk after final NMES session.

Table 2 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Church and colleagues (2006)[27] RCT $N = 176$ enrolled; $N = 165$ analysed at 4 wk; $N = 155$ analysed at 3 mo Included in SR[23,25]	Acute stroke (4–7 d) with new upper limb problem; 46% had shoulder pain NMES ($n = 90$): NMES + stroke unit care CON ($n = 86$): sham NMES + stroke unit care	Electrode size nr 1 channel Electrodes: on supraspinatus and posterior deltoid Limb position nr	Waveform nr; PC 30 Hz PD nr ON:OFF 15:15 s 3 s ramp-up and ramp-down Amplitude comfortable muscle contraction	60 min TID 4 wk	Arm function: • ARAT • Frenchay Arm Test • Star Cancellation Test • Motricity Index Pain: upper limb @ 0, 4, and 12 wk	No differences between groups on any outcomes Subjects with shoulder pain (33% both groups) @ 12 wk	NMES applied very early post-stroke to prevent the development of shoulder pathology and pain. Largest sample size published to date. CON group received sham NMES to blind subjects; however, 71% of subjects in NMES group correctly identified intervention. This study is often quoted because of large sample size and rigorous RCT design.
Faghri and colleagues (1994)[10] RCT $N = 26$ enrolled; $N = 26$ analyzed Identical study was published in Faghri and Rodgers (1997)[26] Included in SR[23,28]	Acute stroke (16–17 d) with flaccid shoulder NMES ($n = 13$): NMES + PT CON ($n = 13$): PT	Electrode size nr 1 channel Electrodes: active on posterior deltoid, 1 on supraspinatus Seated in wheelchair with arm support	Waveform nr PC 35 Hz PD nr ON:OFF: 10:12 s; progressed to ON:OFF 30:2 s on the basis of muscle fatigue, defined as no muscle contraction at max amplitude Amplitude tetanic contraction adequate to reduce sublux	90 min progressed to 6 h/d, based on muscle fatigue 7 d/wk 6 wk	Sublux: GH head displacement Comparing affected with unaffected side: X-ray Pain: max AROM Shoulder ABD based on pain tolerance Arm function: modified Bobath Assessment Chart EMG activity posterior deltoid: change over time comparing affected with unaffected side Upper arm girth: method nr Arm muscle tone: Modified Gross Clinical Scale (0–4) @ 0, 6, and 12 wk	Sublux less @ 6 and 12 wk Pain: less limitation of shoulder ABD due to pain @ 6 wk but not 12 wk Arm function: increased @ 6 wk but not 12 wk Tone: improved @ 6 wk but not 12 wk No significant between-groups differences in all other outcomes	Clear description of NMES programme and measurement techniques Function, EMG, and tone were subjective measures, and there was no placebo Rx or assessor blinding.

Table 2 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Fil and colleagues (2011)[11] RCT $N = 62$ enrolled; $N = 48$ treated; $N = 48$ analyzed Included in SR[23]	Acute stroke ($\leq$2 d in hospital) with flaccid shoulder NMES ($n = 24$): NMES + Bobath CON ($n = 24$): shoulder protection + Bobath	Electrode size nr 1 channel Electrodes: 3 on supraspinatus, mid-deltoid, posterior deltoid Limb position nr	High-voltage PC 60 Hz PD 100 μs ON:OFF 5:5 s Amplitude set to visible contraction without discomfort	10 min/d BID 5 d/wk 2+ wk	Sublux: X-ray • Horizontal and vertical symmetry of shoulder • Vertical distance from humeral head to inferior border of acromion Motor recovery: MAS Tone: Modified Ashworth Scale ROM: goniometry @ d 0 and at D/C (12 + 2 d)	Reduced development of sublux 9 (33%) CON subjects and 0 (0%) NMES subjects @ D/C (12 d) Greater symmetry using NMES No between-groups differences in all other outcomes	Shoulder sublux was prevented despite quite short Rx times.
Kobayashi and colleagues (1999)[12] CCT $N = 17$ enrolled; $N = 17$ analyzed Included in SR[24,30]	Chronic stroke (90–190 d) with shoulder sublux and pain NMES supraspinatus ($n = 6$) NMES deltoid ($n = 6$) CON ($n = 5$): PT	3.5 × 4.0 cm 1 channel Electrodes on supraspinatus: active 5 cm from acromion on supraspinatus fossa; 1 on acromion; minimal contraction of upper trapezius Electrodes on deltoid: active 5 cm distal to acromion on mid-deltoid; one on posterior axilla Sitting with arm on adjacent table	Monophasic (negative) PC 20 Hz 300 μs ON:OFF 15:15 s 3 s ramp-up, 2 s ramp-down Amplitude set to tolerance to reduce sublux and confirmed by X-ray	5 min BID, increasing to 15 min BID 5 d/wk 6 wk	Sublux distance: X-ray—unstressed (relaxed, unsupported) vs. stressed state (3.5 kg weight) Difference between affected and unaffected side Sublux > 5 cm displacement Pain: VAS—15 cm during AROM shoulder ABD MRI examination to identify rotator cuff tear ABD force: strain gauge (3 trials isometric ABD) EMG activity: during shoulder ABD in sitting with arm against thorax Tone pectoralis major: Modified Ashworth Scale @ 0 and 6 wk	Deltoid and supraspinatus NMES improved sublux Deltoid NMES reduced sublux distance Deltoid NMES increased ABD force Deltoid and supraspinatus NMES increased EMG activity No significant between-group differences in all other outcomes	CON subjects refused NMES or were unable to tolerate continuous NMES. Randomized between 2 groups receiving NMES: supraspinatus or deltoid muscle. Mean time since stroke 190 d for CON subjects vs. 90 d for NMES-treated groups. Sample size very small in each group ($n = 5$–6/group), which may explain lack of statistical differences in supraspinatus group. *P*-values showed a strong trend ($p = 0.07$).

Table 2 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Koyuncu and colleagues (2010)[13] RCT $N = 50$ enrolled; $N = 50$ analyzed Included in SR[21,25]	Stroke with shoulder sublux and pain NMES ($n = 25$): NMES + PT CON ($n = 25$): PT	Electrode size nr 1 channel Electrodes: active on posterior deltoid and 1 on supraspinatus—avoiding activation of upper trapezius Sitting in armchair with sling to protect shoulder	Asymmetric biphasic PC 36 Hz 250 μs ON:OFF 10:30 s progressed to 12:2 s 1 s ramp-up and ramp-down Amplitude: tetanic contraction adequate to reduce sublux	5/d (60 min total) 5 d/wk 4 wk	Sublux: X-ray (Van Langenberghe classification) Pain: VAS during PROM and AROM of shoulder flexion and ABD @ 0 and 4 wk	Greater sublux reduction No significant between-groups differences in all other outcomes Pain worsened in CON group and not in NMES group, but did not reach significance.	Subjective measure of pain (VAS) but no subject blinding
Linn and colleagues (1999)[14] RCT $N = 40$ enrolled; $N = 40$ analyzed Included in SR[23,28]	Acute stroke (≤ 2 d) and arm weakness (manual muscle testing $<$ grade 2) NMES ($n = 20$): NMES + PT CON ($n = 20$): PT	Electrode size nr 1 channel Electrodes: on supraspinatus and posterior deltoid Limb position nr	Asymmetric biphasic PC 30 Hz 300 μs ON:OFF 15:15 s 3 s ramp-up and ramp-down included in ON time Amplitude to reduce sublux	Wk 1, 30 min/QID; wk 2–3, 45 min/ QID; wk 4, 60 min/QID 4 wk	Sublux: X-ray—grade (0–4) and vertical displacement of humeral head Pain: goniometry—pain-free passive external rotation Pain rating: NPRS Arm girth: tape measure Motor function: UE section of MAS @ 4 and 12 wk	Sublux score better and less vertical displacement @ 4 wk but not @ 12 wk No significant between-groups differences in all other outcomes Pain increased in both groups.	Blinded assessor Authors reported statistically significant differences in sublux between groups, although P-values > 0.05 (0.06 and 0.07).

Table 2 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Wang and colleagues[15] (2000) RCT A–B–A design $N = 32$ enrolled; $N = 32$ analyzed Results of this RCT were reported in 2 separate publications[15,31] Included in SR[23,25]	Acute ($\leq$21 d) and chronic ($\geq$365 d) stroke with minimum of 9.5 mm shoulder sublux Stratified into 2 groups on the basis of duration post-stroke (acute $n = 16$; chronic $n = 16$), then randomized to receive NMES + standard rehab ($n = 16$) CON: standard rehab ($n = 16$) A–B–A design with 6 wk Rx blocks: A = NMES, B = standard rehab	Electrode size nr 1 channel Electrodes: active on posterior deltoid; 1 on supraspinatus with minimized activation of upper trapezius Limb position nr	Asymmetric biphasic PC 10–24 Hz 300 μs ON:OFF 10:30 s progressed over 6 wk; ON time increased by 2 s every 1–2 d until 24 s ON; OFF time decreased by 2 s every 1–2 d until 2 s Amplitude set to tetanic muscle contraction	Wk 1, 30 min/d TID; wk 2–6, progressed to 6 h/d 5 d/wk 6 wk	Sublux: X-ray—distance from inferior border of acromion to superior aspect of humeral head (mm) PROM: goniometry—shoulder external rotation to pain tolerance Function: F-M Motor function: MAS (0–66) @ 0, 6, 12, and 18 wk	Acute stroke group: Sublux reduced @ 6 wk MAS improved @ 6 wk Minimal regression during wk 6–12 with only standard rehab and without NMES, which was regained during additional 6 wk period of NMES (wk 13–18); however, no significant improvement @ wk 18 compared with wk 6 No significant between-groups differences in all other outcomes Chronic stroke group: no significant differences in any outcomes	No improvement in motor function in individuals with stroke of long duration. In acute stroke, there was a slight reversal of gains when NMES was withdrawn prematurely. The loss was reversed when NMES was reapplied. A total of 32 subjects divided into 4 groups created small group size ($n = 8$).

NMES = neuromuscular electrical stimulation; CON = control; RCT = randomized controlled trial; SR = systematic review; sublux = subluxation; PC = pulsed current; PD = pulse duration; nr = not reported; GH = glenohumeral; TID = three times per day; Rx = treatment; PT = physiotherapy/physical therapy; VAS = visual analog scale; ROM = range of motion; ABD = abduction; EMG = electromyography; ABI = acquired brain injury; ARAT = Action Research Arm Test; AROM = active range of motion; max = maximum; BID = twice per day; MAS = Motor Assessment Scale; D/C = discharge; CCT = controlled clinical trial; MRI = magnetic resonance imaging; PROM = passive range of motion; QID = 4 times per day; NPRS = numerical pain rating scale; UE = upper extremity; F-M = Fugl-Meyer Assessment.

1B. UPPER EXTREMITY STROKE: WRIST AND FINGER EXTENSION

Indications and rationale for using NMES

Hemiplegia after stroke often results in flexor synergy of the wrist, hand, and fingers, which limits functional use of the hand and arm. Activation of the wrist extensors with NMES alone or EMG-triggered NMES (EMG-NMES) during purposeful hand movements can improve strength and active ROM of the wrist extensors. Repetitive, task-specific movements of the wrist and hand using NMES stimulation can prevent disuse atrophy and contractures and encourage functional use of the paretic hand.

Table 3 Summary of the Literature and Recommendations for Use of NMES or EMG-NMES for Wrist and Finger Extension

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
Wrist and finger extensor weakness	**Electrode placement:** Both recording EMG and stimulating electrodes were placed just distal to common extensor origin and halfway down the extensor surface of the forearm (on extensor carpi ulnaris, extensor carpi radialis, or both, aiming for a neutral position of the extended wrist in terms of radial and ulnar deviation) **Body and limb position:** patient seated, elbow flexed 90°, forearm pronated **NMES waveform:** asymmetric biphasic PC **Frequency:** 30–40 Hz to produce tetany[32–39] **Pulse duration:** 200 μs[32,33,39–41] or 300 μs[37,38,42–44] **Current amplitude:** individual maximum tolerated intensity; trying to achieve full wrist and finger ext **Work–rest cycle:** 10:30–60 s to avoid muscle fatigue **Treatment schedule:** average 30 min/d[33,34,37–39,44] **Session frequency:** 5 d/wk[33,38–40,43–46] over 4–8 wk;[32,33,37,38,40,43,45,46] extra wk may be required if applied > 6 mo post-stroke	• Increased muscle recruitment[32] • Increased wrist and finger extension[33,34,37,38] • Increased grip strength[37,38,47] • Increased wrist ROM[33,38,43] • Reduced flexor spasticity and increased reach[32,44] • Increased cortical activation[39] • Improved function (e.g., B&B,[34,39] UE F-M,[35,40,41,44] Barthel Index[38,43,44])
Rationale for recommended NMES protocol	EMG can be used in combination with NMES to detect and encourage voluntary movement and patient involvement. At an EMG threshold preset by the clinician, NMES stimulates contraction of the wrist extensor group and moves the wrist and hand through a functional range. Adding EMG to NMES protocols will require the patient to initiate the contraction; however, several studies have not shown superior outcomes when comparing EMG-NMES with NMES alone.[32,41,48] Electrodes placed over the wrist and finger extensor group using biphasic PC applied using small, portable devices is sufficient to move the wrist into at least 30° ext, without excessive finger ext, to allow finger grasping. Adding a second channel of electrodes on wrist flexors to stimulate wrist extensors and flexors alternately did not produce better clinical outcomes.[49] Pulse frequency should be set to the normal recruitment rate of forearm muscles (30–50 Hz); although higher frequency may produce greater muscle force, the muscle will tend to fatigue more quickly and limit total session duration. Comparison of high- (40 Hz) and low- (20 Hz) frequency stimulation produced similar outcomes,[50] whereas a doublet pattern of 20 Hz produced greater muscle force than continuous use of a single 20 Hz frequency.[51] Work–rest cycles are set to minimize muscle fatigue and allow as many repetitions of the movement as possible in a single session. Cauraugh and colleagues[34] showed that individuals with UE hemiplegia could move more blocks after receiving NMES with ON time set to 10 s than after a similar protocol with only 5 s ON time. Also, longer rest times between contractions will produce sustained muscle tension throughout the treatment session, whereas shorter rest times (5 or 10 s) will cause muscle fatigue and result in less voluntary muscle work over time.[19] Treatment schedule: NMES and EMG-NMES applied to wrist and finger extensors for at least 30 min/d, 5 d/wk, for 4 wk can improve muscle strength. Most studies that produced benefit were applied 150–210 min/wk.[32,33,37–39,41,44] Mangold and colleagues[36] concluded that 12 sessions of NMES applied to the wrist extensors for 25–30 min/d, 4 d/wk, for 4 wk (120 min/wk) was insufficient to produce changes in any outcome for people who had recently sustained a stroke. Hsu and colleagues[52] compared 30 and 60 min duration NMES for 5d/wk for 4 wk; a significant and similar improvement was detected in F-M and ARAT tests in both NMES groups compared with CON; therefore, no advantage was found for 60 min treatments. Most reports have suggested that functional changes are more likely when NMES is applied as soon after stroke as possible, when the patient has at least some ability to initiate hand and wrist movement (Chedoke-McMaster Stroke Assessment stage 5 of recovery).	

Table 3 *continued*

Physiological effect of NMES	NMES and EMG-NMES applied to the wrist extensors can improve upper limb function by increasing grip and wrist extensor strength and improving active ROM of the wrist and hand.[29,53] Increased cortical activity detected using fMRI[54] and transcranial magnetic stimulation tests[55] after NMES application to wrist extensors suggests that this treatment can enhance neuroplasticity and improve motor relearning after stroke. The effect of NMES on wrist flexor spasticity is not yet clear.
Critical review of research evidence	• Studies included in Table 4 evaluated the effect of adding NMES or EMG-NMES to a conventional rehab programme; in all but three studies,[32,45,46] significant improvement in outcomes was detected. NMES or EMG-NMES improved grip and wrist extensor strength in three studies[33,37,38] and increased active ROM of the wrist.[33,38,43] NMES-induced improvements in function were reported in 12 of the studies in Table 4. • Differences in functional outcome between NMES and control treatments were detected using F-M,[40–42,44] B&B,[34,39] and Barthel Index,[38,43,44] whereas MAS,[32,34,45] FIM,[30,38] and ARAT[38,46] were seldom associated with change. Improvements in arm function persisted 32 wk[37] and 6 mo[14] after the end of NMES. • 7 SRs[22,23,29,53,56–58] examined the effects on UE impairments, activity, and function of applying NMES and EMG-NMES to the wrist extensors post-stroke. Inclusion criteria were different for each SR, with the result that no 2 reviews included the same group of studies; thus, it is not surprising that pooled findings resulted in contradictory conclusions. • There are commercially available devices with pre-positioned EMG and NMES electrodes that allow for quick patient set-up or self-administration by the patient for home-based therapy (e.g., NESS Handmaster,[59] Automove).[49,55,60,61] More complicated computer-programmed, multi-channel devices that sequentially activate muscles to cause combined movements of the arm and hand are also available. NMES has also been applied in combination with other therapies such as bilateral movement,[62] positional feedback, and robotic powered devices;[63] however, the added benefit of these complicated and expensive devices has not been shown.[57,64] Patients who elect to use a device that incorporates EMG and NMES should consult a qualified therapist to fit the device properly and train them in how to use it safely and effectively. • There are conflicting results regarding the length and extent of carry-over of the benefits produced by NMES and EMG-NMES treatment (see Table 4).[32,35,37,38,41,44] Persch et al.[65] evaluated patients who had received 12 wk of NMES to wrist extensors and hand using a neuroprosthesis (Bioness H-200) and showed that functional improvements (ARAT, MAS, F-M) were retained 3 mo after ending the intervention; there are also studies that suggest functional gains are retained up to 9 mo after NMES intervention.[41,44] Benefit has been shown for patients who had sustained a stroke $>$ 1 yr before NMES initiation;[34,39] however, Hsu and colleagues[66] studied the response of 90 stroke survivors to 4 wk of NMES and found greater time since stroke and stroke severity were significant predictors of failure to improve on ARAT scores post-intervention.

NMES = neuromuscular electrical stimulation; EMG = electromyography; PC = pulsed current; ROM = range of motion; Hz = Hertz (cycles per second); ext = extension; B&B = Box & Block Test; UE = upper extremity; F-M = Fugl-Meyer; ARAT = Action Research Arm Test; CON = control; fMRI = functional magnetic resonance imaging; rehab = rehabilitation; MAS = Motor Assessment Scale; SR = systematic review.

Table 4 Details of Individual Studies on Use of NMES or EMG-NMES Treatment of Wrist and Hand Post-Stroke

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Barker and colleagues (2008)[32] RCT $N = 42$ enrolled; $N = 33$ analyzed Included in SR[23,57,67]	Chronic stroke (≥6 mo) NMES ($n = 10$): SMART with EMG-NMES NMES ($n = 13$): SMART alone CON ($n = 10$): no intervention	50 mm diameter 1 channel Electrodes on MP of triceps lateral head and on triceps insertion Sitting with arm on specialized table with SMART arm	Biphasic PC 50 Hz 200 μs ON:OFF 5–10:10–20 s; ramp-up and ramp-down 1 s Amplitude max tolerated	60 min/d 3/wk 4 wk	Function: MAS UE Triceps muscle strength: MMT; peak isometric force triceps Resistance to passive elbow movement: Modified Ashworth Scale Reaching distance @ 0, 4, and 12 wk	Both SMART groups improved in function, strength, resistance to stretch, and reach. No differences found between SMART groups.	
Bowman and colleagues (1979)[33] RCT $N = 30$ enrolled; $N = 30$ analyzed Included in SR[22,23,29,53,57,58]	Stroke with no active wrist ext NMES ($n = 15$): positional stimulation feedback training CON ($n = 15$): PT	Electrode size nr 1 channel Electrodes on wrist extensor muscles; exact location nr Positional feedback unit provided visual and auditory feedback of joint position Sitting with forearm on table	Waveform nr; PC 35 Hz 200 μs ON:OFF 6–8:20 s; ramp-up 3 s Amplitude rose exponentially set to fully extend the wrist	30 min/d 5 d/wk 4 wk	Isometric wrist ext torque Isotonic wrist ext measured with 4 resistance levels ROM: electro-goniometer @ 0, 1, 2, 3, and 4 wk	280% increase in ext torque at 30° wrist ext. 70% increase at 30° wrist flexion. 200% gain in ROM.	
Cauraugh and colleagues (2000)[34] RCT with modified cross-over design $N = 11$ enrolled; $N = 11$ analyzed Included in SR[22,23,29,54]	Chronic stroke (≥1 y) NMES ($n = 7$): EMG-NMES + PROM and stretching CON ($n = 4$): PROM and stretching	Electrode size nr 1 channel Electrodes on ext dig comm and ext c. uln Limb position nr	Biphasic PC 50 Hz PD nr ON:OFF 5:25 s; ramp-up and ramp-down 1 s Amplitude set to obtain pure wrist and finger ext	30 min BID 3 d/wk 2 wk	UE function: • B&B • MAS • F-M Force generation wrist and finger ext: EMG • Reaction time • Sustained muscle contraction @ 0 and 2 wk	Improved B&B @ 2 wk Increased sustained contractions wrist and finger ext @ 2 wk No significant between-groups differences in all other outcomes	Very small and uneven groups This study is 1 of 4 published by the same group. Subsequent studies compared NMES with another active treatment (bilateral arm movement) and showed improved motor function. They concluded that NMES was not warranted.
Chae and colleagues (1998)[35] RCT $N = 46$ enrolled; $N = 28$ analyzed Included in SR[22,23]	Acute stroke (≤4 wk) NMES ($n = 14$): NMES + standard rehab CON ($n = 14$): placebo NMES not over MP; sensory-level stimulation over wrist extensor muscles + standard rehab	2.5 cm diameter 1 channel Electrodes on ext dig comm and ext c. radialis Limb position nr	Waveform nr; PC 25–50 Hz 300 μs ON:OFF 10:10 s; ramp-up and ramp-down 2 s Amplitude set to obtain full wrist and finger ext within comfort	60 min/d 7 d/wk 15 sessions	UE motor function: F-M UE disability: FIM self-care component @ 0, 2, 6, and 14 wk	Greater gains in F-M scores No significant between-groups differences on all other outcomes	18 subjects did not complete treatment – questions feasibility of protocol. Reasons not provided. Active treatment-induced visible contraction, whereas placebo NMES produced sensory-level stimulation (similar to TENS). Obvious effects of electrical stimulation questions effectiveness of blinding.

Table 4 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Dorsch and colleagues (2014)[45] RCT $N = 33$ enrolled; $N = 30$ analyzed	Acute stroke ($\leq$4 wk) NMES ($n = 16$): EMG-NMES to 4 muscle groups + PT CON ($n = 17$): PT	Electrode size varied according to muscle size Electrodes: on MP and muscle belly of shoulder flexors, elbow extensors, wrist extensors, and thumb abductors Limb position nr	Asymmetric biphasic PC 70 Hz 100–250 μs ON:OFF 10:10 s; ramp-up and ramp-down 1 s Amplitude individually set between 10 and 80 mA	15–30 contractions/d 5 d/wk 4 wk	Muscle strength: MMT Arm activity: MAS items 6, 7, and 8 @ 0, 4, and 12 wk	No significant between-groups differences on any outcome No adverse reactions	Study showed that it is feasible to apply multi-channel NMES to very weak muscles early on after stroke. CON group received strengthening programme, which may have made showing greater improvement after NMES difficult. Limited sensitivity of MMT to detect change.
Francisco and colleagues (1998)[40] Pilot RCT $N = 9$ enrolled; $N = 9$ analyzed Included in SR[22,23,56,57]	Acute stroke ($\leq$6 wk) NMES ($n = 4$): EMG-NMES + PT CON ($n = 5$): PT	Electrode size nr 1 channel Electrodes: on ext c. radialis Limb position nr	Biphasic PC 20–100 Hz 200 μs ON:OFF 5:5 s Amplitude set for comfort to obtain full wrist ext	30 min BID 5 d/wk × LOS (33 [SD 7.5] d)	Motor function: F-M UE sub-score Function: FIM (grooming, upper body dressing, and feeding) @ hospital admission and D/C	Greater gains in F-M Higher FIM scores	
Gabr and colleagues (2005)[46] RCT Cross-over design $N = 12$ enrolled; $N = 12$ analyzed Included in SR[22,56,57]	Chronic stroke (12–18 mo post-stroke) EMG-NMES ($n = 8$): EMG-NMES at home followed by Ex programme CON ($n = 4$): Ex programme followed by EMG-NMES	5 cm diameter 1 channel Electrodes: on MP of wrist common extensors (near muscle origin) and 2 cm distal to MP Limb position nr	Biphasic PC Frequency nr 100–400 μs ON:10 s, OFF: nr Amplitude nr	35 min BID 5 d/wk 8 wk Ex programme 8 wk	Impairment: F-M Function: ARAT for grasp, grip, pinch, and gross movement ROM: goniometry—wrist ext @ 0, 8, and 16 wk	No significant between-groups differences in any outcomes.	

Table 4 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Heckmann and colleagues (1997)[43] RCT $N = 28$ enrolled; $N = 28$ analyzed Included in SR[22,29,58]	Stroke (23–174 d post-stroke), all right handed NMES ($n = 14$): PT + EMG-NMES CON ($n = 14$): PT	Electrode size nr Electrodes: upper arm extensors, forearm hand extensors, knee flexors, and ankle extensors; placements not specific Sitting position	Biphasic PC 80 Hz 300 μs ON: 1 s, OFF: nr Amplitude ranged from 20 to 60 mA	15 contractions/d 5 d/wk 4 wk	Spasticity: pendulum test AROM wrist and ankle extensors Barthel Index • Self-care • Mobility @ 0 and 5 wk	Greater improvement AROM Greater improvement on Barthel Index No significant between-groups differences in spasticity	
Kraft and colleagues (1992)[41] Non-RCT $N = 22$ enrolled; $N = 18$ analyzed (1 lost to 9 mo follow-up) Included in SR[29,58]	Chronic stroke (≥6 mo post-stroke) Four groups: EMG-NMES ($n = 6$) NMES + B/B ($n = 4$) PNF Ex ($n = 3$) CON: no treatment ($n = 5$)	Electrode size nr 1 channel Electrodes: EMG-NMES on wrist extensors; placement not specific NMES + B/B on wrist extensors – placement not specific Sitting position	EMG-NMES: Biphasic PC 30–90 Hz 200 μs ON: 10 s, OFF: nr Amplitude 20–60 μV NMES + B/B: Biphasic PC 30–90 Hz 300 μs ON:OFF nr Amplitude set to obtain wrist ext from gravity-assisted flexed position	EMG-NMES: 1 h/d 3 d/wk 12 wk NMES + B/B: 30 min/d 5 d/wk 12 wk	Motor recovery: F-M Grip strength: Jamar hand dynamometer Function: Jebsen–Taylor hand function test Rapid movements: finger-tapping test (in less severely affected subjects) @ 0 and 1 wk, 3 and 9 mo	Increased F-M scores in all treated groups EMG-NMES was better than PNF but equal to NMES No significant between-groups differences in all other outcomes	
Lin and Yan (2011)[44] RCT $N = 46$ enrolled; $N = 37$ analyzed Included in SR[22,23]	Acute stroke (≤3 mo) NMES ($n = 23$): NMES + standard rehab CON ($n = 23$): standard rehab	Electrode size nr 2 channels Electrodes: Shoulder on MP of supraspinatus and deltoid Wrist on muscle belly of wrist extensors Limb position nr	Symmetric biphasic PC 30 Hz 300 μs ON:OFF 5:5 s, ramp-up and ramp-down 1 s Amplitude set to max tolerated up to 90 mA	30 min/d (180 cycles/session) 5 d/wk 3 wk	Shoulder spasticity: Modified Ashworth Scale UE function: F-M, UE section ADLs: Modified Barthel Index @ 0, 2, and 3 wk and 1, 3, and 6 mo	Greater improvement in all outcomes @ 3 and 6 mo No significant between-groups differences before 3 mo	Effect of NMES persisted for at least 6 mo compared with standard rehab, which produced shorter term benefit

Table 4 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Powell and colleagues (1999)[37] RCT $N = 60$ enrolled; $N = 48$ analyzed Included in SR[22,23,29,58]	Acute stroke ($\leq$4 wk) NMES ($n = 30$): NMES + PT (Bobath and movement science) CON ($n = 30$): PT	Electrode size nr 1 channel Electrodes: on dorsal forearm distal to elbow and proximal to wrist Limb position nr	Waveform nr; PC 20 Hz 300 μs ON:OFF 5:20 s, progressed to 5:20 s, 5:15 s, 5:10 s, and 5:5 s; ramp-up 1 s, ramp-down 1.5 s Amplitude set to obtain full joint ext	30 min TID 7 d/wk 8 wk	UE function: • ARAT • 9-hole peg test Global handicap and mobility: • Rankin • Barthel Index Pain: VAS Grip strength: Jamar dynamometer Tone: Ashworth Scale @ 0, 4, 8, 20, and 32 wk	Greater total and grip subscore of ARAT @ 8 wk but not @ 32 wk Increased isometric wrist ext strength @ 8 and 32 wk No significant between-groups differences in all other outcomes	
Rosewilliam and colleagues (2012)[38] RCT $N = 90$ enrolled; $N = 66$ analyzed Included in SR[58]	Acute stroke ($\leq$6 wk) with no UE function; ARAT = 0 NMES ($n = 45$): NMES + PT CON ($n = 45$): PT	Electrode size nr 1 channel Electrodes: about 5 cm proximal to wrist and just inferior to ext dig comm origin Limb position nr	Waveform nr; PC 40 Hz 300 μs ON:OFF 15:15 s; ramp-up and ramp-down 6 s, included in ON:OFF times Amplitude set to produce full wrist and finger ext within comfort	30 min BID 5 d/wk 6 wk	UE function: • ARAT score • Barthel Index (independent ADLs) AROM wrist flexion and ext Strength: • MVIC wrist flexion and ext • Grip strength @ 0, 6, 12, 24, and 36 wk	Greater strength, increased AROM of wrist ext Increased grip strength @ 12 wk No significant between-groups differences in all other outcomes	This patient group had severely affected UE after stroke. ARAT score = 0 at baseline.
Shin and colleagues (2008)[39] RCT $N = 14$ enrolled; $N = 14$ analyzed Included in SR[22,58]	Chronic stroke ($\geq$1 year) NMES ($n = 7$): EMG-NMES CON ($n = 7$)	Electrode size nr 1 channel Electrodes: on proximal and distal ends of ext dig comm Sitting position: elbow flexed 90°, forearm pronated, wrist ext 10°	Symmetric biphasic PC 35 Hz 200 μs ON:OFF 5:4 s; ramp-up 0.1 s, ramp-down 2 s Amplitude nr	30 min BID 5 d/wk 10 wk	Function: B&B Tracking test: electrogoniometer fMRI of brain for cortical activation @ 0 and 10 wk	Improvement on B&B Improvement on tracking test @ 10 wk fMRI: changes in cortical activation	Small number per group ($n = 7$).

NMES = neuromuscular electrical stimulation; EMG = electromyography; CON = control; RCT = randomized controlled trial; SR = systematic review; SMART = SensoriMotor Active Rehabilitation Training; MP = motor point; PC = pulsed current; max = maximum; MAS = Motor Assessment Scale; UE = upper extremity; MMT = manual muscle testing; ext = extension; PT = physiotherapy/physical therapy; nr = not reported; ROM = range of motion; PROM = passive range of motion; ext dig comm = extensor digitorum communis muscle; ext c. uln = extensor carpi ulnaris muscle; PD = pulse duration; BID = twice per day; B&B = Box & Block Test; F-M = Fugl-Meyer test; rehab = rehabilitation; TENS = transcutaneous electrical nerve stimulation; ext c. radialis = extensor carpi radialis muscle; TID = 3 times per day; LOS = length of stay; D/C = discharge; Ex = exercise; AROM = active range of motion; PNF = proprioceptive neuromuscular facilitation technique; ADLs = activities of daily living; ARAT = Action Research Arm Test; B/B = bias balance; VAS = visual analogue scale; MVIC = maximum voluntary isometric contraction; fMRI = functional magnetic resonance imaging.

1C. LOWER EXTREMITY STROKE: FOOT DROP, PLANTAR SPASTICITY, AND GAIT IMPROVEMENT

Indications and rationale for using NMES

After a stroke, many individuals have foot drop, characterized by an inability to dorsiflex the ankle and requiring hip hiking to obtain sufficient toe clearance during walking. The abnormal gait causes walking speed to be slow, the physiological cost to be high, and the risk of stumbling and falling to increase. NMES is applied to improve muscle strength of weak foot dorsiflexor muscles, reduce foot drop, and decrease plantar muscle spasticity. By addressing these impairments, gait symmetry, speed, and walking distance can improve.

Table 5 Summary of the Literature and Recommendations for Use of NMES for Foot Drop, Plantar Spasticity, and Gait Improvement

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
Lower extremity foot drop; plantar (gastrocs) spasticity; gait re-education	**Electrode placement:** 1 electrode over the common peroneal nerve, the other over the MP of tib ant or both tib ant and peronei. Additional channel might be considered for gluteus medius stimulation **Body and limb position:** DFL against gravity during gait re-education or with patient sitting or standing (weight-shift Ex) **NMES waveform:** biphasic PC **Frequency:** 30–50 Hz to produce tetany[68–75] **Pulse duration:** 300 μs[72–76] **Current amplitude:** individual maximum tolerated to achieve ankle DFL (varying from neutral to max)[72–78] **Work–rest cycle:** ON:OFF 5–10:6–30 s[70,72,75,76] When using NMES as part of gait retraining, ON:OFF times are controlled by pressure-sensitive heel switch[71,74,76] **Treatment schedule:** 30 min/d[70–76] **Session frequency:** 5 d/wk[71,72,74,75,78] over 3–4 wk[70,72,73,75,78]	• Increase in muscle strength (torque, MMT)[71,73,74] • Increase in ankle DFL[74] • Increased EMG activity[75] • Decrease in ankle plantar flexor (gastrocs) spasticity (Barthel Index, modified Ashworth Scale, CSS)[70,74,75] • Increase in gait speed[68,69,78] • Improved LE function (F-M, Mass Gen Hosp, ambulation)[68] • Improvement in gait kinematics (symmetry, stride length)[68,70,71,76] • Improved balance (Berg Balance Scale)[71]
Rationale for recommended NMES protocol	NMES protocol for foot drop has been used by many research groups,[70,73,74,77,78] and improvements in muscle strength and gait symmetry were achieved using a simple single-channel system that targets tib ant and peronei muscles of the affected leg. An additional channel was also added to stimulate plantar flexors (gastrocs) during stance phase.[76] Chung and associates[71] found that combining activation of ankle DFL during swing phase with activation of gluteus medius during stance phase produced greater gait symmetry, and the effort of walking was reduced.[79] Pulse frequency of 30–50 Hz produces smooth muscle tetany. Higher pulse frequency was used to produce greater muscle force.[77,78] Pulse duration of 300 μs and amplitude that produces comfortable but complete contraction of the ankle DFL and evertors can produce neutral foot position. ON:OFF times are determined most often by using a simple pressure-sensitive heel switch, which triggers the NMES signal at heel-off during swing phase. In this way, tib ant of the affected leg remains contracted during gait in a way that prevents foot drop. NMES has also been shown to improve muscle strength when applied with the patient in sitting or static standing to move the ankle through ROM in a cyclical manner without patient involvement. We recommend using NMES while patients are walking because it has been associated with a therapeutic benefit that persists after the NMES treatment ends.[69] Treatment schedules of between 20 and 30 min per session are progressed as fatigue permits.[70–76] Bakhtiary and Fatemy[77] used a very short, 9-min session of NMES and showed significant improvements in DFL strength and ROM. Most protocols used NMES 3–5 times per wk for at least 3–4 wk.[70,72,73,75,78] Longer treatment programmes given over 6–12 wk may be required.[71,74,76] Patients who have sustained a stroke up to 18 mo before NMES have benefited from this therapy.[71,74] Many devices have been developed in which NMES units are incorporated into a custom-fitted orthotic or brace for easy application by the patient for home use. Examples of these technologically advanced automated devices with in situ electrodes, portable gait-event detection devices (pressure sensor, accelerometers, EMG activity), or both include the Bioness,[80] Odstock Dropped Foot stimulator,[69] and WalkAide.[81] PT involvement typically entails initial sessions to fit and adjust the device, followed by a 2 to 6 wk training period during which the patient adapts to and gradually increases the duration of daily use of NMES.	

Table 5 *continued*

Physiological effect of NMES	Muscles affected by stroke have a higher proportion of fast-twitch, fatiguable fibre types on the paretic side.[16] NMES can produce hypertrophy and increase force generation in muscles weakened by central nervous system infarct.[71,73,77] Newsam and Baker[19] showed increased motor unit recruitment in weakened muscles stimulated with NMES for 4 wk post-stroke. Stimulation of the LE dorsiflexor muscles can reduce spasticity in plantar flexors.[74,75] Burridge and McLellan[82] demonstrated that patients who had ankle plantar muscle spasticity were more likely to respond to NMES treatment protocol. Benefits produced by NMES to tib ant muscles are thought to be mediated through reciprocal inhibition. Reciprocal inhibition occurs through inhibitory interneurons in the spinal cord.[83] Measures of surface EEG before and after 3 mo treatment including NMES applied to ankle dorsiflexors showed altered activation of the primary motor cortex affected by stroke.[84] These cortical changes were associated with significant improvements in several measures of gait.
Critical review of research evidence	• Of 11 RCTs that were reviewed, 9 reported positive effects of NMES on leg impairments, function, or both. Macdonell and colleagues[72] reported that 4 wk of daily cyclical NMES applied for 20 min to affected ankle dorsiflexors in sitting (without patient involvement) did not improve leg spasticity (Barthel Index) or LE function (F-M). Patients in this study had very little voluntary muscle contraction and were within 6 wk of a stroke. The other study that did not detect a difference in gait kinematics, ankle movement, or stroke recovery also applied NMES in a cyclical fashion to patients who had no voluntary activation of the affected leg muscles.[78] Cozean and colleagues[76] found no association between time since stroke and study outcomes, whereas other studies have suggested that the sooner after stroke NMES is applied, the better the outcomes. • Systematic review of this body of research has produced pooled effects that consistently favour NMES over conventional PT treatment (e.g., Bobath techniques) for muscle strength gains[29,53,58] and faster speed of walking.[85,86] Dickstein[87] found increased walking speed after NMES; however, they concluded that none of the increases would have resulted in community ambulation, and therefore they suggested that using NMES was not warranted. A Cochrane review published in 2006 also did not find that NMES increased gait speed over control treatments.[88] Conflicting results among the meta-analyses[29,53,85,86,88] and SRs[22,23,87] that have been published on this topic can be explained by the reviewers combining for analysis heterogeneous patient populations and a wide range of NMES protocols. Each of the large reviews included different sets of studies and excluded some of the controlled clinical trials included in the present review.[22,23] • A recent SR involving 33 studies found no conclusive evidence to suggest that more sophisticated and often expensive types of devices produce better outcomes than the simple protocols.[89] This conclusion is similar to that of a subcommittee of the American Congress of Rehabilitation Medicine, which found insufficient evidence to support the use of electrical stimulation orthotic substitute devices over traditional ankle–foot orthosis without NMES.[67]

NMES = neuromuscular electrical stimulation; gastrocs = gastrocnemius muscle; MP = motor point; tib ant = tibialis anterior muscle; MMT = manual muscle testing; DFL = dorsiflexion; Ex = exercise; EMG = electromyography; CSS = Composite Spasticity Score; PC = pulsed current; LE = lower extremity; F-M = Fugl-Meyer Assessment; Mass Gen Hosp = Massachusetts General Hospital Functional Ambulation Class; ROM = range of motion; PT = physiotherapy/physical therapy; EEG = electroencephalogram; RCT = randomized controlled trial; SR = systematic review.

Table 6 Details of Individual Studies on Use of NMES in Lower Extremity Stroke for Foot Drop, Plantar Spasticity, and Gait Improvement

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Bakhtiary and Fatemy (2008)[77] RCT $N = 40$ enrolled; $N = 35$ analyzed Included in SR[58]	Stroke patients with PFL spasticity NMES ($n = 20$): NMES + Bobath + 10 min infrared heat CON ($n = 20$): Inhibitory Bobath + 10 min infrared heat	Electrode size nr 1 channel Electrodes: active on MP of tib ant; anode on fibular head Limb position nr	Faradic-type PC 100 Hz 100 μs ON:OFF 4:6 s; no ramp time Supramaximal contraction (25% over intensity for max contraction)	9 min/d 20 sessions	PFL spasticity: Modified Ashworth Scale DFL ROM: goniometer DFL strength: MMT Soleus H-reflex amplitude @ before and after each treatment session	Greater ankle DFL ROM Greater DFL muscle strength Lower PFL spasticity No significant between-groups differences in H-reflex	Unique NMES protocol: very short treatment sessions (9 min) applying high NMES intensity (25% above max). No mention of whether this level of stimulation was uncomfortable.
Cheng and colleagues (2010)[70] RCT $N = 18$ enrolled; $N = 15$ analyzed Included in SR[23,67]	Chronic stroke (≥3 mo) with PFL spasticity NMES ($n = 9$): PT + NMES + ambulation CON ($n = 9$): PT + ambulation training	Electrode size nr 1 channel Electrodes: on MP of tib ant and over common peroneal nerve below fibular head Standing in a harness on the Balance Master rocker board	Waveform nr; PC 40 Hz PD nr ON:OFF 10:10 s Amplitude at max contraction with no discomfort	30 min 3 d/wk 4 wk	DFL muscle strength: dynamometer Dynamic spasticity of DFL: GAITRite Active ankle ROM: electrogoniometer Dynamic balance: Balance Master Gait kinematics and functional gait performance: GAITRite @ 0 and 4 wk	Decreased ankle spasticity Greater improvement in gait symmetry and functional gait ability No significant between-groups differences in all other outcomes	NMES applied to patient standing on rocker board (simulated proprioceptive feedback during weight-shift perturbation). Study was conducted in a research lab; however, easy to replicate in PT.
Chung and colleagues (2014)[71] RCT $N = 18$ enrolled; $N = 18$ analyzed	Chronic first stroke with weak tib ant and gluteus medius (<grade 2 MMT) NMES ($n = 9$): NMES to tib ant and gluteus medius + gait training CON ($n = 9$): gait training	Electrode size nr 1 channel Electrodes: on gluteus medius 5 cm below iliac crest and 3 cm above greater trochanter and on tib ant halfway between knee and ankle	Symmetric biphasic PC 40 Hz 200 μs ON:OFF time triggered by foot switch; gluteus medius during stance and tib ant during swing phase of gait; ramp-up and ramp-down 0.5 s Amplitude set to gain 10° DFL in sitting	30 min/d 5 d/wk 6 wk	Gait parameters: GAITRite • Velocity • Cadence • Stride length affected and non-affected sides Muscle strength: handheld dynamometer, gluteus medius and tib ant Dynamic balance function: Berg Balance Scale @ 0 and 6 wk	Better gait parameters Greater muscle strength, gluteus medius and tib ant Improved dynamic balance function	Small study with objective and sensitive outcome measures Improved gait symmetry was achieved by avoiding foot drop (tib ant stimulation) and also preventing dropping of contralateral pelvis during single limb support (stance).

Table 6 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Cozean and colleagues (1988)[76] RCT $N = 36$ enrolled; $N = 32$ analyzed Included in SR[22,23]	Stroke with PFL spasticity and ability to walk with 1-person assist 4 groups: NMES ($n = 10$) EMG ($n = 9$) EMG-NMES ($n = 8$) CON ($n = 9$): PT	Electrode size and number nr 2 channels Electrodes: on tib ant (stimulated during swing phase) and gastrocnemius-soleus complex (stimulated during stance phase)	Waveform nr; PC Frequency nr 300 μs Frequency set to produce smooth tetanic contraction ON:OFF time determined by foot switch Amplitude set to max contraction within tolerance	30 min/d 3 d/wk 6 wk	Gait analysis using video motion-capture system: • Knee and ankle angles during swing phase • Step length • Stance time • Gait cycle time Joint reaction force: force plate @ 0, 2, 4, 6, and 10 wk	EMG-NMES improvements in knee and ankle flexion angles during swing phase No significant between-groups differences on all other outcomes	None of the patients achieved a normal gait pattern. Gait improvement related to age and side of stroke (right-sided weakness better than left-sided weakness). Results not associated with time post-stroke. Subjects > 1 yr since stroke and with severe leg spasticity showed marked improvement with EMG-NMES.
Macdonell and colleagues (1994)[72] RCT $N = 38$ enrolled; $N = 38$ analyzed Included in SR[22,23]	Acute stroke ($\leq$6 wk) All subjects had weak DFL (at least grade 2) NMES ($n = 20$): NMES + PT CON ($n = 18$): PT	Electrode placement, size, and number nr Aim to produce neutral ankle DFL Sitting position (non-weight bearing) NMES triggered manually after patient attained max voluntary contraction	Waveform nr PC 30–50 Hz 300 μs ON:OFF 10:30 s Amplitude set to max within tolerance to obtain neutral DFL against gravity	20 min/d, progressed to 30–40 min/d 5 d/wk for cyclical NMES 3 d/wk NMES was combined with functional activities 4 wk	Barthel Index F-M Mass Gen Hosp Electrophysiological tests: • Foot tap frequency • Activity in tib ant • Hmax/Mmax: gastrocnemius-soleus complex Vibratory inhibition of H-reflex Fmean/Mmax ratio: flexor hallucis brevis @ 0, 4, and 8 wk	No significant between-groups differences in all outcomes	Example of cyclical NMES: no patient involvement, and NMES was not used functionally during gait. Authors attribute lack of difference to severity of stroke in several patients.

Table 6 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Merletti and colleagues (1978)[73] RCT $N = 49$ enrolled, $N = 49$ analyzed Included in SR[22,23,29,53,86]	Acute ($\leq$1 mo) and chronic ($\leq$15 mo) stroke NMES ($n = 24$): NMES + PT + neuromuscular facilitation CON ($n = 25$): PT + neuromuscular facilitation (Kabat and Bobath)	Electrode size nr 1 channel Electrodes: on tib ant and peroneus muscle or on peroneal nerve in popliteal fossa and over fibular head Either sitting or walking	Monophasic PC 30 Hz 300 μs ON:OFF 1.5:3 s Amplitude set to achieve max functional movement	20 min/d 6 d/wk 4 wk	Max voluntary dorsiflexor ankle torque: isometric brace @ 0 wk and twice/wk for 4 wk	Muscle strength was 3 times greater than CON	One of the earliest published reports showing potential benefits of NMES on post-stroke hemiparesis
Sabut and colleagues (2011)[74] $N = 51$ enrolled; $N = 51$ analyzed Included in SR[67,89]	Chronic stroke ($\geq$3 mo) with unilateral foot drop NMES ($n = 27$): NMES + PT CON ($n = 24$): PT	Electrode size nr 1 channel Electrodes: on common peroneal nerve and on MP of tib ant NMES triggered during swing phase of gait using heel switch	Waveform nr; PC 35 Hz 280 μs ON:OFF nr Amplitude set to produce muscle contraction within patient comfort	20–30 min/d 5 d/wk 12 wk	PFL spasticity: Modified Ashworth Scale DFL strength: MMT Ankle DFL AROM: goniometry LE motor function: F-M @ 0 and 12 wk	Decreased PFL spasticity Greater DFL strength Greater AROM DFL Greater change in LE motor recovery	A 12-wk, supervised, clinic-based rehab programme that added NMES showed better recovery than conventional rehab alone.
Yan and colleagues (2005)[75] RCT $N = 46$ enrolled; $N = 41$ analyzed Included in SR[23,58,89]	First acute stroke ($\leq$2 wk) NMES ($n = 13$): NMES + PT Placebo ($n = 15$): sham NMES + PT CON ($n = 13$): PT	Electrode size nr 2 dual-channel stimulators were connected with a programme timer to form 1 stimulating unit Electrodes: on quads, hams, tib ant, and medial gastrocnemius-soleus complex Side-lying position with affected leg supported in a sling	Waveform nr; PC 30 Hz 300 μs ON: 5 s to stimulate swing phase; OFF: nr Amplitude max tolerable (20–30 mA)	30 min/d 5 d/wk 3 wk 15 sessions	Spasticity: CSS Strength: MVIC ankle dorsiflexion EMG of tib ant and medial gastrocnemius-soleus complex TUG (7 to 8 m walk distance) without assistance @ 0, 1, 2, 3, and 8 wk post-stroke	Improved CSS Increased ankle DFL torque Increased EMG activity of agonist 84.6% NMES returned home vs. 53.3% and 46.2% in placebo and control groups No significant between-groups differences on TUG	Multi-channel unit allowed NMES to be delivered reciprocally to limb muscles to mimic normal gait.

Table 6 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Yavuzer and colleagues (2006)[78] RCT $N = 25$ enrolled; $N = 25$ analyzed	First stroke ($\leq$6 mo) with Brunnstrom LE score stage 1–3 NMES ($n = 12$): NMES + PT CON ($n = 13$): PT	Electrode size nr Electrodes: on tib ant close to insertion points Limb position nr	Surge-alternating PC 80 Hz PD nr ON:OFF 10:50 s; ramp-up 2 s, ramp-down 1 s Amplitude set to produce muscle contraction without discomfort	10 min/d 5 d/wk 4 wk	Recovery: Brunnstrom Stage LE Gait kinematics: • Walking velocity • Step length • % stance phase on paretic side • Sagittal plane • Kinematics pelvis, hip, knee, and ankle • Max ankle DFL angle at swing • Max ankle PFL at initial contact @ 0 and 4 wk	Increased walking velocity No significant between-groups differences on all other outcomes	Negative results may be explained by NMES being applied without voluntary contraction of ankle DFL (cyclical). Relatively short treatment sessions (10 min).

NMES = neuromuscular electrical stimulation; CON = control; RCT = randomized controlled trial; SR = systematic review; PFL = plantar flexor; nr = not reported; MP = motor point; tib ant = tibialis anterior muscle; PC = pulsed current; max = maximum; DFL = dorsiflexor; ROM = range of motion; MMT = manual muscle testing; PT = physiotherapy/physical therapy; F-M = Fugl-Meyer test; Mass Gen Hosp = Massachusetts General Hospital Functional Ambulation Class; Hmax/Mmax = maximum H reflex/maximum motor response; Fmean = F-wave mean; AROM = active range of motion; LE = lower extremity; quads = quadriceps; hams = hamstring muscles; CSS = Composite Spasticity Score; MVIC = maximum voluntary isometric contraction; EMG = electromyography; TUG = timed up-and-go test; PD = pulse duration.

2. Musculoskeletal Conditions

2A. ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Indications and rationale for using NMES

Pain and weakness secondary to both ACL injury and post-surgical trauma is a common issue for patients after ACL reconstruction.[90] Presynaptic reflex inhibition (alteration of neural signalling) of quadriceps (quads) inhibits appropriate recruitment of motor neurons.[91] Muscle atrophy, particularly in type 1 muscle fibres post-injury and post-surgery, results in reduced muscle strength (60%–80% decrease in isometric quads strength), which jeopardizes joint function and has been shown to be linked to gait abnormalities (velocity, stride length, and pace).[92] Weakness of the quads post–ACL injury has been reported to be related to reduced functional performance,[93] a greater potential for re-injury,[93] and a higher risk of developing OA.[94] NMES is indicated post–ACL reconstruction to elicit an electrically induced muscle action to augment volitional recruitment and strengthen the quads; secondary to improved strength and biomechanics, NMES might reduce pain.

Table 7 Summary of the Literature and Recommendations for Use of NMES in Anterior Cruciate Ligament Reconstruction

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
ACL reconstruction	**Electrode placement:** No standardized location reported in the literature. Recommended placement based on a synthesis of the literature: (1) quads on femoral nerve or muscle belly of rec fem or vastus intermedius and on MP or muscle belly of VM[95–97]or (2) quads (as above) and on hams (over muscle bellies of biceps femoris and semitendinosis or semimembranosis).[98–101] Some studies placed electrodes on VL.[102,103] **Limb position:** knee flexed to ~65° **NMES waveform:** low-frequency biphasic[95,97,98,101,104–107] or medium-frequency burst-modulated AC[99,103,108–110] **Frequency:** 30–50 Hz PC[95,97,101,104–107] or 2500 Hz AC in 50 Hz bursts[99,110,111] **Pulse duration:** 250–400 μs[97,100,102,103,105–107,112,113] **Current amplitude:** individual max tolerated intensity; minimum at strong but comfortable muscle contraction[95,97,99,100,105,106,109,112,113] **Work–rest cycle:** ON:OFF 6–10:12–50 s;[95,98,101,103,105,106] use lower duty cycle–e.g., work–rest 1:3–1:5–if the muscle is weaker to limit fatigue associated with an electrically induced muscle contraction **Treatment schedule:** initiate ideally within 1 wk post-op:[98–101] 12–15 contractions/session[98,99,102,103,108–110,112] **Session frequency:** 3 × wk over 4–6 wk, particularly in the first 6 wk post-op[98,101,110]	• Reduced pain (NPRS, VAS)[98,105] • Improved muscle strength (isometric and isokinetic, dynamometry, tensiometry)[99,100,102–104,107–110,112,113] • Reduction in loss of muscle volume or thickness (CT, MRI, US imaging)[100,107,113] • Self-reported function (ADL scale)[108] • Gait parameters (motion analysis)[103] • Achieving clinical milestones[108] • Limb circumference (tape measure)[105,110] • Functional performance (lateral step-up, anterior reach)[100,101]

Table 7 *continued*

Rationale for recommended NMES protocol	When reviewing the studies, difference in methodologies is obvious. It is evident that regardless of whether the stimulator used was a low-frequency PC or a medium-frequency burst-modulated AC device, the authors used some common parameters: (1) initiation of NMES on POD 1–2 and in some studies 1 wk post-op, (2) amplitude raised to max tolerated, and (3) 10–20 contractions/session in most cases. A study that used 300 contractions/d for 12 wk showed no advantage for strength until 52 wk post-op.[104] For athletes who had not fully recovered strength at 6 or more mo post-op, initiating NMES at 6 or more mo post-op was beneficial.[107] With respect to ON:OFF parameters, the studies show that short OFF periods (2–20 s) were applied only when ON times were short (5–6 s), frequency was low (20–30 Hz), or both. Short ON time or low frequency of stimulation results in motor unit sparing and thus slower onset of fatigue, which, in turn, reduces the OFF time needed for recovery. The literature does not show that strength improves using short ON and OFF times. 2 studies using short OFF periods[95,107] compared 2 contrasting NMES protocols without a CON group; thus, the relative usefulness of these 2 protocols for strengthening cannot be elucidated. A further 2 studies[97,106] showed no strength gain. Eriksson and Häggmark,[96] with 5:6.5 s ON:OFF and an unusually high frequency of 200 Hz, used oxidative capacity as the only outcome measure, perhaps reflecting their intent to use Ex training to improve endurance, not strength. Strength was not measured in 2 other studies.[101,105] Accordingly, our recommendations for strengthening quads are to initiate NMES as early as possible, even on POD 1 and ensure that the intensity elicits a maximum tolerated contraction; 10–15 contractions, 10–15 s ON:OFF duration, 3–5 times that of the ON time. Position the limb within the resting length of the quads (e.g., 65° flexion) to facilitate max force production.[114] Some earlier studies used full extension, which is not advised because it places high strain on the ACL. In addition, studies with the knee $<30°$ flexion have produced inferior outcomes.[108]
Physiological effect of NMES	In animal models, there is cellular and molecular evidence of positive changes in muscle with NMES after ACL surgery. NMES minimized connective tissue density in muscles and reduced MMP-2, increased both type IV collagen mRNA and protein levels,[91] and minimized the accumulation of atrogenes and myostatin as well as prevented reduction in muscle mass early post-transection.[115]
Critical review of research evidence	• We reviewed the individual RCTs identified by our search protocol as well as 2 SRs. • Conclusions of the SRs were that the addition of NMES to rehabilitation Ex can improve strength[92,116] and function[92] at 6–8 wk post-op but is inconclusive for functional performance at 6 wk and self-reported function at 12–16 wk post-op.[116] • Earlier trials focused on use of NMES to reduce atrophy secondary to the prolonged immobilization post-surgery. Current ACL reconstruction protocols have significantly reduced duration of immobilization; accordingly, recent trials have focused on the use of NMES to address quads weakness secondary to both the original trauma and that incurred during surgery. • NMES (using optimized parameters) + Ex is better than CON (Ex alone or Ex + sham NMES), especially when initiating treatment earlier post-op. • Individual RCTs have limitations: In some cases, there is a risk of bias due to subjects, therapists, or outcome assessors being not blinded to group allocation. Some trials used parameters, particularly intensity, that are unlikely to induce improvements in strength. There are some instances of incomplete reporting or management of missing data points. • Interpretation of the findings is complicated by differences in knee position, electrode position, type of stimulator (battery powered vs. console[109]), stimulation parameters, type of graft (quads vs. hams), duration of immobilization, time delay in initiating NMES (POD 2 vs. 3 wk vs. 24 wk), and failure to track compliance. • Feasibility has been demonstrated: Recent studies have shown that patients tolerate NMES well even when initiated on POD 1–2. • No adverse effects have been associated with NMES in this population.

NMES = neuromuscular electrical stimulation; ACL = anterior cruciate ligament; quads = quadriceps muscle; rec fem = rectus femoris muscle; MP = motor point; VM = vastus medialis; hams = hamstring muscles; VL = vastus lateralis; AC = alternating current; PC = pulsed current; max = maximum; post-op = post-operative; NPRS = numerical pain rating scale; VAS = visual analogue scale; CT = computed tomography; MRI = magnetic resonance imaging; US = ultrasound; ADL = activities of daily living; POD = post-operative day; Ex = exercise; MMP-2 = matrixmetalloproteinase-2; mRNA = messenger ribonucleic acid; RCT = randomized controlled trial; SR = systematic review; CON = control.

Table 8 Details of Individual Studies on Use of NMES in ACL Reconstruction

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Anderson and Lipscomb (1989)[104] RCT $N = 100$ enrolled; $N = 96$ analyzed Included in SR[92]	ACL recon using semitendinosis and gracilis ± meniscal repair POD 1 NMES + immobilization in flex 60° ($n = 20$) Immobilization in flex 60° ($n = 20$) Immobilization in flex + CPM ($n = 20$) TENS + immobilization in ext ($n = 20$) Immobilization in ext ($n = 20$)	Electrode size and placement nr	Biphasic PC 35 Hz 150 μs ON:OFF 10:110 s Amplitude nr No simultaneous voluntary contraction with NMES	10 h/d (300 contractions) 7 d/wk 12 wk	Thigh volume: circumferential measure @ 0, 6, 12, 28, 52, and 78 wk Varus/valgus stress test: X-ray with 15 lb stress @ 78 wk ACL laxity: KT-1000 @ 28 and 78 wk Strength: Cybex @ 28, 52, and 78 wk	Increased strength @ 52 and 78 wk Increased ROM and less patellofemoral crepitus (no time frames provided) No significant between-groups difference in all other outcomes	Unusually demanding protocol 10 h/d × 12 wk Pulse duration short to elicit effective strengthening of quads. Several key features of protocol not reported. Technical difficulties with the stimulator precluded use of NMES for 5 patients for extended periods. Methods for assessing patellofemoral crepitus not described.
Currier and colleagues (1993)[98] Non-RCT $N = 17$ enrolled; $N = 17$ analyzed Included in SR[92]	ACL recon Patellar tendon NMES ($n = 7$) from POD 1 NMES ($n = 7$) from POD 1–3 Then NMES + PEMF CON ($n = 3$)	8 × 12.5 cm 2 channels Electrodes: over femoral triangle and on VM and muscle bellies of the biceps femoris and medial hams Knee in full ext	2500 Hz AC 50 Hz burst rate NMES group: ON:OFF 15:50 s Ramp up 5 s NMES/PEMF group: ON:OFF 10:50 s Ramp-up 5 s Amplitude set for each patient pre-op at 50% of MVC Simultaneous voluntary contraction during NMES	10 contractions 1–3/d post-op Then 3 d/wk Total 6 wk	Thigh girth: tape measure @ pre-op and 6 wk Pain: VAS comparing 3 sessions each of NMES with NMES + PEMF Torque MVIC: Biodex – only for NMES + PEMF group @ pre-op and 6 wk	NMES and NMES + PEMF reduced loss of thigh girth @ 6 wk NMES + PEMF was less painful than NMES alone (sessions 1–3 vs. sessions 4–6) Torque decrease averaged 13.1% using NMES + PEMF @ 6 wk	Lack of randomization and small sample size warrant caution in extrapolating findings to clinical practice. Torque comparisons were not available.
Delitto and colleagues (1988)[99] RCT $N = 20$ enrolled; $N = 20$ analyzed Included in SR[116]	ACL recon 2–3 wk post-op NMES ($n = 10$) CON ($n = 10$): Ex	Electrode size nr 2 channels Electrodes: on quads and hams co-contraction In 65° knee flex	2500 Hz AC 50 Hz burst rate ON:OFF 15:50 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	15 contractions 5 d/wk 3 wk	Isometric flex and ext torque: Cybex @ 0 and 3 wk	Increased torque	Compliance with voluntary Ex was not monitored.

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Draper and Ballard (1991)[95] RCT (groups matched for age and gender) $N = 30$ enrolled; $N = 30$ analyzed Included in SR[116]	ACL recon POD 1 NMES ($n = 15$): EMG-BF NMES ($n = 15$) during voluntary contraction Subjects were trained using device pre-op Both groups standard rehab POD 1–6 wk	5×10 cm 1 channel Electrodes: active on femoral nerve; dispersive 5–7 cm prox to patella on VM	Waveform nr; PC 35 Hz ON:OFF 10:20 s Ramp-up and ramp-down 4:2 s Amplitude set to tolerance, increasing each session No simultaneous voluntary contraction with NMES	30 min TID 7 d/wk 4 wk	Isometric peak torque as % of non-operated limb: Cybex @ wk 6 ROM: goniometer weekly @ wk 1–6	Strength gain in group with EMG–BF greater than NMES alone No significant between-groups difference in all other outcomes	Initial intensity of stimulation likely suboptimal (initially only 15 mA, ultimately 40 mA). Compliance with home programme was tracked with a log. No CON group for comparison
Ediz and colleagues (2012)[105] RCT $N = 29$ enrolled; $N = 26$ analyzed	ACL recon Hams autograft (aged 18–40 yr) NMES ($n = 15$): POD 4 + Ex POD 1 CON ($n = 14$): Ex POD 1	6×8 cm Channel number nr Electrodes: on quads, hams, triceps surae	Waveform nr; PC 30 Hz 300 μs ON:OFF 10:20 s Amplitude max tolerable without discomfort No simultaneous voluntary contraction with NMES	20 min/d 5 d/wk 6 wk	Effusion: numerical bulge-dancing patella Swelling: difference in circumference @ mid-centre of the patella between operated and non-operated knees Pain: average daily resting pain International Knee Documentation Committee scoring system Tegner Activity Scale @ 0, 1, 2, 8, 12, and 24 wk	Less effusion @ 7 d Less swelling @ 7 d Lower pain scores @ 7 d–12 wk No significant between-groups difference in all other outcomes	The primary purpose was to examine swelling and pain. Strength was not measured.
Eriksson and Häggmark (1979)[96] RCT $N = 8$ enrolled; $N = 8$ analyzed Included in SR[92]	ACL recon Casted post-op NMES ($n = 4$): NMES + Ex CON ($n = 4$): Ex	Electrode size nr 1 channel Electrodes: through hole in cast on distal quads and above the femoral nerve @ the groin 10° knee flex	Waveform nr; PC 200 Hz PD nr ON:OFF 5–6:5 s Self-adjusted voltage to below pain threshold No simultaneous voluntary contraction with NMES	1 h/d 5 d/wk 4 wk	Biopsy of VL • Atrophy • SDH concentration @ 0, 1, and 5 wk	Less muscle atrophy Increased oxidative enzyme	A frequency of 200 Hz is unusual in NMES literature. High frequency results in rapid muscle fatigue and may not be ideal for strengthening.[117] Reliability within or between assessors of classification of biopsy sample was not established. Patients immobilized after surgery.

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Fitzgerald and colleagues (2003)[108] RCT $N = 48$ enrolled; $N = 43$ analyzed Included in SR[116]	ACL recon NMES ($n = 21$): NMES + Ex CON ($n = 22$): Ex	6.98 × 12.7 cm 1 channel Electrodes on VL and VM Supine full knee ext	2500 Hz AC 75 Hz burst rate ON:OFF 10:50 s Ramp-up and ramp-down 2:2 s Amplitude max tolerated (minimum full, sustained, tetanic contraction with palpable evidence of superior glide of patella and no fasciculations) No simultaneous voluntary contraction with NMES	10 contractions (11–12 min) 2 d/wk Mean Rx time for both groups: 10+ wk Ex programme progressed individually	Quad strength: Biodex isometric @ 60° flex Self-reported function: ADL scale Achievement clinical milestones: proportion of successful subjects Pain: NPRS @ 0, 12, and 16 wk	Greater strength @ 12 and 16 wk Greater proportion achieved clinical criteria for advancing to agility training @ 16 wk Better ADL score @ 12 and 16 wk No significant between-groups difference in NPRS	Single blinded Authors noted that the programme was less effective than prior studies; session frequency and leg position might explain this difference. ADL score was a subjective measure, and there was no blinding of subjects.
Hasegawa and collegues (2011)[100] RCT $N = 20$ enrolled; N analyzed nr	ACL recon Semitendinosis autograft (aged 13–54 yr) NMES ($n = 10$): POD 2 + Ex CON ($n = 10$): Ex	4 channels active simultaneously Electrodes: on quads, hams, tib ant, triceps surae Supine with knee ext	Monophasic PC 20 Hz 250 μs ON:OFF 5:2 s Amplitude set to max tolerable and individually progressed No simultaneous voluntary contraction with NMES	20 min/d 5 d/wk 4 wk	Muscle thickness: (US still imaging) @ pre-op and @ 4 and 12 wk Quads strength: Cybex normalized peak torque @ 60°/s pre-op and @ 4 and 12 wk Muscle function: Lysholm scores @ pre-op and 6 mo post-op	Increased thickness VL and triceps surae Less decline in quads strength Greater recovery of quads strength @ 12 wk No change in Lysholm scores	Unexpected finding given that the frequency (20 Hz) and duty cycle were less than typically used (50–80 Hz) for muscle strengthening. Frequency of 20 Hz may have limited fatigue associated with stimulation.
Lepley and colleagues (2015)[109] RCT Parallel longitudinal design $N = 43$ enrolled; $N = 36$ analyzed	ACL recon +10 healthy CON NMES ($n = 9$): post-op wk 1–6 + eccentric Ex from post-op wk 6 + PT NMES ($n = 12$): NMES alone post-op wk 1–6 + PT Eccentric Ex alone ($n = 9$): from post-op wk 6 + PT CON ($n = 13$): PT wk 1–6	7 × 13 cm 1 channel Electrodes: on VL and VM @ 60° knee flex	2500 Hz AC 75 Hz burst rate ON:OFF 10:50 s Ramp-up 2 s Amplitude max tolerable No simultaneous voluntary contraction with NMES Eccentric Ex: 4 sets of 10 @ 60% 1 RM; 2 min rest between sets	10 contractions 2 d/wk 6 wk	Strength: % MVIC change in quads strength (3 trials normalized to body weight) @ 90°/flex Quads activation: % change scores in Central Activation Ratio using superimposition burst technique Relationship change between quads activation and strength Quads activation and strength compared with healthy controls @ pre-op, 12 wk post-op, and return to play	Increased quads strength recovery using NMES + eccentric Ex or eccentric Ex alone No significant between-groups difference in all other outcomes	Eccentric Ex was the key determinant for improvements in muscle activation and strength (the authors contend that the stimulator they used was not powerful enough to overcome the inhibition of the muscle).

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Lieber and colleagues (1996)[106] RCT $N = 40$ enrolled; N analyzed nr Included in SR[92]	ACL recon 2–6 wk post-op and 90° knee flex NMES ($n = 20$): NMES CON ($n = 20$): Ex Both groups allowed therapist-monitored home Ex	Electrode size and placement nr	Custom-built device Asymmetric biphasic PC 50 Hz 250 μs ON:OFF 10:20 s (for both NMES and voluntary Ex) Ramp-up and ramp-down 2:2 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	30 min/d (60 contractions) 5 d/wk 4 wk Eccentric Ex increased 15%, 25%, 35%, and 45% of the injured limb's max volitional torque @ wk 1, 2, 3, and 4, respectively	Knee ext torque: torque transducer Transducer recorded muscle tension for each contraction over the 4-wk period for every subject, both NMES and Ex @ 6, 8, 12, 24, and 52 wk	No between-groups differences in all outcomes	The authors attempted to match the groups during training on the parameter of activity (Nm*Min). However, the voluntary Ex group still performed 30% more activity than NMES. Thus, on the basis of training intensity the study favoured the Ex group. Fatigue-inducing protocol of 300 contractions/wk might account for lack of benefit.
Paternostro-Slugo and colleagues (1999)[111] RCT $N = 49$ enrolled; $N = 47$ analyzed Included in SR[116]	Aged 17–40 yr Post–ACL recon ($n = 25$) Post–ACL patellar ligament repair ($n = 24$) NMES ($n = 16$): NMES + Ex TENS + Ex ($n = 14$) CON ($n = 17$): Ex	Electrode size nr 4 channels Electrodes: on MP, VL, rec fem, VM, hams	Monophasic PC 2 sets: set 1, 30 Hz, 200 μs; set 2, 50 Hz, 200 μs Set 1: ON:OFF 5:15 s, 6 min rest between sets Set 2: ON:OFF 10:50 s Amplitude tolerance level, strong visible muscle action No simultaneous voluntary contraction with NMES	Set 1: 12 contractions repeated 4 × (total 48) Set 2: 12 contractions BID (total 120 contractions/d) 7 d/wk 6 wk	Quads and hams strength: • Isometric (45° flex) • Isokinetic (60°/s) @ 6, 12, and 52 wk	No significant between-groups differences in strength	Tracked compliance Double blinded PD less than ideal to elicit muscle strengthening. No. of contractions for training greater than usual. Fatigue-inducing protocol of 500 contractions/wk might account for lack of benefit.
Rebai and colleagues (2002)[107] RCT $N = 10$ enrolled; $N = 10$ analyzed Included in SR[92]	ACL recon (6–24 mo post-injury) POD 3–4 NMES 80 Hz + Ex ($n = 5$) NMES 20 Hz + Ex ($n = 5$) Ex standardized 2 h/d, 5 d/wk	Electrode size nr Electrodes: on MP of 3 superficial heads of quads Knee ~75° flex	Asymmetric balanced biphasic PC NMES 20 Hz: amplitude set to achieve ≥ 25% MVIC NMES 80 Hz: amplitude set to achieve ≥ 35% MVIC 300 μs For 20 Hz group, ON:OFF 15:10 s; for 80 Hz group, ON:OFF 15:75 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	20 Hz: 144 contractions (60 min) 80 Hz: 36 contractions (54 min) 5 d/wk 12 wk	Muscle and fat volumes: MRI @ pre-op and 12 wk Quads and hams isokinetic strength: 90°/s, 180°/s, and 240°/s through 0–60° flex comparing the operated with contralateral limb @ 1 wk pre-op and 12 wk	Less deficit in muscle strength in 20 Hz group than in 80 Hz group @ 180°/s and 240°/s comparing operated with contralateral limb No difference in quads peak torque deficit @ 12 wk comparing pre- with post-op No effects on hams (less affected by strength loss) Less fat accumulation in NMES 20 Hz No significant between-groups differences in all other outcomes	The 20 Hz group received 4 times the number of quads contractions. Neither 20 Hz nor 80 Hz is ideal for muscle strengthening. 2 h of Ex is unusually high. No CON group for comparison.

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Ross (2000)[101] RCT $N = 20$ enrolled; N analyzed nr Included in SR[92]	ACL recon 1 wk post-op Aged 22–42 yr NMES ($n = 10$): NMES + CKC Ex CON ($n = 10$): CKC Ex Standard rehab both groups from POD 1	4 × 8.9 cm 2 channels Electrodes: on prox VL and distal VM and hams (prox medial hams and distal biceps femoris	Symmetric biphasic PC 50 Hz 200 μs ON:OFF 15:35 s, 3 s ramp-up Amplitude max tolerable No simultaneous voluntary contraction with NMES	30 min/d 5 d/wk 3 wk Then 3 d/wk for 2 wk	Anterior joint laxity: KT-1000 Unilateral squat to max knee flex Lateral step-up: max 15 s Anterior reach test: distance reached @ 0 and 6 wk	Better unilateral squat Better lateral step test @ 6 wk No significant between-groups differences in all other outcomes	Pilot study intended to determine reliability of outcome measures.
Sisk and colleagues (1987)[97] RCT $N = 24$ enrolled; $N = 22$ analyzed Included in SR[116]	ACL recon Knee immobilized in flex post-op NMES ($n = 11$): NMES POD 4–5 + Ex CON ($n = 11$): Ex Ex both groups from POD 2	10 × 5 cm 1 channel Electrodes through window in cast: 5 cm prox to patella and 3 cm distal to femoral triangle	Symmetrical biphasic PC 40 Hz 300 μs ON:OFF 10:30 s Rise time 0.5 s Amplitude self-adjusted to max comfortable No simultaneous voluntary contraction with NMES	8 h/d 7 d/wk 6 wk	MVIC quads @ 70°–80° flex: KinCom dynamometer—highest of 3 max trials, ratio of torque to body weight @ 7, 8, and 9 wk	No significant between-groups difference in any outcomes	8 h/d, 7 d/wk atypical; fatiguing protocol might account for lack of benefit.
Snyder-Mackler and colleagues (1995)[102] RCT Multicentre trial $N = 129$ enrolled; $N = 110$ analyzed Included in SR[92]	ACL recon (mixed grafts—e.g., Achilles, patellar semitendinosis, or gracilis) NMES ($n = 31$): NMES high intensity NMES ($n = 25$): NMES low intensity NMES ($n = 20$): NMES mixed high and low intensity CON ($n = 34$): high-intensity Ex from 1 wk post-op	1 channel High-intensity group: 8.9 cm diameter Electrodes: on proximal and distal VL Knee flex 65° Low-intensity group: 4 × 5 cm Electrodes: on proximal and distal VL Knee flex 90°	High-intensity group: 2500 Hz AC 75 Hz burst rate ON:OFF 11:120 s Low-intensity group: Waveform nr; PC 55 Hz 300 μs ON:OFF 15:50 s 15 min Amplitude max tolerated for each contraction No simultaneous voluntary contraction with NMES	High-intensity group: 15 contractions 3 d/wk 4 wk Low-intensity group: 15 contractions QID 5 d/wk 4 wk	Quads strength: NMES superimposition technique @ 4 wk Knee flex during stance @ 4 wk	Greater strength with high-intensity NMES and mixed-intensity NMES No effect using low-intensity NMES or Ex No significant between-groups differences in all other outcomes	Compliance monitored Suggests NMES using AC at high intensity is more effective than NMES using portable, battery-powered, low-frequency devices at lower intensity; however, it is important to note that groups also used different duty cycles, no. of contractions, and knee positions.

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Snyder-Mackler and colleagues (1994)[112] Analysis of a sub-sample of $N = 52$ from RCT reported in Snyder-Mackler (1995) [95] Included in SR[116]	ACL recon 2–6 wk post-op Aged 15–43 yr NMES ($n = 31$): NMES console device NMES ($n = 21$): NMES battery-powered device Standard rehab all groups from wk 1	Console device: 10.2 × 12.75 cm 1 channel Electrodes: on VM and prox VL Sitting knee flex 65° Battery device: 4 × 5 cm Electrodes: on VM and prox VL Sitting knee flex 90°	Console device: 2500 Hz AC 75 Hz burst rate 400 μs 50% duty cycle ON:OFF 11:120 s Battery device: Waveform nr; PC 55 Hz 300 μs 15 min ON:OFF 15:50 s Intensity max tolerated for each contraction No simultaneous voluntary contraction with NMES	Console device: 15 contractions 3 d/wk 4 wk Battery device: 13 contractions; QID 5 d/wk 4 wk	Quads strength: • MVIC ext torque compared with uninvolved quads expressed as % • Using burst superimposition technique	Linear relationship between quad torque and training intensity Training with medium-frequency units resulted in greater torque	Training intensities monitored. Suggests training with console units may be superior to that with portable units, but caution is required in interpretation because the parameters were different.
Snyder-Mackler and colleagues (1991)[103] RCT $N = 10$ enrolled; $N = 10$ analyzed Included in SR[92]	ACL recon 3–6 wk post-op Aged 18–28 yr NMES ($n = 5$): NMES + Ex CON ($n = 5$): Ex Ex = 15 co-contractions of 15 s duration @ 60–90° flex 2 × /d, 7 d/wk	Electrode size nr 1 channel Electrodes: 4 on quads VM and VL and on hams distal short head of biceps and proximal medial hams Sitting knee flex 60°	2500 Hz AC 75 Hz burst rate 50% duty cycle 400 μs ON:OFF 15:50 s; ON time included 3 s ramp Amplitude max tolerable, increasing each contraction No simultaneous voluntary contraction with NMES Monitored with Cybex to ensure no net ext torque	15 co-contractions of hams and quads 3 d/wk 4 wk	Gait analysis: motion analysis Quads strength: KINCOM isokinetic @ 90°/s and 210°/s; max peak and average torque over 3 trials Joint laxity: KT-1000 @ 4 wk	Increased quads strength Better gait parameters (cadence, stance time, and walking velocity) No significant between-groups differences in joint laxity	Log book used to check compliance with Ex. CON group also seen 3 d/wk to check Ex. Caution required in interpretation because of the small number of subjects.

Table 8 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Taradaj and colleagues (2013)[110] RCT $N = 80$ enrolled; N analyzed nr	ACL recon Soccer players 6 mo post-op NMES ($n = 40$): NMES + Ex CON ($n = 40$): Ex Both groups received standard 6 mo rehab post-op	8 × 6 cm 1 channel each leg Electrodes: on quads bilaterally, exact location nr @ knee flex 60°	2500 Hz AC 50 Hz burst rate ON:OFF 10:50 s 55–67 mA Amplitude set to produce a strong, visible motion, but no ROM was permitted during stimulation No simultaneous voluntary contraction with NMES	10 contractions 30 min BID (3 h between treatments) 3 d/wk 4 wk	Strength: tensometry Muscle circumference: tape measure Ease of motion: goniometry pendulum test @ 1 and 3 mo	Increased strength Increased thigh circumference No significant between-groups differences in goniometry	Blinded assessor Large sample size Ex programme is not applicable to early post-op period: aggressive nature of Ex would likely jeopardize the recon. This study supports starting NMES late (i.e., 6 mo) in athletes who have not regained strength as expected.
Wigerstad-Lossing and colleagues (1988)[113] RCT $N = 23$ enrolled; $N = 26$ analyzed Included in SR[116]	ACL recon (patellar tendon) POD 2 NMES + Ex ($n = 13$) CON ($n = 10$): Ex (10 min/h, 8/d)	4 × 10 cm 1 channel Electrodes through window in cast: 5 cm distal to inguinal ligament and 10 cm proximal to patella base on VL	Asymmetrical balanced biphasic PC 30 Hz 300 μs ON:OFF 6:10 s +2 s ramp up Intensity max tolerated (65–100 mA) Simultaneous voluntary quads contraction	4 sets of 10 min 10 min intervals between sets (132 quad contractions) 3 d/wk NMES group instructed to reduce home Ex to 50% on NMES days	Knee extension strength: • Cybex • MVIC @ 30° and 60° flex • Isokinetic @ 30°/s and 180°/s @ pre-op and 6 wk CSA: CT @ pre-op and 6 wk Oxidative and glycolytic enzyme activity: biopsy @ pre-op and 6 wk	Less reduction in isometric strength Less reduction in CSA Less decrease in oxidative and glycolytic enzyme activity	Compliance in control group was addressed by attending PT 1 × /wk. Results suggest that use of NMES, applied very early post-op, prevents secondary muscle weakness. (Note that in the 1980s, patients were immobilized in a cast post-op for extended periods.)

NMES = neuromuscular electrical stimulation; ACL = anterior cruciate ligament; CON = control; RCT = randomized controlled trial; SR = systematic review; POD = post-operative day; flex = flexion; CPM = continuous passive motion; TENS = transcutaneous electrical nerve stimulation; ext = extension; nr = not reported; PC = pulsed current; ROM = range of motion; recon = reconstruction; PEMF = pulsed electromagnetic fields; VM = vastus medialis; hams = hamstring muscle; MVC = maximum voluntary contraction; pre-op = pre-operatively; post-op = postoperatively; VAS = visual analog scale; MVIC = maximum voluntary isometric contraction; Ex = exercise; max = maximum; quads = quadriceps muscle; EMG = electromyography; BF = biofeedback; prox = proximal; TID = 3 times per day; PD = pulse duration; VL = vastus lateralis muscle; SDH = succinate dehydrogenase; Rx = treatment; ADL = activities of daily living; NPRS = numerical pain rating scale; tib ant = tibialis anterior muscle; US = ultrasound; AC = alternating current; RM = repetition maximum; Nm*Min (defined as activity = muscle tension × contraction duration; BID = twice per day; MP = motor point; rec fem = rectus femoris muscle; MRI = magnetic resonance imaging; CKC = closed kinetic chain; QID = 4 times per day; rehab = rehabilitation; CSA = cross-sectional area; CT = computed tomography; PT = physiotherapy/physical therapy.

2B. PATELLOFEMORAL PAIN SYNDROME

Indications and rationale for using NMES

Quads muscle weakness, indicated by reduced peak torque, is believed to play a key role in PFPS.[118] Weakness of the vastus medialis (VM) is thought to be particularly important[119] because the VM normally counterbalances the vastus lateralis muscle; VM weakness may be a cause of patellar mal-alignment, with the resultant abnormal tracking of the patella in the trochlear groove.[120] It is uncertain whether quads weakness is the cause or a consequence of pain in PFPS.[121] NMES activation of the quads, particularly of the relatively weaker VM, may facilitate normal tracking of the patella in the trochlear groove.

Table 9 Summary of the Literature and Recommendations for Use of NMES in PFPS

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
PFPS	**Electrode placement:** No standardized location reported in the literature. Recommended placement is based on a critical review of the literature: 2 electrodes, 1 over the rec fem and vastus intermedius muscle bellies, the other over the VM.[122,123] Recommendation is to position electrodes in line with the orientation of the muscle fibres.[124,125] **Limb position:** No standardized location reported in the literature. From a clinical perspective, it is advisable to avoid the portion of the ROM that is provocative – i.e., position within the pain-free range. **NMES waveform:** low-frequency biphasic PC[122,123,126,127] **Frequency:** 35–50 Hz[122,123,126,127] **Pulse duration:** 250–500 μs[122,123,126,127] **Current amplitude:** individual max tolerated intensity[122,123,126–128] **Work–rest cycle:** ON:OFF 6–10:10–50 s; OFF times should be consistent with the treatment goals: shorter rest period ($\leq$10 s) for endurance training, 30–50 s for strengthening purposes[122,123,126–128] **Treatment schedule:** 12–15 contractions per session, as is typically reported in NMES literature relating to quads weakness[98,99,102,103,108–110,112] **Session frequency:** ideally, 3 d/wk over 4–6 wk[127]	✓ Reduction in pain (VAS)[123,126,128] ✓ Increased force-generating capacity (EMG)[127] ✓ Deactivation of VL[127]
Rationale for recommended NMES protocol	In accordance with evidence for the importance of selective strengthening of VM,[129] electrode placement should target VM and either rec fem and vastus intermedius or femoral nerve. Other recommended parameters are in accordance with those sufficient to elicit a strengthening effect. In contrast, using a short rest period and high number of reps (e.g., $\geq$ 60 reps/d) is thought to target muscle endurance rather than strength.[130] Effects of an endurance-type protocol were shown by delayed onset of quads fatigue in PFPS using 35 Hz (main frequency) and 60 contractions daily, 7d/wk, for 6 wk.[123,126]	
Physiological effect of NMES	NMES can assist in recruitment of motor fibres of VM, which are typically relatively weaker in PFPS than are other muscles of the quads mechanism. NMES activates sensory fibres; this may also be a factor in reducing PFPS pain.	

Table 9 *continued*

Critical review of research evidence	• Effectiveness has been examined in 1 SR[131] consisting of 12 RCTs, of which 4 involved NMES for PFPS. The review was descriptive in nature. Authors of the SR concluded that combined NMES + Ex provided no added benefit than Ex alone for strengthening quads and noted that because Ex was part of the intervention, it was not possible to determine the possible benefits of NMES alone. In drawing conclusions, however, the authors did not consider whether NMES parameters in any of the RCTs were optimal for strengthening VM; potential parameters contributing to the lack of benefit include low frequency,[122,123,126] low pulse charge,[128] high number of daily contractions,[122,123,126] and, in 1 study, use of an insensitive measure to assess change in muscle strength (manual muscle test).[128] • Interpretation of the literature is further complicated by comparison between 2 different forms of stimulation, sometimes without a sham group.[126] Increased strength was shown in 2 RCTs that compared mixed versus fixed NMES frequency and low versus high NMES frequency.[123,126]These results cannot be interpreted as strong evidence because there was no CON group. • NMES was applied for 6 wk without Ex in a controlled cohort study of 10 subjects with PFPS. The finding of increased force generation of the VM and decreased activation of VL using EMG as an outcome measure demonstrates the potential benefit of NMES.[127] • Feasibility has been demonstrated. • No adverse effects have been associated with NMES in this population. • The literature does not indicate that NMES is not effective in the management of PFPS; this has not been conclusively demonstrated.

NMES = neuromuscular electrical stimulation; PFPS = patellofemoral pain syndrome; rec fem = rectus femoris muscle; VM = vastus medialis; ROM = range of motion; PC = pulsed current; max = maximum; quads = quadriceps muscle; VAS = visual analog scale; EMG = electromyography; VL = vastus lateralis; reps = repetitions; SR = systematic review; RCT = randomized controlled trial; Ex = exercise; CON = control.

Table 10 Details of Individual Studies on Use of NMES in PFPS

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Akarcali and colleagues (2002)[128] RCT $N = 44$ enrolled; $N = 44$ or 42 analyzed (tables report 42 or 44) Included in SR[131]	PFPS $>$ 2 mo Aged 15–45 yr NMES ($n = 22$): HVPC + Ex CON ($n = 22$): Ex	4×4 cm 1 channel Electrodes: on VM 4 cm superior to and 3 cm medial to superomedial border patella Weight bearing with comfortable knee flex position	High-voltage PC 60 Hz 65–75 μs ON:OFF nr Amplitude max tolerable without pain Simultaneous voluntary contraction with NMES	10 min 5 d/wk 6 wk	Pain: VAS Strength: Lovett's manual muscle test @ 0, 3, and 6 wk	Less pain @ 3 wk No significant between-groups differences in all other outcomes	Parameters unlikely to increase strength (waveform combines rapid decay of intensity with very short pulse duration). Thus, equal increase in strength may be explained by Ex effects alone. Manual muscle test may be insensitive to improvement No blinding
Bily and colleagues (2008)[122] RCT $N = 38$ enrolled; $N = 36$ analyzed @ 12 wk; $N = 29$ analyzed @ 1 yr Included in SR[131]	PFPS NMES ($n = 19$): NMES + Ex CON ($n = 19$): Ex	5×13 cm 2 channels Electrodes: on prox and distal quads	Asymmetrical biphasic PC 40 Hz 260 μs ON:OFF 5:10 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	20 min BID (160 contractions/d) 60 min rest between sessions 5 d/wk 12 wk	Pain: VAS max Function: Kujala PFPS Score Strength: seated isometric with strain gauges @ 0, 12 wk, and 1 yr	No between-groups differences	High number of repetitions, 800 contractions/wk, is typically used for training muscle endurance. However, the authors expected that quads strength would increase. No blinding Study was underpowered to detect change in pain.
Callaghan and Oldham (2004)[123] RCT $N = 80$ enrolled; $N = 79$ treated; $N = 74$ analyzed Included in SR[131]	PFPS NMES ($n = 38$): Experimental device NMES ($n = 41$): Conventional device	Conventional device: 5×9 cm 2 channels Electrodes: on quads; exact location nr Experimental device: 10×17 cm 1 channel Electrodes: on quads, upper lateral and distal medial	Conventional device: Asymmetrical biphasic PC 35 Hz 300 μs ON:OFF 10:50 s Experimental device: Asymmetrical balanced biphasic PC 200 μs 5 pulse train frequencies (125, 83, 50, 2.5, and 2 Hz) ON:OFF 10:50 s Amplitude set to highest comfortably tolerable No simultaneous voluntary contraction with NMES	60 min/d (60 contractions) 7 d/wk 6 wk	Lower extremity isometric and isokinetic torque @ 90°/s, Biodex Quads fatigue: EMG Knee flex in squatting: goniometer Patellar pain: VAS Step test: number until onset of pain Quads CSA: US imaging Function: Kujala PFPS Score @ 0 wk and within 1 wk after final NMES session Double blind	Similar improvements: Strength Fatigue Squatting Pain Step test CSA Function	Findings indicate that NMES is equally effective when delivered using mixed- vs. fixed-frequency pattern. This was a comparison between 2 types of NMES; with neither a CON nor a sham comparison, it is not possible to evaluate the effect of NMES. Short-term results

Table 10 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Callaghan and colleagues (2001)[126] RCT $N = 16$ enrolled; $N = 14$ analyzed Included in SR[131]	PFPS 6 mo–3 yr NMES 1, experimental: simultaneous mixed frequency NMES 2, conventional: sequential mixed frequency	Electrodes: Size nr 2 channels Electrodes: on quads; exact location nr	NMES 1: Asymmetrical balanced biphasic PC Low-frequency background with superimposed pattern of high-frequency bursts 200 μs ON:OFF 10:50 s Amplitude max tolerable NMES 2: Asymmetrical biphasic PC Wk 1–4, 8 Hz × 2 min, 35 Hz × 20 min, 3 Hz × 3 min; wk 5–6, 8 Hz × 2 min, 45 Hz × 20 min, 3 Hz × 3 min 250–350 μs ON:OFF nr Amplitude nr No simultaneous voluntary contraction with NMES	NMES 1: 1 h/d (60 contractions) 7 d/wk 6 wk NMES 2: 1 h/d (60 contractions) Wk 1–2, 5 d/wk; wk 3–4, 3 d/wk; wk 5–6, 2 d/wk	Isometric and isokinetic ext torque: Biodex Muscle fatigue rate: EMG Pain: VAS Function: Kujala PFPS Score Step test Knee flex: max squat range Quads CSA: US scan @ 0, 7, 8, and 9 wk	Similar improvements: Strength Pain Function Step test Squat	Rationale was to improve both muscle fatigue (low Hz) and strength (high Hz). Findings indicated that NMES is equally effective when delivered using mixed sequential- vs. mixed simultaneous-frequency pattern. Small sample. No CON or sham group.

NMES = neuromuscular electrical stimulation; PFPS = patellofemoral pain syndrome; RCT = randomized controlled trial; SR = systematic review; HVPC = high-voltage pulsed current; Ex = exercise; CON = control; VM = vastus medialis; PC = pulsed current; nr = not reported; max = maximum; VAS = visual analog scale; prox = proximal; quads = quadriceps muscle; BID = 2 times per day; flex = flexion; CSA = cross-sectional area; US = ultrasound; ext = extension; EMG = electromyography.

2C. DEGENERATIVE ARTHRITIS AND OSTEOARTHRITIS

Indications and rationale for using NMES

Weak quads, loss of functional capacity and endurance (e.g., stair climbing, distance walking, timed up-and-go), pain, and stiffness are common reports of people with symptomatic knee OA.[132] NMES is indicated to strengthen weak quads muscles, train endurance, minimize atrophy, and increase ROM at the joint.[4,133,134]

Table 11 Summary of the Literature and Recommendations for Use of NMES in Knee OA

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
Knee OA	**Electrode placement:** large electrodes placed on quads muscle belly proximally on rec fem and distally on VM, VL, or both[135–138] **Limb position:** sitting; hip flexed to 90°, knee flexed 60–90° 135,136,138 **NMES waveform:** low-frequency biphasic PC[135–139] **Frequency:** 50 Hz[135–139] **Pulse duration:** 250–300 μs[135–140] **Current amplitude:** individual max tolerated intensity[135,138,140] **Work–rest cycle:** ON:OFF 10:50 s (1:5 ratio)[135,137,139] **Treatment schedule:** 15–20 contractions with Ex[135–137,139] **Session frequency:** 3 d/wk, 4–8 wk[135–140]	✓ Strength (OHAUS dynamometer, Kin-Com, 1 RM, 10 RM)[136,139,140] ✓ Improved self-reported function (WOMAC, SF-36)[135–137,140,141] ✓ Improved function (SCT, 6MWT, 25-metre walk test, TUG)[135,136,138–142] ✓ Pain (WOMAC)[136]
Rationale for recommended NMES protocol	NMES parameters for knee OA vary in the literature. A frequency of 50 Hz was used in 5 studies in Table 12; it was combined with an ON:OFF duration of 10:50 s in 3 studies and of 10:10 s or 10:30 s in 2 studies. Muscle strength increased in 3 of 4 studies that measured strength.[136,139,140] Function and endurance increased in 3 (1 a marginal effect) of 4 studies that measured endurance.[135,136,138] Pain decreased in 4 of 6 studies that measured pain.[136–138,140] The recommended protocol is based on 5 studies.[136–140] A further study used AC at 50 Hz burst rate with no resulting benefit for strength, pain, or function. This result may be due to using a protocol that consisted of a low number of contractions/wk (30) with neither supervised volitional Ex nor a self-management programme (e.g., home Ex, ROM).[141] In contrast, NMES using 45 contractions/wk combined with Ex improved quads activation and strength after knee surgery.[143] NMES using max tolerated amplitude at each session appears to have been the most effective. In contrast, amplitude, increased gradually up to 40% of MVIC over a 9-wk treatment period, increased strength but not more so than intensive Ex.[136] A study that used an endurance type of protocol (25 Hz, 5:5 ON:OFF, 180 contractions 3 d/wk, max tolerated amplitude) showed increased strength and function.[140] This protocol might be an alternative to the one recommended earlier, but additional study of this protocol is needed. Patterned NMES is not recommended because the single study using this approach showed results for the experimental groups that were not better than sham; furthermore, within-group benefits for the experimental group were seen at some measurement intervals but not others.[142]	
Physiological effect of NMES	NMES can cause beneficial adaptations mediated by muscular and neural mechanisms. Tetanic contractions elicited by pulses of high intensity and short duration induce a high metabolic stress in the muscle, contribute to the reversal of inadequate motor unit recruitment, and improve the maximal capability of the neuromuscular system through increased force-generating capacity of the muscle and also through intensified voluntary activation.[5]	

Table 11 *continued*

Critical review of research evidence	• We reviewed the individual RCTs identified by our search protocol as well as 2 recent SRs.[144,145] • 1 of the SRs examined NMES specifically for quads strengthening in elderly people with knee OA.[144] 6 studies met the criteria; although a meta-analysis was not possible, the authors stated that a best-evidence analysis showed moderate evidence in favour of NMES alone or combined with isometric quads Ex for strengthening. • The literature on NMES in knee OA has some limitations. In some cases, randomization methods were not fully described, sample size was not calculated, or observed power was not reported. Some studies had high unexplained drop-out rates.[135,138,140] • Studies can also be criticized for risk of bias because subjects and therapists were not blinded to group allocation. This will almost always be the case in RCTs involving NMES because it is difficult to design sham NMES: Electrical current at amplitude less than contraction threshold (i.e., TENS-type current) would not suffice because TENS has been shown to reduce pain in knee OA, which might in turn affect function and quality of life. • Interpretation of the literature is complicated by the use of a variety of NMES parameters and outcome measures. • A recent large RCT[135] showed significant effect of NMES on functional outcomes. • Feasibility has been demonstrated. • No adverse effects have been associated with NMES in this population.

NMES = neuromuscular electrical stimulation; OA = osteoarthritis; quads = quadriceps muscle; rec fem = rectus femoris muscle; VM = vastus medialis muscle; VL = vastus lateralis muscle; PC = pulsed current; max = maximum; Ex = exercise; RM = repetition maximum; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 = Short Form (36) Health Survey; SCT = stair-climbing test; 6MWT = 6-min walk test; TUG = timed up-and-go test; AC = alternating current; ROM = range of motion; MVIC = maximum voluntary isometric contraction; RCT = randomized controlled trial; SR = systematic review; TENS = transcutaneous electrical nerve stimulation.

Table 12 Details of Individual Studies on Use of NMES in Knee OA

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Bruce-Brand and colleagues (2012)[135] RCT $N = 41$ enrolled; $N = 32$ analyzed @ 8 wk; $N = 26$ analyzed @ 14 wk	Knee OA Aged 55–75 yr NMES ($n = 14$): home-based NMES group Home-based resistance training group ($n = 14$) CON ($n = 13$): standard care (arthritis education, pharmacological therapy, PT)	Electrodes 194, 83, 74, and 66 cm^2 2 channels fitted into a garment Electrodes: on quads on rec fem, VL, & VM Sitting knee flex 60°	Symmetric biphasic PC 50 Hz 100–400 μs changing dynamically during ON time ON:OFF 10:50 s, +1 s ramp-up) Amplitude: max tolerable intensity No simultaneous voluntary contraction with NMES	NMES: 20 min/d (20 contractions) 5 d/wk 6 wk Resistance training: 30 min 3 d/wk 6 wk	Primary: Functional capacity: • 25 m walk test • Chair rise test • SCT Secondary: WOMAC SF-36 Strength: Biodex • Peak isometric and isokinetic torques @ 0, 1, 8, and 14 wk CSA by MRI @ 0 and 8 wk	Functional capacity (timed walk, chair rise, stair climb) improved using NMES and resistance training compared with CON @ wk 8 and 14 Assessors were blinded.	Adherence monitored using patient-logged data. NMES device also recorded usage.
Durmuş and colleagues (2007)[136] RCT $N = 50$ enrolled; $N = 50$ analyzed Included in SR[144,145]	Knee OA Women aged 42–74 yr NMES ($n = 25$): NMES CON ($n = 25$): BF-assisted isometric Ex	Electrode size nr NMES: 2 channels Electrodes: on quads on rec fem and VM and on MP of VL Knee flex 60° CON: Recording electrodes: on rec fem, VM, and VL Knee flex 25–30° All sessions at clinic	NMES: Asymmetric biphasic PC 50 Hz 200 μs ON:OFF 10:10 s Amplitude set to visible muscle contraction (70–120 mA) No voluntary Ex program CON: Voluntary muscle contraction. ON:OFF 10:50 s Muscle potentials transduced to visual and auditory signals	20 min (60 contractions) 5 d/wk 4 wk	Pain: VAS • At rest • During activity • At night WOMAC: pain, disability, and stiffness Strength: 1 RM and 10 RM Functional capacity: • 50 m timed walk • SCT @ 4 wk	Significant improvement in both groups on all outcomes. No significant between-groups differences @ 4 wk	A protocol of high daily reps, short rest period, and low NMES intensity might have compromised NMES effectiveness for strengthening. Study suggests that NMES is as effective as BF-assisted Ex. NMES combined with Ex was not studied, and there was no sham or untreated CON group. Blinding of subjects, study staff, and assessors nr. Risk of bias cannot be evaluated.

Table 12 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Gaines and colleagues (2004)[137] RCT $N = 43$ enrolled; $N = 38$ analyzed Included in SR[145]	Knee OA Aged $>$ 60 yr NMES ($n = 20$): NMES home-based + arthritis self-help course CON ($n = 18$): arthritis self-help course only (12-hr, community-based education about OA, pain management, Ex, etc.)	10.2 $\times$ 12.7 cm 1 channel Electrodes: on quads on VL and VM Limb position: nr	Symmetric biphasic PC 50 Hz 300 μs ON:OFF 10:50 s, ramp-up 3 s Amplitude: wk 1–4, 10%–20% MVC; wk 5–8, 20%–30% MVC; wk 9–12, 40% MVC 12-hr community-based education, 1 h/wk No simultaneous voluntary contraction with NMES	15 min/d (15 contractions) 3 d/wk 12 wk	NMES pain diary score (1–10 numerical scale): before and 15 min after each NMES session MPQ pain intensity @ 0, 4, 8, 12, and 16 wk AIMS @ 0 and 12 wk	Pain diary scores decreased immediately after 74% of all NMES sessions No significant between-groups differences on all other outcomes	Assessors were not blinded for the baseline MVC test for the NMES group. Only outcomes were self-reported pain. NMES amplitude was low for wk 1–8; furthermore, the authors were unable to check whether the subjects used the prescribed amplitude.
Imoto and colleagues (2013)[138] RCT $N = 100$ enrolled; $N = 82$ analyzed	Knee OA Aged 50–75 yr NMES ($n = 50$): NMES + education guide + strengthening, stretching, + ROM Ex CON ($n = 50$): education guide	Electrodes 7.5 $\times$ 13 cm Quads on rec fem and VM Subjects sitting knee flex 90°	Symmetric biphasic PC 50 Hz 250 μs ON:OFF 10:30 s Amplitude max tolerable Simultaneous voluntary contraction against resistance with NMES	20 min/d d/wk nr 8 wk	Primary: TUG NPRS Secondary: Lequesne index ADL scale @ 8 wk	Marginal effect on TUG Improved NPRS Improved Lequesne index Improved ADL @ 8 wk Blinded assessor	Drop-out subjects were accounted for in the analysis. Study focused on pain and function. Muscle strength was not measured.
Oldham and colleagues (1995)[142] RCT $N = 30$ enrolled; $N = 28$ analyzed Included in SR[145]	OA knee Aged $>$ 55 yr Patterned NMES group ($n =$ nr) NMES ($n =$ nr): NMES uniform frequency (interpulse interval constant) NMES random frequency (varying interpulse interval) group ($n =$ nr) CON: sham NMES ($n =$ nr)	7.6 $\times$ 12.7 cm 1 channel Electrodes: on quads on VL and VM Limb position: nr	Asymmetric balanced biphasic PC Patterned NMES: replicated the discharge rate of a fatigued normal quad motor unit with mean frequency = 8.4 Hz NMES uniform and random frequency = 8.4 Hz Sham NMES: 1 pulse/3 min All NMES groups: 300 μs ON:OFF 30:15 s Amplitude set to minimum required to produce a visible contraction No simultaneous voluntary contraction with NMES	3 consecutive h/d 7 d/wk 6 wk	Strength: MVIC Endurance: a sustained MVIC CSA: US scanner Functional capacity: • Sit to stand • 10 m timed walk test Nottingham Health Profile (part II) @ 1, 2, 3, 4, 5, 6, 8, 10, 12, and 18 wk Double blind	No significant between-groups differences	Inconclusive results mainly because significant within-group effects were limited to specific weeks during the study. The low frequency, long ON times, brief OFF times, low intensity, and 280 contractions/wk are typical of muscle endurance training protocols. This may explain lack of strengthening effects; however, endurance effects were also limited to specific weeks during the study.

Table 12 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Palmieri-Smith and colleagues (2010)[141] RCT $N = 30$ enrolled; $N = 30$ analyzed Included in SR[145]	Women with knee OA Kellgren and Lawrence score 2–3 NMES ($n = 16$): NMES CON ($n = 14$): no intervention	6.9 × 12.7 cm 1 channel Electrodes: on quads on rec fem and VM Subjects seated; knee flex 90°	2500 Hz AC 50 Hz burst rate ON:OFF 10:50 s, including 2 s ramp-up Amplitude max tolerable to produce at least 35% MVIC No simultaneous voluntary contraction with NMES	10 contractions 3 d/wk 4 wk	Quads strength and activation using superimposition technique WOMAC score: pain, stiffness, disability 12.19 m (40 ft) timed walk test @ 0, 5, and 16 wk	No significant between-groups differences	In each group, 50% of subjects reported asymptomatic knees at baseline. In addition, weakness and activation failure were relatively mild. Findings of non-effectiveness in mild OA may not apply to advanced OA. 10 contractions, 3d/wk × 4 wk without any other intervention (Ex, education, self-help techniques, etc.) are not likely to prove beneficial 1 wk post-intervention. Subjects and assessors not blinded; high risk of bias.
Rosemffet and colleagues (2004)[140] RCT pilot study $N = 37$ enrolled; $N = 26$ analyzed Included in SR[144,145]	Knee OA Median age 60 yr NMES ($n = 8$): sitting Ex group ($n = 10$) NMES + Ex ($n = 8$)	Electrode size nr Limb position: seated	Monophasic PC 25 Hz 250 μs ON:OFF 5:5 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	30 min/d (180 contractions) 3 d/wk 8 wk Supervised Ex training: 75 min/d 2 d/wk 8 wk	WOMAC Knee pain: VAS Quads strength: dynamometer Functional capacity: 6MWT @ 0 and 8 wk	All groups improved on pain and WOMAC scores NMES + Ex increased strength compared with either NMES or Ex alone @ 8 wk No significant between-groups differences in all other outcomes	A total of 11 non-compliant subjects were lost to follow-up; group assignment of missing subjects nr. Some aspects of this protocol are more reflective of endurance training (low frequency, short ON:OFF times, high reps). All 3 groups showed improved endurance. Authors stated that strength was analyzed after adjusting for pain. Reason and procedure for doing this were not explained; baseline pain scores were similar.

Table 12 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Talbot and colleagues (2003)[139] RCT $N = 38$ enrolled; $N = 34$ analyzed Included in SR[144,145]	Knee OA Aged $>$ 60 yr NMES ($n = 20$): NMES home-based + arthritis self-help course CON ($n = 18$): arthritis self-help course (12-hr, community-based education about OA, pain management, Ex, etc.)	10.2 $\times$ 12.7 cm 1 channel Electrodes: on quads; exact placement nr Limb position nr	Symmetric biphasic PC 50 Hz 300 μs ON:OFF 10:50 s; ramp-up 3 s Amplitude: wk 1–4, 10%–20% MVC; wk 5–8, 20%–30% MVC; wk 9–12, 40% MVC No simultaneous voluntary contraction with NMES Education: community-based 1 hr/wk for 12 wk	15 min/d (15 contractions) 3 d/wk 12 wk	Primary: Quads peak torque: KinCom @ 0, 4, 8, 12, and 24 wk Secondary: Physical activity: accelerometer, pedometer • Daily step count • Total activity vector Functional performance: • 30.5 m walk-turn-walk • SCT • Chair rise test Pain: MPQ @ 0, 12, and 24 wk	Increased peak quad torque @12 wk No significant between-groups differences in all other outcomes	Assessors were not blinded; high risk of bias. Adherence assessed using patient log book and a concealed metre in the device. Amplitude was low up until wk 9.

NMES = neuromuscular electrical stimulation; OA = osteoarthritis; CON = control; RCT = randomized controlled trial; PT = physiotherapy/physical therapy; quads = quadriceps muscle; rec fem = rectus femoris muscle; VL = vastus lateralis muscle; VM = vastus medialis; flex = flexion; PC = pulsed current; max = maximum; SCT = stair-climbing test; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 = Short Form (36) Health Survey; RM = repetition maximum; CSA = cross-sectional area; MRI = magnetic resonance imaging; SR = systematic review; BF = biofeedback; Ex = exercise; nr = not reported; MP = motor point; VAS = visual analogue scale; MVC = maximum voluntary contraction; MPQ = McGill Pain Questionnaire; AIMS = Arthritis Impact Measurement Scale–2; ROM = range of motion; TUG = timed up-and-go test; NPRS = numerical pain rating scale; ADL = activities of daily living; MVIC = maximum voluntary isometric contraction; US = ultrasound; AC = alternating current; 6MWT = 6-min walk test; reps = repetitions.

2D. TOTAL JOINT REPLACEMENT

Indications and rationale for using NMES

Quads weakness secondary to end-stage knee OA[146,147] and post-surgical trauma is very common in patients after total knee arthroplasty (TKA).[146–148] NMES is commonly used after TKA to strengthen the quads and to provide an adequate training dose for those lacking sufficient volitional quads activation; it engages neurophysiological mechanisms thought to facilitate strength gains and provides a general physical stress to the quads' neuromuscular system. The goal is to attenuate the dramatic strength loss immediately post-operation, which typically persists for 1 year. NMES is also used to address quads weakness after total hip arthroplasty.

Table 13 Summary of the Literature and Recommendations for Use of NMES in TKA and THA

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
TKA and THA	**Electrode placement:** quads; large electrodes placed proximally and distally on the belly of the muscles, typically rec fem and VM.[143,149–154] Recommendation is to position electrodes in line with the orientation of the muscle fibres.[124,125] **Limb position:** sitting; knee flexed 60–90°[143,152–154] **NMES waveform:** low-frequency biphasic PC[149–151,153–156] or 2500 Hz burst-modulated AC[143,152] **Frequency:** 50 Hz PC (range 40–75 Hz) or AC @ 50 Hz burst rate **Pulse duration:** 250–400 μs[149,150,153,155–157] **Current amplitude:** individual max tolerated intensity (use large electrodes for better comfort and to reach more motor units)[143,149–155,157] **Work–rest cycle:** ON:OFF 5–10:8–80 s. Ratio of 1:2 or 1:3 recommended when using 10–50 Hz PC.[153,154] Ratio of 1–8 recommended when using 2500 Hz AC.[143,152] **Treatment initiation:** ideally on POD 1 or 2 **Session frequency:** For increasing quads activation and strength as well as function, 10–30 contractions/d, 3 d/wk, for 6 wk.[143,152,153] For increased function, 1–2 h/d, 5d/wk, for 6 wk.[149–151] **Indication:** Use combined with (not simultaneously with) supervised active Ex, resisted Ex, or both.	• Improved muscle strength: isometric, isokinetic[143,152–155,157] • Muscle activation[143,145,152–155] • Reduction in loss of muscle volume or thickness[154,157] ✓ Improved self-reported function or disability (WOMAC, KOOS, Knee Society Score, Oxford Knee Score)[153,154,156] ✓ Improved function (SCT, 3MWT, 6MWT, TUG)[149,150,152–154,156] ✓ Improved walking speed[149,150,152,153,156] ✓ Perceived health status (SF-36)[149]
Rationale for recommended NMES protocol	NMES protocols in the literature for TKA generally adhere to 1 of 2 types. Low number of contractions, 3 d/wk, with max tolerated amplitude and knee restrained in 60° flexion appears to significantly enhance muscle strength and activation; functional benefits are also seen. Protocols that incorporate a very high number of reps (100–500 contractions/d) at max amplitude generally do not demonstrate a strengthening effect and are thought to target muscle endurance.[4] However, even functional outcomes appear limited using this type of protocol.[149–151,154] For example, investigators applied an endurance-type NMES protocol during continuous passive motion and reported benefits for knee extensor lag, 14° less than CON, and LOS a half-day shorter than CON; it is not clear whether these are clinically important differences.[151] In summary, our recommendations are to use a protocol targeting strength and function, combining low reps with rest periods that prevent muscle fatigue. There is some evidence for beginning NMES pre-op.[154,156] 2 small RCTs examined NMES effects on quads in patients undergoing THA.[155,157] Because there were only 2 studies and their designs and protocols are quite different, it is difficult to be confident that the parameters recommended for TKA are equally ideal for THA patients. The literature offers explanations for why NMES combined (non-simultaneously) with Ex is the optimal approach to muscle strengthening.[5]	
Physiological effect of NMES	A profound loss of quads strength, marked failure of voluntary muscle activation, and a decrease in quads CSA occur after TKA. The loss of strength is largely explained by a combination of failure of voluntary muscle activation and atrophy. Failure of voluntary muscle activation (not explained by increased pain) explains much more of the strength loss than atrophy.[5,148,158] NMES has been shown to decrease atrophy and reduce muscle protein breakdown.[159–161] Ex programmes that encourage high-intensity muscle contractions and interventions such as NMES that facilitate activation appear to counter the large deficit in quads strength.[5]	

Table 13 *continued*

Critical review of research evidence	• We reviewed the individual RCTs identified by our search protocol as well as the most recent SR[162] and 1 descriptive review of NMES post-TKA.[163] • 2 studies met the SR inclusion criteria. 1 study treated patients who had been designated as suitable for TKA but who were not yet pre-op; this study is included in our review of NMES for OA (Table 12).[142] Authors of the SR were not able to reach conclusions about the second study; it is not included here because it is a PhD thesis and is not widely available. • Interpretation of the literature is difficult because of wide variation in use of NMES parameters. 3 studies applied NMES using low contraction–repetition rates 3 d/wk and showed improved strength, muscle activation, and function. 2 of these studies had a good sample size (*N*s = 66 and 200); the third was a study with 8 subjects, each acting as his or her own control. All 3 studies appeared to fully describe their methods of treatment, measurement, and statistical analysis; the protocols could easily be replicated for clinical application. Follow-up was 6[143] or 12 mo,[152,153] with some loss to follow-up at 12 mo.[152] There is possible risk of bias because of the lack of blinding.[143,153] Overall, these protocols can be used with considerable confidence that they provide benefit post-TKA. • It should be noted that the effects of a PT-supervised, specialized, progressive-resistance Ex programme[152] performed 2–3 d/wk for 6 wk post-TKA were not enhanced by adding NMES. More important, however, traditional community-based rehabilitation without NMES did not produce the same results as the Ex programme.[152] • As noted previously, NMES studies are difficult to design with convincing blinding of subjects and therapists. Electrical current at amplitude less than contraction threshold (i.e., TENS-type current) would not suffice because TENS has been shown to reduce pain in the knee with OA, which might in turn affect function and quality of life. Assessors should always be blinded; Table 14 shows this was not always the case. • Incomplete reporting of methods confounds attempts to evaluate some of the protocols involving high contraction–repetition rates.[149,150,156] Furthermore, conflicting results among these studies create doubt about possible clinical usefulness. The uncertainty is compounded by unexplained findings within studies, for example, improved function according to chair-rise and stair-climbing tests but not according to walking tests, perceived disability (WOMAC), or health status (SF-36).[154] • Feasibility has been demonstrated; furthermore, recent studies have shown that patients tolerate NMES even on POD 1–2. • No adverse effects have been associated with NMES in this population. • Further studies are needed on the use of NMES for strength training in THA.

NMES = neuromuscular electrical stimulation; TKA = total knee joint arthroplasty; THA = total hip joint arthroplasty; quads = quadriceps muscle; rec fem = rectus femoris muscle; VM = vastus medialis muscle; PC = pulsed current; AC = alternating current; max = maximum; POD = post-operative day; Ex = exercise; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; KOOS = knee osteoarthritis outcome scale; SCT = stair-climbing test; 3MWT = 3 min walk test; 6MWT = 6 min walk test; TUG = timed up-and-go test; SF-36 = Short Form (36) Health Survey; reps = repetitions; CON = control; LOS = length of stay; pre-op = pre-operatively; RCT = randomized controlled trial; CSA = cross-sectional area; SR = systematic review; *N* = total number; PT = physiotherapy/physical therapy; TENS = transcutaneous electrical nerve stimulation; OA = osteoarthritis.

Table 14 Details of Individual Studies on Use of NMES in Total Joint Replacement

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Avramidis and colleagues (2011)[149] RCT $N = 76$ enrolled; $N = 70$ analyzed Included in SR[163]	TKA POD 2 Aged 60–75 yr NMES ($n = 38$): NMES + Ex CON ($n = 38$): Ex	7×7 cm 1 channel Electrodes: on quads on VM and lateral thigh Knee extended	Biphasic PC 40 Hz 300 μs ON:OFF 8:8 s Amplitude max tolerable sufficient to produce contraction No simultaneous voluntary contraction with NMES	2 h BID (500 contractions/d) d/wk nr 6 wk	Functional capacity: Walking speed—3MWT Oxford Knee Score Knee Society Function Score SF-36 @ 0, 6, 12, and 52 wk	Greater walking speed Higher Oxford Knee Score @ 6 and 12 wk SF-36 sub-group scores improved more, some scores at all measurement times, some scores only @ 12 wk No significant between-groups differences in all other outcomes	3 NMES group patients withdrew because of NMES intolerance. High number of repetitions, as in Avramidis and colleagues'[150] 2003 study. Assessors were blinded, and sample size was adequate to detect a significant difference.
Avramidis and colleagues[150] (2003) RCT $N = 30$ enrolled; $N = 30$ analyzed	TKA POD 2 Aged 58–81 yr NMES ($n = 15$): NMES + Ex CON ($n = 15$): Ex	7 cm diameter 1 channel Electrodes: on quads on VM and lateral thigh Knee extended	Asymmetric biphasic PC 40 Hz 300 μs ON:OFF 8:8 s Amplitude max tolerable sufficient to produce contraction No simultaneous voluntary contraction with NMES	2 h BID (500 contractions/d) d/wk nr 6 wk	Functional capacity: Walking speed 3MWT Physiologic Cost Index Hospital for Special Surgery Knee Score @ 0, 1, 6, and 12 wk	Increase in walking speed @ 6 and 12 wk No significant between-groups differences in all other outcomes	Blinding of investigators and study staff nr; possible risk of bias. High no. of repetitions, consistent with a focus on functional capacity rather than strength.
Gotlin and colleagues (1994)[151] RCT $N = 40$ enrolled; $N = 40$ analyzed	TKA POD 1 Aged 64–66 yr NMES ($n = 21$): NMES + PT CON ($n = 19$): Sham NMES + PT	Electrode size nr 1 channel Electrodes: on quads over femoral nerve and VM Positioned in CPM device NMES delivered over final 40° of knee ext	Waveform nr; PC 35 Hz ON:OFF 15:10 s Amplitude set to 80% of that required to evoke a visual contraction on the un-operated limb	1 h BID (288 contractions/d) Daily until D/C	Extensor lag @ pre-op and D/C LOS: D/C when patient could ambulate 45 m with cane and climb 5 stairs independently	Reduced extensor lag (5.67° [SD 1.93] compared with increased lag of 8.32° [SD 2.52] in CON) Shorter LOS @ D/C	Measuring knee ROM post-op using a handheld goniometer may compromise accuracy because of an inability to locate bony landmarks. Therapist blinded; assessor blinding nr. Outcomes specific to immediate post-op period.
Gremeaux and colleagues (2008)[155] RCT $N = 32$ enrolled; $N = 29$ analyzed	THA patients admitted <2 wk post-op to a rehab unit NMES ($n = 16$): NMES + PT CON ($n = 16$): PT	8×10 cm 2 channels Electrodes: on quads 2 cm distal to the inguinal fold and 2 cm prox to superior pole of patella and on calves distal to knee joint and at soleus muscle—tendon junction Knee extended	Biphasic PC 10 Hz 200 μs ON:OFF 20:20 s Amplitude max tolerable, progressed throughout training programme	60 min/d (90 contractions) 5 d/wk 5 wk Mean in-patient LOS 25 d; remaining visits were on an outpatient basis	Quads strength operated and un-operated leg Functional capacity: • 6MWT • 200 m fast-walk test • FIM Rehab hospital LOS @ 0 and 6.5 wk	Increased strength gain in operated limb Improved peak force ratio of operated to un-operated limb Improved FIM score @ 6.5 wk No significant between-groups differences in all other outcomes	Endurance-type protocol; however, strength gain was significant but not endurance.

Table 14 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Levine and colleagues (2013)[156] RCT non-inferiority trial $N = 70$ enrolled; $N = 66$ analyzed @ 6 wk; $N = 53$ analyzed at 6 mo Included in SR[163]	TKA 14 d pre-op NMES ($n = 35$): NMES + unsupervised at-home ROM Ex CON ($n = 35$): PT-supervised strengthening and ROM Ex	Electrode size nr Electrode placement nr	Waveform nr; PC 75 Hz 300 μs ON:OFF 4:10 s Amplitude max tolerable	20–30 min/d (~100 contractions/d) Initiated 14 d pre-op 14 d Re-initiated POD 1 20–30 min/d 60 d	Pain/function: Knee Society Score WOMAC Functional capacity: TUG AROM @ 6 wk and 6 mo	Non-inferiority of NMES + ROM Ex on all outcomes @ 6 mo However, non-inferiority was not shown for knee ext and TUG @ 6 wk No between-groups difference in patient satisfaction	Focus was on function; strength was not measured.
Petterson and colleagues (2009)[152] RCT $N = 200$ enrolled; $N = 168$ analyzed @ 12 wk; $N = 149$ analyzed @ 52 wk Included in SR[163]	TKA Post-op 4 wk Aged 50–85 yr NMES ($n = 100$): NMES + progressive Ex CON ($n = 100$): progressive Ex Community care ($n = 41$): eligible but not randomized); received standard care (average 22.8 PT visits)	7.6 × 12.7 cm Electrodes: on quads on rec fem and VM @ 60° knee flex Ex targeted quads, hams, gastrocs, soleus, hip abductors, and hip flexors; weights increased to always maintain a 10 RM intensity level Initiated at 20 reps, increasing to 30 reps	2500 Hz AC 50 Hz burst rate 400 μs ON:OFF 10:80 s Amplitude max tolerance with minimum 30% MVC No simultaneous voluntary contraction with NMES	10 contractions 2–3 d/wk 6 wk NMES and CON average 17 OPD visits	Isokinetic quads strength Quads activation: burst superimposition technique Functional capacity: • SCT • TUG • 6MWT ROM Knee Outcome Survey SF-36 @ 3 and 12 mo (NMES and CON) @ 12 mo (community care group) Blinded assessors	NMES and CON improved equally on strength, activation, and function @ 3 and 12 mo NMES and CON increased strength and function (TUG, 6MWT, SCT) compared with community care @ 12 mo No significant between-groups differences in all other outcomes	The implication is that a progressive Ex programme is more effective than a standard community rehab programme; NMES does not add to the benefit of a progressive Ex programme.
Stevens and colleagues (2004)[143] Non-RCT $N = 8$ enrolled; $N = 8$ analyzed	TKA bilateral post-op 3–4 wk Aged 61–76 yr NMES ($n = 5$): NMES applied to initially weaker leg + Ex CON ($n = 3$): Ex	7.6 × 12.7 cm Electrodes: on quads on VM and prox rec fem Knee flexion 60°	2500 Hz AC 50 Hz burst rate ON:OFF 10:80 s, ramp-up 2–3 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	10 contractions 3 d/wk 6 wk	Strength: Kin-Com Muscle activation: burst superimposition technique @ 0, 3, 9, 12, and 24 wk Blinded assessors	Strength and activation in 4 of 5 NMES-treated legs equalled or surpassed that of the initially stronger legs @ 3 wk Strength advantage maintained @ 24 wk Initially weaker CON legs remained weaker than stronger contralateral legs at all times	The cross-transfer effect of NMES (increased strength of untreated limb muscles) is well documented. It is therefore likely that the untreated knees in this study also benefited from NMES; this means that the treated knees had more ground to cover to equal or surpass the strength of the untreated knees.

Table 14 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Stevens-Lapsley and colleagues (2012)[153] RCT $N = 66$ enrolled; $N = 60$ analyzed @ 6 wk; $N = 58$ analyzed @ 26 wk; $N = 55$ analyzed @ 52 wk Included in SR[163]	TKA POD 2 NMES ($n = 35$): NMES at home + standard rehab CON ($n = 31$): standard rehab group	7.6 × 12.7 cm 1 channel Electrodes: on quads on distal medial thigh and prox lateral thigh 60° knee flex Subjects did not voluntarily contract muscles during NMES Progressive ext both groups; weights increased to always maintain a 10 rep max intensity level Initiated at 20 reps, increasing to 30 reps	Symmetric biphasic PC 50 Hz 250 μs ON:OFF 15:45 s Amplitude max tolerable No simultaneous voluntary contraction with NMES	15 contractions BID 6 wk	Strength quads and hams: MVIC Quads activation: burst superimposition technique Functional capacity: • SCT • 6MWT • TUG ROM: • Knee flex • Knee ext WOMAC SF-36 Patient-rated GRS @ 0, 3.5, 6.5, 13, 26, and 52 wk	Improved quads and hams strength Improved TUG, SCT, and 6MWT Improved knee ext @ 3.5 wk; trend @ 52 wk Trend to better ext range @ 52 wk Improved WOMAC scores @ 52 wk Improved SF-36 @ 52 wk Improved GRS @ 3.5 and 52 wk No significant between-groups differences at other times	The NMES device tracked compliance at home. Assessors were not blinded; possible risk of bias. Comparing NMES intensity with strength and activation gain showed that higher training intensities were associated with greater gains. A total of 10 NMES subjects reached the output limit of the stimulator for 3 or more sessions.
Suetta and colleagues (2004)[157] RCT $N = 36$ enrolled; $N = 30$ analyzed	THA POD 1 NMES ($n = 11$): NMES + standard rehab CON ($n = 13$): resistance training + standard rehab CON ($n = 12$): standard rehab	5.0 × 8.9 cm One channel Electrodes: on quads 5 cm below inguinal ligament and 5 cm above patella Standard rehab Ex programme was performed daily at home after D/C 1 d/wk subjects visited the clinic for performance review Resistance training took place in clinic, and all sessions were supervised by a physical therapist for 12 wk	Biphasic PC 40 Hz 250 μs ON:OFF 10:20 s included 2 s ramp-up and ramp-down Amplitude max tolerable Limb position nr No simultaneous voluntary contraction with NMES	1 h/d (120 contractions/d) 12 wk	Quads strength CSA: CT Functional capacity: • Gait speed • SCT • Sit-to-stand LOS (combined acute surgical + in-patient rehab) @ 0, 5, and 12 wk	Resistance training increased strength compared with standard rehab @ 5 wk Standard rehab and NMES @ 12 wk Resistance training improved CSA compared with NMES and standard rehab @ 5 and 12 wk Resistance training and NMES improved sit-to-stand compared with standard rehab @ 12 wk Resistance training reduced LOS compared with standard rehab (10 [SD 2.4] d vs. 16 [SD 7.2] d) NMES LOS (12 [SD 2.8] d) trended to be less than standard rehab No significant between-groups differences in all other outcomes	Some assessors were blinded to group assignment.

Table 14 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Walls and colleagues (2010)[154] RCT $N = 17$ enrolled; $N = 14$ analyzed	TKA 8 wk pre-op Aged 49–80 y NMES ($n = 9$): home-based pre-op CON ($n = 5$): standard pre-op care Both groups: standard post-op rehab	193, 83, 74, and 66 cm^2 Electrodes: self-adhesive in a garment on quads—VM and VL proximally and distally Knee flexion 60°	Symmetric biphasic PC 50 Hz 100–400 μs (dynamically changing) ON:OFF 5:10 s + 1 s ramp-up Amplitude max tolerable No simultaneous voluntary contraction with NMES	72 contractions/d Pre-op 8-wk period Wk 1–2, 3 d/wk "conditioning period"; Wk 3–8, 5 d/wk POD 1 was start of standard rehab for both groups without NMES	Quads strength: Biodex: MVIC CSA Functional capacity: • Chair rise test • SCT • 25 m timed walk WOMAC SF-36 @ 8 wk and immediately pre-op and @ 6 and 12 wk post-op Blinded assessor	Function: Improved chair-rise test @ end of 8-wk pre-op programme Function improved: • SCT • Chair-rise test @ 12 wk post-op No significant between-groups differences in all other outcomes	Compliance with NMES programme assessed by device recording and patient report (97–99%). High number of reps 5 d/wk might account for absence of strength effects and finding of improved endurance. The study sample was extremely small, which might be the main reason for lack of benefit.

NMES = neuromuscular electrical stimulation; CON = control; RCT = randomized controlled trial; SR = systematic review; TKA = total knee joint arthroplasty; POD = post-operative day; Ex = exercise; quads = quadriceps muscle; VM = vastus medialis muscle; PC = pulsed current; max = maximum; BID = twice per day; nr = not reported; 3MWT = 3 min walk test; SF-36 = Short Form (36) Health Survey; PT = physiotherapy/physical therapy; CPM = continuous passive motion; D/C = discharge; pre-op = pre-operative; LOS = length of stay; ROM = range of motion; post-op = post-operative; THA = total hip joint arthroplasty; prox = proximal; 6MWT = 6 min walk test; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; TUG = timed up-and-go test; AROM = active range of motion; ext = extension; rec fem = rectus femoris muscle; gastrocs = gastrocnemius muscle; RM = repetition maximum; reps = repetitions; AC = alternating current; MVC = maximum voluntary contraction; OPD = outpatient department; SCT = stair-climbing test; MVIC = maximum voluntary isometric contraction; flex = flexion; GRS = Global Rating Scale; hams = hamstring muscle; CSA = cross-sectional area; CT = computed tomography; VL = vastus lateralis muscle.

3. Critical Illness and Advanced Disease States

Indications and rationale for using NMES

Skeletal muscle proteins break down in advanced disease states, and during prolonged periods of immobilization, to provide energy for vital metabolic functions—for example, gluconeogenesis in the liver. This leads to varying degrees of loss of skeletal muscle mass and, in some patients, polyneuropathy. Muscle weakness and fatigue impede patients' capacity to exercise, are known to delay extubation, extend length of stay in ICU, and delay patients achieving independent mobility and returning to their former independence.[164,165] The goal of NMES in advanced disease states is to prevent or reverse skeletal muscle wasting for persons who are not able to exercise. Conditions include advanced COPD, CHF, sepsis, and reduced consciousness during critical illness, malignancy, and periods of mechanical ventilation.

Table 15 Summary of the Literature and Recommendations for Use of NMES in Critical Illness and Advanced Disease States

Indication	Parameter Recommendations	Outcome Measures Demonstrating Benefit
Advanced COPD, heart failure, sepsis, consciousness disturbance, malignant disease, and during mechanical ventilation	**Electrode placement:** LE muscle groups bilaterally; primarily quads, frequently also hams and calf muscles **Limb position:** ICU patients in supine with knee supported in 30–40° flex;[166,167] CHF patients sitting with knee flex 90°;[168,169] COPD patients sitting with knee flex 65–90°170–172 **Waveform:** biphasic low-frequency PC **Frequency:** 50 Hz[166,169–180] **Pulse duration:** 350–400 μs **Work–rest cycle:** COPD patients, ON:OFF 6–8:12–24 s (1:2 or 1:3 ratio; shorter ON times paired with shorter OFF times); ICU and CHF patients, ON:OFF 2–5:4–10 s (1:1 or 1:2 ratio; shorter ON times paired with shorter OFF times) **Treatment schedule**: 30–60 min/d. Alternatively, 30 min, gradually increasing to 60 min.[169,170,175,177,180] Total time divided among the muscle groups. **Session frequency:** COPD patients, 5–7 d/wk for 6–8 wk; ICU patients, daily until extubation or D/C from ICU; CHF patients, 5–7 d/wk for 8–10 wk. **Current amplitude:** individual max tolerated intensity. For COPD patients, a strong muscle contraction is the minimum acceptable response; in the ICU, a muscle contraction is not always observed.	• Muscle protein degradation (urinanalysis; biomarker analysis)[181,182] • Thigh circumference (CT)[167,183] • Cross-sectional area (by CT but not when measured by anthropometry or DEXA scan)[169,172,175,184,185] • Strength of LE muscles (isometric or isotonic dynamometry, MRC score),[169,170,172–174,176,178,179,185–192] Ex capacity (6MWT, Incremental Shuttle Walking Distance, Endurance Shuttle Walk Test)[168,170,171,173,174,178,180,186,189,190] • Prevention of muscle atrophy (US, biopsy)[166,168,177,182] • Levels of function (transfers, PFIT)[179,190,192,193] • Cardiopulmonary function (O_2 uptake, min ventilation, heart rate, Borg Symptom Score, spirometry)[168,171,186,192] • Breathlessness (MRC dyspnoea scale, SGRQ, Borg Scale, Maugeri Foundation Respiratory Failure Questionnaire)[178,189] • Duration of weaning from ventilation and decreased ICU length of stay[185,193] • QOL (SF-36, Chronic Respiratory Questionnaire, Maugeri Foundation Respiratory Failure Questionnaire)[168–171,178,189–191] • Safety and feasibility[194]
Rationale for recommended NMES protocol	The majority of studies selected parameters to minimize muscle fatigue—i.e., short ON times of 2–6 s. This is in sharp contrast to studies involving musculoskeletal injuries and knee surgery, as shown in Tables 7–14. A frequency of 50 Hz was repeatedly associated with preserved muscle mass and with improved strength and functional capacity; it is therefore recommended for NMES in this population. Other frequencies were used: 35 and 50 Hz were compared and were found to provide equal benefit after daily treatment in the ICU;[174] there was also no immediate difference in respiratory function in COPD patients after a single session using 15 or 75 Hz.[195] In 3 ICU studies, frequency was set at 100 Hz.[167,182,183] Some benefit was seen, but there is no evidence that 100 Hz was more beneficial than 50 Hz, and it is known to cause rapid fatigue. The 2 studies involving CHF population differed in their settings for frequency and daily treatment duration: 1 used 15 Hz for 120 min BID,[168] and the other used 50 Hz[169] for 60 min/d; both showed numerous benefits compared with CON. A progression of ON time, total treatment duration/d, and number of sessions/wk was frequently found in the literature.	

Table 15 *continued*

Physiological effect of NMES	The literature has shown that NMES preserves muscle strength and muscle mass and reduces rate of muscle degradation. Maintaining muscle strength and endurance facilitates maintenance of functional capacity. Nápolis and colleagues[180] suggested that most of the benefit of NMES was related to neural adaptations because true hypertrophy was rarely found in patients with COPD. However, increase in CSA has been shown in patients with COPD[172] and ICU patients.[184] Burke and colleagues[196] posited that improvement in walking distance and Ex tolerance in critically ill persons was due to gains in muscle strength and endurance because NMES appears to have little effect on the physiological processes associated with Ex or on quads' oxidative capacity. Increase in type II and decrease in type I fibres has been shown.[175] Nápolis and colleagues[180] studied COPD patients and found that NMES improved Ex tolerance more in patients with better preserved muscle. These patients also tolerated higher current amplitude, which he suggested might explain the results and which also underscores the importance of high stimulation intensity.
Critical review of research evidence	• We reviewed the individual RCTs identified by our search protocol as well as 6 SRs.[196–201] • Inclusion criteria for the SRs varied with respect to patient populations: Patients with COPD, chronic heart failure, or thoracic cancer;[198] patients in the ICU;[200] and critically ill patients with a variety of conditions.[196,197,201] Authors reported that heterogeneity in study designs and outcome measures generally precluded meta-analyses. • CON groups vary in the literature (Table 16): NMES is compared with active limb mobilization, sham NMES, usual care, or an untreated contralateral leg.[167,176,183,187,202] • Among the studies in Table 16, only 3 showed no benefit,[187,202,203] 2 of which used the untreated limb as CON. Cross-transfer effect of NMES is well documented: NMES applied to 1 limb leads to some strength gain in the untreated limb. Using the untreated limb as CON means that the treated limb must make up extra ground to show a significant strength difference between the 2 limbs. However, other reasons might explain lack of benefit in 2 of the negative studies: 1 applied NMES for a shorter duration (20 min/d)[187] than all other ICU studies, and both used very small sample sizes, which might have compromised power to find a difference.[202] The remaining negative study involved ambulant patients with non–small-cell lung cancer; no other NMES study in this population has confirmed the non-effectiveness of NMES. • Initiation of NMES in critically ill patients varies from 1 to 7 d post-intubation but commonly begins within 3 d of intubation. NMES has also been beneficial for long-term ICU-stay patients who started treatment only after 30 d of being bedbound.[192] • Optimal time for initiating NMES in patients with severe COPD has not been established. In most studies, the inclusion criteria required FEV_1 to be $< 50\%$ of predicted value, a 6MWT < 400 m, or both. Results showed actual mean FEV_1 was between the 30% and 54% predicted in the majority of studies; in 1 study, FEV_1 was 15%–25% predicted.[186] There is some indication that NMES should be initiated before COPD-associated muscle wasting develops.[180] • NMES treatment of COPD, shown in Table 16, is noticeably different when compared with that for patients with orthopaedic or musculoskeletal conditions. The common approach in critical illness is to apply NMES 5–7 d/wk for 6–8 wk. However, treatment in the ICU might be applied only during periods of unconsciousness or mechanical ventilation, and the possible benefit of continuing NMES after extubation and D/C from ICU has not been studied. • Individual studies have limitations: There is a risk of bias due to lack of blinding of subjects, therapists, and outcome assessors; sample size is small in some studies (range 15–120 subjects, and as low as 8 in studies that used an untreated limb as CON); and study endpoints vary widely among the studies. • Feasibility has been demonstrated; authors consistently reported that treatment was well tolerated. • Safety has been examined in a controlled series of 50 patients with no adverse effects reported.[194] • Parry and colleagues[193] reported a minor adverse effect for 1 patient: Post–NMES training, the patient experienced a transient desaturation to 86% for > 1 min, requiring an increase in fraction of inspired oxygen for 1 h. No other study has investigated the cycling apparatus used by Parry and colleagues with mechanically ventilated patients. • In COPD patients, inflammatory markers were found not to be stimulated by NMES.[172]

NMES = neuromuscular electrical stimulation; COPD = chronic obstructive pulmonary disease; LE = lower extremity; quads = quadriceps muscle; hams = hamstring muscle; ICU = intensive care unit; flex = flexion; CHF = congestive heart failure; PC = pulsed current; D/C = discharge; max = maximum; CT = computed tomography; DEXA = dual-energy X-ray absorptiometry (measures bone mineral density); MRC = Medical Research Council; 6MWT = 6-minute walk test; US = ultrasound; PFIT = Physical Function in Intensive Care Test; SGRQ = St George's Respiratory Questionnaire; QOL = quality of life; SF-36 = Short Form (36) Health Survey; BID = twice per day; CON = control; CSA = cross-sectional area; Ex = exercise; RCT = randomized controlled trial; SR = systematic review; FEV_1 = forced expiratory volume in 1 s.

Table 16 Details of Individual Studies for Use of NMES in Critical Illness and Advanced Disease States

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Abdellaoui and colleagues (2011)[186] RCT $N = 15$ enrolled; $N = 15$ analyzed Included in SR[196,198,199]	Severe COPD Acute episode requiring ICU admission NMES ($n = 9$) CON ($n = 6$): usual care	5×5 cm 2 channels Electrodes: on bilateral quads and hams Supine lying	Symmetric biphasic PC 35 Hz 400 μs ON:OFF 6:12 s Amplitude max tolerated, at least a visible contraction	1 h/d 5 d/wk 6 wk In-patient treatment followed ICU D/C	Isometric quads strength Functional capacity: 6MWT Muscle oxidation Muscle fibre typology: biopsy @ 0 and 6 wk	Improved strength Improved 6MWT Improved muscle-oxidative stress (some measures and some tests showed no change) Increased proportion of type 1 and IIa/IIx fibres; increased size of type 1 fibres	Blinding nr; possible risk of bias.
Bouletreau and colleagues (1987)[181] Cross-over design: washout period 1 d $N = 10$ enrolled; $N = 10$ analyzed Included in SR[200,201]	Acute stroke, post-op respiratory failure, or ventilated patients	Electrode size nr Electrodes: on bilateral calf and thigh muscles; exact location nr Supine lying	Waveform nr; PC 1.75 Hz 3,000 μs ON:OFF nr Amplitude: visible muscle contraction	30 min BID 4 d NMES 4 d CON	Muscle protein degradation by urinary excretion: • Urea • Nitrogen • Creatinine • 3-methyl histodine Daily @ 0–8 d	Reduced 3-methyl histidine and creatinine excretion during 4 d NMES period No significant between-groups differences in other outcomes	NMES parameters as reported by authors. Discomfort would be likely at 3,000 μs, and tetany is unlikely at 1.75 Hz
Bourjeily-Habr and colleagues[173] (2002) RCT $N = 18$ enrolled; $N = 18$ analyzed Included in SR[198]	Moderate to severe COPD Aged < 70 yr NMES ($n = 9$) CON ($n = 9$): usual care	8×6 cm Electrodes: on bilateral quads, hams, and calf muscles Knee flex 90° fixed	Biphasic PC 50 Hz PD nr ON:OFF 0.2:1.3 s Amplitude: visible muscle contraction	20 min/d 3 d/wk 6 wk Amplitude increased each wk	Functional capacity: • Incremental SWT • Ex capacity Isokinetic quads and hams strength Peak O_2 uptake @ 0 and 6 wk	Increased SWT Increased muscle strength @ 6 wk No significant between-groups differences in all other outcomes	Assessor blinded. Contraction would be very brief using a 0.2 s ON duration.
Chaplin and colleagues (2012)[174] RCT $N = 29$ enrolled; $N = 20$ analyzed	Acute COPD, hospitalized patients NMES ($n = 14$) @ 35 Hz NMES ($n = 15$) @ 50 Hz No CON	Electrode size nr Electrodes: on bilateral quads Limb position nr	Symmetric biphasic PC 35 Hz or 50 Hz 300 μs ON:OFF 15:5 s Amplitude max tolerated	30 min/d 7 d/wk until hospital D/C	Quads isometric strength Functional capacity: Endurance SWT @ baseline and D/C	Both groups improved on strength and SWT No significant between-groups differences	No CON or placebo group. Study showed that low- and high-frequency NMES have similar outcomes.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Dal Corso and colleagues (2007)[175] RCT Crossover design $N = 17$ enrolled; $N = 17$ analyzed Included in SR[198]	Moderate to severe COPD NMES ($n = 17$) CON ($n = 17$): treated with sensory-level stimulation	Electrode size nr 4 channels Electrodes: on bilateral quads Knee flex 20–30° Self-applied NMES at home	Waveform nr PC NMES 50 Hz, 400 μs; CON 10 Hz, 50 μs ON:OFF wk 1, 2:10 s; wk 2, 5:25 s; wk 3–4, 10:30 s; wk 5–6, 10:20 s NMES amplitude max tolerated, minimum a visible contraction; CON group 10 mA, no visible contraction	Wk 1, 15 min/d; wk 2, 30 min/d; wk 3–6, 1 h/d 5 d/wk 6 wk	Isokinetic quads strength Leg muscle mass (DEXA) Median CSA of type I and II fibres and capillary:fibre ratio in VL Functional capacity: 6MWT @ 0 and 6 wk	Reversed baseline relative atrophy of type II fibres Type II fibre increase was inversely related to baseline mass and strength Decreased type I fibre CSA No significant between-groups differences in all other outcomes	Assessor not blinded; therefore, risk of bias.
Dirks and colleagues (2015)[182] RCT $N = 9$ enrolled; $N = 6$ analyzed	ICU, ventilated patients, acute illness APACHE II $\geq$ 25 NMES ($n = 9$): unilateral treatment CON: placebo NMES	5×5 cm 2 channels Electrodes: bilateral on muscle belly of rec fem and VL Limb position nr	Symmetric biphasic PC Warm-up, 5 Hz, 250 μs; stimulation phase, 100 Hz, 400 μs; cool-down, 5 Hz, 250 μs ON:OFF 5:10 s Amplitude: full visible quads contraction increased as muscle fatigue occurred CON: zero amplitude	Warm-up, 5 min; stimulation phase, 30 min; cool-down, 5 min BID until D/C Minimum 3 d Max 9 d	Muscle biopsy • Fibre type CSA • Satellite cell content mRNA levels of selected genes Content and phosphorylation status of key proteins, including mTOR @ 0 and after final NMES d	No atrophy in NMES leg versus significant atrophy in CON leg (both type I and type II fibres) 6 genes involved in muscle protein regulation more highly expressed in patients than healthy controls Phosphorylation of mTOR significantly greater using NMES	Patients in this cohort were more critically ill than in most other studies.
Falavigna and colleagues (2014)[187] RCT $N = 25$ enrolled; $N = 11$ analyzed Included in SR[196]	ICU, ventilated patients Mean APACHE II score = 15 NMES: unilateral treatment CON: untreated leg	Electrode size nr Electrodes: on MP quads and tib ant Limb position nr	Symmetric biphasic PC 50 Hz 400 μs ON:OFF 9:9 s Amplitude visible contractions	20 min/d each muscle group Daily, continuing after awakening until patients were graded 4 out of 5 for muscle strength on Oxford Scale Average treatment 10.2 (SD 9.0) days	Muscle strength: MRC scale • Hip flex • Knee ext • Ankle DFL Thigh and calf circumference ROM: ankle DFL and PFL @ end treatment	Increased ankle DFL ROM No significant between-groups differences in all other outcomes	Assessor blinded. Cross-transfer effect might affect results.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Gerovasili and colleagues (2009);[166] Routsi and colleagues (2010);[185] Karatzanos and colleagues (2012)[188] RCT $N = 52$ enrolled; $N = 52$ analyzed Included in SR[196,197,199–201]	ICU patients with MRC score < 48 of 60 for muscle strength NMES ($n = 24$) CON ($n = 28$): usual care	9×5 cm Electrodes: on bilateral VL, VM, and peroneus longus Knee flex about 40°	Waveform nr; PC 45 Hz 400 μs ON:OFF 12:6 s Contraction confirmed visually or by palpation	24–48 h after admission 55 min/d 7 d/wk Duration of stay in ICU: 8 (SD 6) d	Gerovasili and colleagues (2009): LE muscle mass, US @ 0 and 7–8 d Routsi and colleagues (2010): duration of weaning from mechanical ventilation @ 48 h free of mechanical ventilation; incidence of CIP @ awakening Karatzanos and colleagues (2012): Muscle strength – MRC scale @ awakening and ICU D/C	Gerovasili and colleagues (2009): NMES preserved muscle mass Routsi and colleagues (2010): Shorter weaning duration; reduced CIP incidence Karatzanos and colleagues (2012): MRC scores higher for hip flex, knee ext, and ankle DFL Preserved muscle strength	Study not blinded; therefore, risk of bias. The results are reported in 3 separate articles.
Giavedoni and colleagues (2012)[176] RCT $N = 11$ enrolled; $N = 11$ analyzed Patients were their own controls	Patients with severe COPD exacerbation; acute episode in hospital NMES: unilateral treatment CON: untreated limb	Electrode size nr 1 channel Electrodes: on VM and femoral triangle Limb position nr	Asymmetric biphasic PC 50 Hz 0.4 s (*sic*) ON:OFF 8:20 s Amplitude max tolerated	Initiated within 48 h of admission 30 min/d 7 d/wk 2 wk Continued at home post-D/C	Spirometry @ 4 wk post-admission Isometric quads strength @ 0 and 16 d	Strength improved in treated leg and decreased in CON leg Significant correlation between strength gain and training intensity No significant between-groups differences in spirometry	Study not blinded; therefore, risk of bias. 0.4 s (400 ms) pulses are extremely uncomfortable.
Gruther and colleagues (2010)[177] RCT $N = 33$ enrolled; $N = 33$ analyzed Included in SR[196,199–201]	ICU patients, various illnesses Groups stratified: acute (<7 d) and long term (>14 d) NMES ($n = 16$) CON ($n = 17$): sensory-level protocol	5×5 cm and 5×10 cm 4 channels Electrodes: on bilateral VM and VL Limb position nr	Biphasic PC 50 Hz 350 μs ON:OFF 8:24 s NMES group: max tolerated amplitude CON group: sensory-level amplitude, no visible contraction	Wk 1, 30 min/d; wk 2–4, 60 min/d 5 d/wk 4 wk	Muscle thickness quads: US • Vastus intermedius • Rec fem @ 4 wk	Long-term group showed positive results—greater muscle thickness—i.e., NMES did not retard muscle loss when applied early.	Fully blinded study
Hirose and colleagues (2013)[184] Non-RCT $N = 15$ enrolled; $N = 15$ analyzed Included in SR[196]	ICU patients with reduced consciousness and paralysis, 1 or both legs NMES ($n = 9$): recruited over a 5-yr period CON ($n = 6$): no intervention; recruited over a 1 y period	Electrode size nr Electrodes: on quads, hams, and calf muscles ant and post Limb position nr	Waveform nr Frequency nr PD nr ON:OFF 10:10 s Contraction confirmed visually: 30–40 mA	Initiated d 7 30 min/d each muscle group 5 d/wk 2 wk	CSA: CT @ 2 wk	CSA was preserved.	The extended period over which subjects were recruited (5 yr) might have affected standardization of procedures.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Kaymaz and colleagues (2015)[178] Non-RCT $N = 50$ enrolled; $N = 50$ analyzed	Severe COPD NMES ($n = 23$); subjects too dyspnoeic to participate in endurance training CON ($n = 27$): endurance training	Electrode size nr Electrodes: on quads and deltoid Limb position nr	Symmetric biphasic PC 50 Hz 300–400 μs ON:OFF nr Amplitude max tolerated	NMES group: 15 min/d 2 d/wk 10 wk Endurance group: Treadmill walking 15 min Cycling 15 min Active strength Ex UE and LE, 3 d/wk for 8 wk	Muscle strength: MMT SWT: incremental and endurance Dyspnoea: MRC scale SGRQ Psychological status Body composition (bioelectrical impedance) QOL @ 0 and 8 wk	Increased strength UEs and LEs Increased SWT Improved dyspnoea Improved SGRQ Improved psychological status No significant between-groups differences in all other outcomes	The implication is that NMES can replace active Ex in individuals too dyspnoeic to Ex.
Kho and colleagues (2015)[179] RCT $N = 36$ enrolled; $N = 34$ treated; $N = 29$ analyzed	ICU, ventilated patients NMES ($n = 16$) CON ($n = 18$): sham NMES	Electrode size nr Electrodes: on bilateral VM, VL, tib ant, and gastrocs Limb position nr	Asymmetric balanced biphasic PC 50 Hz 400 μs (quads); 250 μs (tib ant and gastrocs) ON:OFF 5:10 s (quads, ramp-up and ramp-down 2:1 s), 5:5 s (tib ant and gastrocs) Amplitude: NMES visible muscle contraction below pain level Sham NMES: zero	60 min/d or 30 min BID Daily Mean NMES sessions: 9.1 (SD 8.7) Mean sham sessions: 10.8 (SD 9.5)	Primary: Sum of all LE muscle strength: MRC score @ ICU awakening and hospital D/C Secondary: Strength: dynamometry • Each LE muscle • Grip @ ICU awakening, ICU D/C, and hospital D/C Ventilation duration ICU Hospital LOS Functional capacity: • Walking distance • Functional Status Score for ICU @ ICU awakening, ICU D/C, and hospital D/C Max inspiratory pressure Post hoc test for ICU: acquired weakness—MRC score < 48 @ awakening Hospital mortality	Secondary outcomes: Increased LE strength from awakening to ICU D/C and awakening to hospital D/C Increased walking distance @ hospital D/C Improved Functional Status Score from awakening to ICU D/C No significant between-groups differences in all other outcomes	All clinicians and assessors were blinded to study groups. Target enrolment not achieved, leading to statistically under-powered study.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Maddocks and colleagues (2009)[203] RCT $N = 16$ enrolled; $N = 16$ analyzed Included in SR[198]	Lung cancer NMES ($n = 8$) CON ($n = 8$): usual care	7 cm diameter Electrodes: on bilateral quads Limb position nr Self-applied NMES at home	Biphasic PC 50 Hz 350 μs ON:OFF: wk 1, 2:18 s; wk 2, 5:25 s; wk 3–4, 10:30 s Visible contraction, amplitude increasing as tolerated	Wk 1: 15 min/d; wk 2–4: 30 min/d 5 d/wk 4 wk	Quads strength Functional capacity • SWT • Daily step count: accelerometer @ 0 and 4 wk	No significant between-groups differences Result favoured NMES on all outcomes.	Study not blinded; therefore, risk of bias
Meesen and colleagues (2010)[183] Partly RCT $N = 25$ enrolled; $N = 25$ analyzed Included in SR[196,200]	ICU, ventilated patients with post-op coronary artery bypass, COPD, or pneumonia were randomized to NMES or CON NMES ($n = 11$): unilateral treatment CON ($n = 10$): untreated leg Acute stroke patients were assigned to CON ($n = 4$)	Electrode size nr NMES subjects Right leg: 1 channel Electrodes: on rec fem and VM Supine lying with half-roll pillow behind knee Left leg: Usual care Acute stroke patients right leg: usual care	Symmetric biphasic PC Set 1: 5 Hz, 250 μs, ON:OFF 90:30 s, 5 min; Set 2: 60 Hz, 330 μs, ON:OFF 10:20s, 6 min Set 3: 100 Hz, 250 μs, ON:OFF 10:20 s, 8 min Set 4: 80 Hz, 300 μs, ON:OFF 7:14 s, 8 min Set 5: 2 Hz, 250 μs, ON:OFF 90:30 s, 5 min Amplitude: visible muscle contraction	30 min/d 7 d/wk Duration of intubation	Thigh circumference @ 4, 7, 10, 13, and 16 days	Increased thigh circumference compared with untreated leg and treated CON legs	6 subjects excluded from analysis; unexplained dropouts might affect the validity of the findings
Nápolis and colleagues (2011)[180] RCT Crossover design: 2-wk washout period $N = 30$ enrolled; $N = 30$ analyzed Included in SR[198]	Stable moderate to severe COPD: GOLD classification II and III Compared NMES in better and worse- preserved muscle function and structure	Electrode size nr Electrodes: on bilateral quads Limb position nr Self-applied NMES at home	Symmetric biphasic PC NMES, 50 Hz, 300–400 μs; sham, 50 Hz, 200 μs ON:OFF: Wk 1, 2:10 s Wk 2, 5:25 s Wk 3–4, 10:30 s Wk 5–6, 10:20 s Sham 2:10 s Amplitude NMES max tolerated each session: 30.3 (SD 5.8) @ wk 1 to 48.6 (SD 8.3) @ 6 wk Sham NMES: 10 mA	Wk 1, 15 min/d; wk 2, 30 min/d; wk 3–6, 1 h/d 5 d/wk 6 wk Sham 15 min/d 3 d/wk 6 wk	Body composition at baseline Pulmonary function Functional capacity: • 6MWT • Ex capacity: submaximal cardiorespiratory Ex measures Isokinetic quads strength @ 0 and 6 wk each arm of crossover	Ex capacity, but not 6MWT, improved in a subgroup that had higher baseline values of fat-free mass. This group was also able to train at higher current intensity. No significant between-groups differences in all other outcomes.	Assessor blinded. Compliance with at-home protocol checked by patient diary. However, investigators could not be certain that subjects used devices as prescribed.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Neder and colleagues (2002)[170] RCT Crossover $N = 15$ enrolled; $N = 15$ analyzed Included in SR[198]	COPD, moderate to severe MRC scale 4–5 NMES early ($n = 9$) NMES late ($n = 6$)	Electrode size nr Electrodes: on bilateral quads Sitting position, knee flexed, not supported Self-applied NMES @ home	Symmetric biphasic PC 50 Hz 300–400 μs ON:OFF: Wk 1, 2:18 s; wk 2: 5:25 s; wk 3–4, 10:30 s Amplitude max tolerated each session	Wk 1, 15 min/d; wk 2–4, 30 min/d 5 d/wk 6 wk	Isokinetic quads strength and endurance Functional capacity: max and endurance Ex QOL: Chronic Respiratory Disease Questionnaire @ 6 wk	Increased quads strength and endurance Increased max and endurance Ex capacity Improved dyspnoea domain of QOL tool	NMES device recorded usage. Not assessor blinded; therefore, risk of bias.
Nuhr and colleagues (2004)[168] RCT $N = 34$ enrolled; $N = 32$ analyzed Included in SR[198]	Chronic heart failure NMES ($n = 15$) CON ($n = 17$): sensory stimulation	130 cm^2 4 channels Electrodes: on bilateral quads and hams Sitting position Self-applied NMES at home	Symmetric biphasic PC 15 Hz 500 μs ON:OFF 2:4 s NMES group: strong contractions, 25%–30% MVC CON group: restricted amplitude	2 h BID 7 d/wk 10 wk	Respiratory function: • Peak VO_2 • Heart rate BP Muscle biopsy Functional capacity: • Cycle ergometer • 6MWT QOL @ 0 and 10 wk	Increased peak heart rate and systolic blood pressure, suggesting increased aerobic capacity Fibre type transitioned from fast to slow twitch Increased 6MWT Improved QOL No significant between-groups difference in cycle ergometer outcome	Blinding unclear NMES device recorded usage.
Parry and colleagues (2014)[193] Parallel groups $N = 24$ enrolled; $N = 24$ analyzed	ICU, patients with sepsis $>$ 48 h NMES ($n = 16$): NMES-driven cycling CON ($n = 8$): usual care	Electrode size nr Electrodes: on bilateral quads, hams, glutei, calf muscles Supine lying using motorized cycle ergometer	Monophasic PC 30–50 Hz 300–400 us ON:OFF: Cycle software turned current ON and OFF depending on cycling stage Amplitude set to visible contraction in all muscle groups	20–60 min/d 5 d/wk until D/C from ICU Awake patients Ex actively with motorized cycle	Time to reach functional milestones Levels of function on awakening: PFIT Return to functional independence Incidence and duration of delirium: De Jonghe 5-point scale @ awakening, @ ICU D/C, and @ hospital D/C	Decreased no. of d to recover from delirium in cycling group Trend toward better outcomes on all other measures	A singular approach to designing NMES-induced Ex in the ICU. Although beneficial, the results may not warrant using this set-up rather than the simple applications used in other studies.
Poulsen and colleagues (2011)[202] RCT $N = 8$ enrolled; $N = 8$ analyzed Patients were their own controls Included in SR[196,199–201]	ICU, ventilated male patients with septic shock NMES: unilateral treatment CON: untreated limb	5 × 5 cm distally; 5 × 9 cm proximally 2 channels 3 electrodes: on VM and VL and 5 cm distal to the inguinal fold Limb position nr	Waveform nr PC 35 Hz 300 μs ON:OFF 4:6 s Amplitude 50% above just visible contraction	60 min/d 7 d continuous	Quads volume reduction: CT @ 7 d	Equal loss of quads volume	Assessor blinded Small sample size, low stimulation amplitude, and use of the untreated limb as CON may explain the variance in results compared with similar studies.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Quittan and colleagues (2001)[169] RCT 2 groups $N = 42$ enrolled; $N = 33$ analyzed Included in SR[198]	Refractory heart failure; awaiting transplant NMES ($n = 17$) CON ($n = 16$): usual activity	130 cm^2 4 channels Electrodes: on bilateral quads and hams Sitting position Self-applied NMES at home All subjects seen for review 1 × /wk	Symmetric biphasic PC 50 Hz 700 μs ON:OFF 2:6 s Amplitude at strong contraction 25–30% of MVC	Wk 1–2, 30 min/d; wk 3–8: 60 min/d 5 d/wk 8 wk	Primary: Knee flexors isometric and isokinetic peak torque; knee extensors isometric and isokinetic peak torque: Cybex CSA: CT Secondary: Muscle endurance: decline of MVIC over 20-min period of contractions ADL score related to leg strength New York Heart Association functional classification SF-36 @ 8 wk	Increased peak torques, isometric and isokinetic, flexor, and extensor muscles Increased CSA Increased endurance Improved QOL Improved classification, New York Heart Association No significant between-groups difference in any other outcomes	Assessor blinded. Home use of NMES device logged in patient diary Actual usage could not be confirmed.
Rodriguez and colleagues (2012)[167] RCT $N = 16$ enrolled; $N = 14$ analyzed Patients were their own controls Included in SR[196,199–201]	ICU, ventilated patients with sepsis NMES ($n = 16$): unilateral treatment CON ($n = 16$): untreated limb	Electrodes 8 cm diameter: on VM Electrodes 5 cm diameter: on biceps brachii Half-lying position, limbs supported with knees and elbow joints in about 30° flex	Biphasic PC 100 Hz 300 μs ON:OFF 2:4 s Amplitude set to visible contraction	30 min BID For duration of intubation (median 14 d)	Muscle strength: MRC scale Arm and thigh circumference Biceps thickness: US @ awakening (median 10 d) @ last NMES session (median 13 d)	Increased biceps and quads strength: @ awakening @ last NMES session No significant between-groups difference in any other outcomes	Sample size was calculated to show a difference in muscle strength: possibly underpowered for other outcomes. Assessors were blinded. 1 patient had a burn resulting from incorrect setting of the device.
Sillen and colleagues (2014)[189, 190] RCT $N = 120$ enrolled; $N = 120$ analyzed	Severe to very severe COPD NMES ($n = 39$): low frequency NMES ($n = 41$): high frequency CON ($n = 40$): voluntary strength training	Electrodes 8 × 12 cm, bilateral; on quads Electrodes 4 × 6 cm, bilateral; on calf muscles Sitting position, knees supported in about 65° flexion	Symmetric biphasic PC High-frequency NMES group: 75 Hz 400 μs Low-frequency NMES group: 15 Hz 400 μs ON:OFF 8:8 s Max tolerated intensity CON: Bilateral leg extension and leg press Ex @ 70% of 1 RM; 4 sets of 8 reps each	18 min BID 5 d/wk 8 wk	Isokinetic quads strength Quads endurance Lower limb fat-free mass Functional capacity: • 6MWT • Cycling endurance • ADL • Ex-induced dyspnoea and fatigue pre–post each session Mood status Health status @ 8 wk Single blind	Increased quads strength and endurance in 75 Hz and strength-training groups Improved 6MWT in all groups; however, only NMES decreased symptoms of dyspnoea and fatigue during 6MWT Cycling endurance, lower limb fat-free mass, mood status, health status, and ADL improved in all groups No significant between-groups difference in any other outcomes	The authors concluded that higher frequency is indicated if strength is the desired outcome, but low frequency and active Ex are equally beneficial for improving fatigue and dyspnoea.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Vieira and colleagues (2014)[171] RCT $N = 24$ enrolled; $N = 20$ analyzed	Men with moderate-level, stable COPD NMES ($n = 11$): NMES + usual respiratory PT CON ($n = 9$): usual respiratory PT, electrodes applied, no current	Electrode size nr Electrodes: bilateral, on quads Sitting position, knees flexed, not supported	Symmetric biphasic PC 50 Hz 300–400 μs ON:OFF: wk 1, 2:18 s; wk 2, 5:25 s; wk 3–8, 10:30 s NMES amplitude max tolerated CON no current	60 min BID 5 d/wk 8 wk	Pulmonary function Fat-free mass Thigh circumference Functional capacity: • 6MWT • Ex tolerance time • Borg dyspnoea and leg score • Mechanical efficiency % TNF-α and β-endorphin levels QOL (SGRQ) @ 8 wk Double blind	Increased FEV_1, FEV_1/FVC Increased 6MWT Increased Ex tolerance time Reduced Borg scores Increased mechanical efficiency % Reduced TNF-α, increased β-endorphin levels Increased thigh circumference Improved QOL No significant between-groups difference in fat-free mass	Study size was calculated before enrolment. Focus was on functional capacity. Strength not directly measured; however, thigh circumference and fat-free mass increased. The authors suggested that increased mechanical efficiency of quads reduced respiratory demands during Ex.
Vivodtzev and colleagues (2012)[172] RCT 2 groups $N = 22$ enrolled; $N = 20$ analyzed Included in SR[198]	Severe COPD NMES ($n = 13$): NMES CON ($n = 9$): sham NMES NMES self-applied at home	Electrode size nr Electrodes bilateral: on quads and calf muscles Sitting position	Waveform nr PC NMES group: 50 Hz 400 μs ON:OFF 6:16 s CON group: 5 Hz 100 μs Continuous Amplitude max tolerated	Quads: 35 min/d Calf muscles: 25 min/d 5 d/wk 6 wk	CSA quads and calf muscles Muscle strength and endurance Functional capacity: SWT Cardio-respiratory function Biopsy: insulin-like growth factor hormone, muscle fibre typology, etc. Plasma levels of pro-inflammatory cytokines Muscle anabolic to catabolic balance @ 6 wk Double blind	Increased CSA, increased strength, and endurance Strong association between training intensity and increases in CSA and SWT Improved muscle anabolic to catabolic balance No significant between-groups difference in other outcomes	Sample size was calculated. Home use was logged in patient diaries. Non-responders to NMES on SWT outcome tolerated low intensity compared with responders, 5% (SD 3) vs. 22% (SD 9) MVIC. The authors suggested that the sham protocol might have had some effect—e.g., through central activation systems.

Table 16 *continued*

Author (Date), Study Design, and Study Size	Population Comparison Groups	Electrode Parameters: Size, Channels, Placement, and Limb Position	Stimulation Parameters: Waveform, Frequency, Pulse Duration, ON:OFF Time, and Amplitude	Treatment Schedule: Min/D Repetitions, D/Wk, and Total Wk Progression	Outcome Measures and Timing	Statistically Significant Results, NMES Compared with CON	Comments
Vivodtzev and colleagues (2006)[191] RCT $N = 17$ enrolled; $N = 17$ analyzed Included in SR[198]	Severe COPD with low body weight and quads MVIC $< 50\%$ predicted In-patient rehab setting during or post–acute episode NMES ($n = 9$): NMES + usual rehab CON ($n = 8$): usual rehab	Two 4×8 cm and two 4×4 cm 2 channels Electrodes: bilateral, on quads Supine lying	Symmetric biphasic PC 35 Hz 400 μs ON:OFF 7:8 s Amplitude at tolerance level	30 min/d 4 d/wk 4 wk	Quads strength: MVIC –tensiometer Functional capacity: 6MWT Total muscle mass Cardio-respiratory measures BMI QOL: MRF-28 @ 4 wk	Increased strength Improved dyspnoea score on MRF-28 Increased muscle mass No significant between-groups difference in any other outcome	Assessor not blinded for muscle strength measurement. Trend toward benefit in some outcomes might have reached significance with longer duration treatment, higher NMES frequency, or both.
Zanotti and colleagues (2003)[192] RCT $N = 24$ enrolled; $N = 24$ analyzed Included in SR[196,198,199]	ICU, COPD patients, ventilated with tracheostomy, $\geq$30 d on bed rest NMES ($n = 12$): NMES + active limb mobilization CON ($n = 12$): active limb mobilization	Electrode size nr Electrodes bilateral: on quads and glutei muscles Supine lying	Asymmetric biphasic PC Set 1: 8 Hz, 250 μs, 5 min Set 2: 35 Hz, 350 μs, 25 min ON:OFF nr Amplitude nr in terms of muscle contraction or mA but increased over time	30 min BID 5 d/wk 4 wk	Muscle strength: @ 0 and every alternate d Cardiovascular function: • Heart rate • Respiration rate • O_2 saturation Acquired continuously Functional capacity: transfer from bed to chair: no. of d	Increased strength Decreased heart rate Fewer d needed before patient could transfer from bed to chair	Blinding of assessors nr; possible risk of bias.

NMES = neuromuscular electrical stimulation; CON = control; RCT = randomized controlled trial; SR = systematic review; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; quads = quadriceps muscle; hams = hamstring muscle; PC = pulsed current; max = maximum; D/C = discharge; 6MWT = 6 min walk test; nr = not reported; post-op = post-operative; BID = twice per day; flex = flexion; PD = pulse duration; SWT = shuttle walk test; Ex = exercise; DEXA = dual-energy X-ray absorptiometry (measures bone mineral density); CSA = cross-sectional area; VL = vastus lateralis muscle; APACHE = Acute Physiology and Chronic Health Evaluation; rec fem = rectus femoris muscle; mRNA = messenger ribonucleic acid; mTOR = mechanistic target of rapamycin; MP = motor point; tib ant = tibialis anterior muscle; MRC = Medical Research Council scale; DFL = dorsiflexor muscle; ROM = range of motion; PFL = plantarflexor muscle; VM = vastus medialis muscle; LE = lower extremity; CIP = critical illness polyneuromyopathy; US = ultrasound ext = extension; ant = anterior; post = posterior; CT = computed tomography; UE = upper extremity; MMT = manual muscle testing; SGRQ = St George's Respiratory Questionnaire; QOL = quality of life; gastrocs = gastrocnemius muscle; LOS = length of stay; $VO_{2\ peak}$ = peak oxygen uptake; BP = blood pressure; PFIT = Physical Function in Intensive Care Test; MVIC = maximum voluntary isometric contraction; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; ADL = activities of daily living; SF-36 = Short Form (36) Health Survey; RM = repetition maximum; reps = repetitions; PT = physiotherapy/physical therapy; TNF-α = tumor necrosis factor alpha; MRF-28 = Maugere Foundation Respiratory Failure questionnaire.

4. Equipment and Application

Stimulator

A wide variety of devices deliver NMES, including battery-operated, portable devices that deliver only NMES and combination units that deliver NMES as well as other electrical currents such as TENS, interferential current therapy, and high-voltage pulsed current (HVPC). NMES can also be applied using alternating current (AC)–powered (plug-in) devices that, in addition to offering multiple waveforms, offer other types of modalities such as ultrasound. Typically, devices with high power output (>80 mA) are required when using large electrodes (e.g., 10 × 13 cm), activating multiple muscles, or stimulating large muscle groups. Smooth tetanic muscle contractions are difficult to achieve when using devices with insufficient power output. The technical specifications should be listed in device manuals.

Stimulator features

Preprogrammed NMES protocols

Most NMES stimulators display parameters in digital rather than analog form (dials). One of the features associated with digital devices is the availability of preprogrammed protocols, in which the stimulus parameters are set by the manufacturer. These protocols would not be updated after purchase and may not even initially reflect the latest research, as shown in the tables in this document. Such protocols may be helpful for people who are not knowledgeable about NMES, but physical therapists must understand and be able to rationalize their choice of NMES parameters so that they can customize and modify treatment over time on the basis of a patient's characteristics and responses and the desired clinical outcomes.

Saved protocols

Devices commonly allow therapists to customize and save a few protocols. This feature saves time setting up the device for a repeat treatment of a particular patient. However, some parameters (e.g., pulse amplitude) cannot be saved and need to be set at each treatment.

Locking

Once settings have been selected for a particular patient, they can be "locked in" so that the patient or uninformed provider cannot adjust them inadvertently. This feature is particularly helpful when patients take equipment home or use equipment in unsupervised settings.

Compliance meters

Many devices permit tracking of how patients use them at home. Some devices track the total time the stimulator has been activated, and others track the duration and number of treatment sessions over a particular time period. This feature can be invaluable in understanding why NMES treatments appear to be ineffective for some patients.

Constant stimulation mode (continuously ON)

It is essential that therapists be aware of ON and OFF current cycles. Amplitude should be adjusted only when delivering current to the patient. Most devices have a safety feature that ensures that amplitude can be adjusted only during an ON cycle. For some portable devices, activating a "constant stimulation" button prevents the current from cycling OFF at the preprogrammed time, allowing more time to adjust the current amplitude to the desired level.

Reciprocal–synchronous (also called alternating–simultaneous)

Most NMES devices provide two channels, which can be used to deliver NMES to different muscles or to different locations on the same muscle. Devices with two channels usually have a switch that dictates whether the current flows simultaneously through both channels (synchronous) or automatically alternates between the channels (reciprocal) so that one muscle, or muscle group, is activated while the other channel is in the rest phase of the cycle. Reciprocal stimulation is helpful when the objective is to move joints through more than one direction of range—for example, wrist flexion and extension—in which case, it is important that the muscles contract reciprocally rather than simultaneously.

Automatic shut-off

It may be possible to program when a device will shut off completely, typically measured in minutes (15, 30, or 60 min) or following a preset number of work–rest cycles (ON:OFF times). Using this feature, patients will always receive the prescribed treatment program without the patient or clinician having to track the number of repetitions.

Electrodes

Self-adhesive electrodes

Self-adhesive, pre-gelled electrodes come in a variety of sizes and shapes and are relatively convenient to use because they do not require a clinician to use tape or straps to secure them in place. However, repeated use of pre-gelled electrodes leads to rapid loss of conductivity and deteriorating adhesiveness because of the buildup of skin cells and oils on the adhesive surface. In addition, loss of adhesion and drying of the gel may cause the edges to begin lifting, which can dramatically increase current density, cause uneven distribution of current, increase the risk of burn, and potentially result in electrode

movement. At the very least, it can cause the patient discomfort. Patients occasionally develop sensitivity to the gum in self-adhesive electrodes, which may result in skin irritation (see ''Safety Concerns'' section).[204] Clinicians should monitor the skin under self-adhesive electrodes: If an itchy rash develops, discontinue using them. The same self-adhesive electrodes should never be used for more than one patient.

Carbon rubber electrodes

Carbon-impregnated, silicone rubber electrodes used with electrode-specific gel and held in place using tape or straps produce the best electrical conduction and most even distribution of current across the electrode surface. The position of these electrodes can easily be adjusted, facilitating an optimal set-up for patients. The electrodes can also be used many times before they need replacing. However, patients can develop sensitivity to carbon rubber electrodes. Some carbon rubber electrodes have a pre-gelled adhesive layer; in this case, follow the precautions and procedures that apply to self-adhesive electrodes (see preceding section).

Electrode gel

Electrode gel that is specifically designed to optimize conduction of electrical current is recommended. Electrode-specific gel will promote optimal and even conduction of current and could be more comfortable for the patient because better electrode conduction means that the desired muscle contraction can be produced at lower current amplitude.

Electrode sponges

Sponges moistened with tap water may be used to couple carbon rubber electrodes and the skin; this is a good option when using larger electrodes. Sponges should be appropriately moistened (not too wet or too dry) and should be replaced when they become dirty to maintain their conductivity. It is recommended that a sufficient number of sponges be available to enable complete drying before reuse; this will limit the growth of water-borne bacteria such as *Pseudomonas aeruginosa*.[205]

Securing electrodes

When the optimal electrode placements have been determined, electrodes should be secured firmly with tape or straps to keep the entire electrode area, including the edges, in contact with the skin. Skin moves when the muscle contracts; thus, unsecured electrodes can lead to uneven current distribution and hot spots on the skin, which could cause an electrical burn or, at the very least, discomfort.

Patient set-up

Electrodes

The number, size, polarity, and location of electrodes need to be selected on the basis of patients' goals and target muscle characteristics.

Electrode polarity

Cathode: The negatively charged electrode. The lead wire is typically coloured black at one end.

Anode: The positively charged electrode. The lead wire is typically coloured red at one end.

Electrode positioning

Monopolar electrode placement: Place the cathode on the motor point (MP) of the target muscle and the anode proximally on the target muscle, on a nearby muscle supplied by the same nerve, or over the supplying nerve. This placement should be considered when the waveform produces more current flow in either the positive or the negative direction, thereby creating a circuit with clearly defined cathode and anode—for example, biphasic asymmetrical unbalanced pulsed current (PC). Monopolar set-up is often indicated when targeting small muscles.

Bipolar electrode placement: Place both electrodes on the muscle belly or at the proximal and distal ends of the muscle or muscle group. This placement should be considered when the waveform produces equal current flow in positive and negative directions. Both electrodes are considered active, and each electrode has a positive and negative phase (cathodal and anodal) during each pulse.

When possible, orient the electrodes parallel to the longitudinal direction of the muscle fibres to reduce resistance to current flow.[124,125] Ask the patient where the stimulus is felt, and observe the resulting muscle action. Be prepared to move the electrodes if the desired muscle action is not elicited.

Locating the motor point

The MP is the point on the skin over a muscle where a contraction can be electrically induced with the lowest current amplitude. Because skin and tissue resistance to current is lowest at that point, patient discomfort is minimized, and tolerance is maximized. Placing electrodes over MPs is said to be crucially important in improving the effectiveness of NMES:[206] Higher training intensity is associated with greater gains in muscle strength, so it is important to use all possible techniques to maximize motor unit recruitment.[206] There are charts depicting MPs; however, these are approximate because MPs vary significantly among individuals, and a more precise location should be confirmed by ''scanning.''[206] To scan, or ''surf,'' for an MP, fix the anode over the nerve trunk or muscle belly of the patient's target muscle. Then fix the gelled cathode in the palm of your own hand and apply gel to the fingertip of that hand. Move your gelled fingertip over the approximate area of the MP; the spot that produces the strongest tingling sensation at your fingertip defines the MP.

A pen electrode can also be used to surf for the MP. Fix the anode over the nerve trunk or muscle belly of the patient's target muscle. Move the pen electrode (cathode)

over the approximate area of the MP (holding it for 3–5 s in each spot using low amplitude) until you observe a visible muscle contraction.[206] If a pen electrode is not available, you may use a small, gelled electrode, but be aware of unwittingly creating a large field of effect by spreading the gel over a large area.

Electrode size

The size of the electrode should be selected on the basis of the size of the target muscle and the required depth and spread of current. Larger electrodes promote deeper current penetration. In addition, using larger electrodes tends to be more comfortable for the patient because of reduced current density. Smaller electrodes are useful for isolating specific muscles and for stimulating smaller muscles. Current density is greater using smaller electrodes, and stimulation therefore tends to be less comfortable and poses greater burn risk.

Standard electrode sizes (e.g., 5 × 5 cm square or 5 cm in diameter) are used for medium-sized muscles (e.g., forearm, calf, shoulder). For larger muscles (e.g., quadriceps, hamstrings, lumbar spine), larger electrodes should be used (e.g., 5 × 10 cm, 10 × 10 cm, or larger) to allow for better dispersion of the current. Using small electrodes on a large muscle produces inadequate motor unit recruitment, whereas using electrodes that are too large can cause the current to activate unwanted adjacent muscles (e.g., upper trapezius fibres when treating shoulder subluxation).

Electrode spacing

When electrodes are placed close together, the current will travel more superficially; wider spacing will promote deeper penetration and greater spread of the current. Electrodes are generally placed further apart when using a monopolar electrode placement because the anode need not be placed on the muscle.

Limb position

Limbs should be positioned in the mid-range of muscle length to produce the strongest muscle contraction. For example, when stimulating quads for musculoskeletal conditions, the knee should be positioned in approximately 65° flexion.[108] Avoiding lengthened or shortened positions of muscles should be incorporated into all NMES strengthening programmes. Muscle groups also need to be considered: For example, to enable the external rotators of the shoulder to be stimulated in their mid-length position, the patient's upper arm should be positioned in the coronal plane.

When muscles are very weak, consider placing the limb relative to gravity to enable an appropriate challenge to the existing muscle strength. For example, muscles with grade 1 or 2 strength should preferentially be stimulated with the limb in a gravity-assisted or gravity-neutral position; grade 3 muscles should be in a gravity-resisted position.

When motor relearning is a goal, the patient should preferentially use a functional position. For example, when retraining lower extremity muscles, patients may benefit from using NMES while standing or walking, rather than sitting with their lower leg dangling over the edge of the plinth or bed.

Voluntary contraction

Whether patients should voluntarily contract their muscles during NMES treatment depends on whether the goals of treatment include motor relearning, functional recovery (e.g., in neuro-rehabilitation programmes), or both or isolated muscle strengthening (e.g., many orthopaedic conditions).

The combination of voluntary effort, motor imagery (thinking or imagining the muscle action), and NMES appears to have greater potential to induce plasticity of the motor cortex post-stroke than either electrical stimulation or exercise training alone.[207] Furthermore, carry-over of benefit after the end of NMES in a stroke treatment program is more likely when the muscle stimulation is superimposed on a functional and meaningful muscle action.[32,41,150] Concurrent activation with both electrical stimulation and voluntary muscle contraction may recruit different types of muscle fibres and result in a more complete muscle contraction.

When the main goal of NMES is muscle strengthening, concurrent voluntary contractions are not required: The benefit of NMES without voluntary assistance has been shown in many studies. However, NMES is not intended as a stand-alone treatment. Patients receiving NMES should, in addition, undertake a comprehensive therapeutic exercise programme (supervised or at home). When patients are unable to perform voluntary contractions—for example, sedated patients in the ICU—NMES is applied alone.

Denervated muscles

This article focuses on applying NMES to select innervated muscles; this occurs through depolarization of the motor nerves rather than the muscle fibres directly. If there is damage to the lower motor neurons or neuromuscular junctions (i.e., partial or complete denervation), electrically induced muscle contraction occurs through direct depolarization of the sarcolemma. This requires a much longer phase duration for the NMES pulse (100–300 ms), thus more electrical charge, to produce a contraction. In fact, most portable NMES stimulators will not provide the parameters required to elicit a contraction of a denervated muscle. As a result, the possible benefit of applying NMES to denervated muscles has not been clearly established.[208]

Safety concerns

Lack of sensation

Several conditions for which NMES is indicated result in impaired sensation as a result of nerve damage. Although intact sensation is not considered to be an

absolute contraindication, a lack of patient feedback significantly increases the risk of adverse reactions.[1] When sensation is altered either by neurological condition (e.g., post-stroke, spinal cord injury) or by damage to superficial sensory nerves (e.g., as a result of surgical incision), it is important to determine whether the altered nerve supply has affected the ability to discriminate between different sensations (pins and needles vs. intense buzz) or the ability to detect a painful and potentially tissue-damaging stimulus. The physical therapist must monitor the situation very carefully, such as by performing frequent skin checks and assessing patient discomfort or potential damage.

Concurrent use of NMES and cold packs

Concurrent application of a cold pack over the electrodes during electrical stimulation will numb the area and block nerve transmission along the sensory fibres. Reducing a patient's awareness of pain or developing tissue damage resulting from the electrical stimulation creates an unsafe practice situation. In addition, the thin film of surface water that forms on the skin with the application of cold will allow a superficial passage of electrical current across the skin, rather than enabling the current to travel through the underlying tissues.

Skin irritation and skin burn

It is common to observe a slight reddening of the skin under the electrodes after applying NMES because of the increased blood supply to the area; however, it resolves spontaneously once the stimulation is switched off. Mild skin irritation is sometimes seen due to allergic factors (electrode compounds, electrode gel, self-adhesive gum, tape) or mechanical factors (skin abrasion from tape removal). Chemical and electrical factors can also be the cause of burns. A chemical burn may be caused when using direct current or monophasic PC (not typical for NMES) by the buildup of new acids and bases formed by electrolysis where the electrode sits on a patient's skin. An electrical burn may be caused by current density being too high; this is a particular risk when delivering high-current amplitudes through relatively small electrodes.

Common approach to applying NMES

A general approach to promoting safe and effective use of therapeutic modalities has previously been presented.[1] Briefly, this approach involves taking the following steps:

- Consult a resource that provides a comprehensive list of relevant contraindications and precautions for NMES treatments as well as references and a rationale for conditions that increase the likelihood or severity of an adverse reaction or reduce intended benefits.[1]
- Develop a strategy to mitigate risks before, during, and after treatment. The most common risks associated with NMES treatment are (1) electrical surge or shock should the equipment malfunction; (2) skin irritation or allergy at the electrode sites; (3) pain during treatment if the current amplitude is not adjusted slowly and on the basis of patient feedback; and (4) post-treatment muscle soreness.

Most risks can be mitigated by establishing clear lines of communication between the therapist and the patient and creating a therapeutic relationship that encourages frequent and honest patient feedback.

- Explain the risks and benefits before obtaining consent from the patient or substitute decision maker. Explain clearly what the patient is likely to feel and what common adverse signs should be watched for during treatment. Many physical therapists use consent forms that patients must sign; however, these documents should be used in conjunction with a dialogue with the patient or substitute decision maker that confirms understanding and provides an opportunity to ask questions.
- Conduct a sensory test using sharp–dull discrimination over the area where NMES is to be applied.
- Swab the relevant skin sites using an alcohol wipe or wet cloth to remove any topical products that could increase skin resistance to current flow.
- Apply the treatment, and encourage the patient to participate in the treatment in the manner determined (see "Voluntary Contraction" section). To protect the joint against potential injury, caution is required in eliciting strong muscle contractions when volitional muscle control is lacking.
- Check the skin under the electrodes after the stimulation is complete and more frequently during treatments, if indicated (see "Skin Irritation and Skin Burn" section).
- Remove all gel and tape residue from the skin using an alcohol swab or wet cloth.
- Remind and instruct patients and caregivers to monitor patients' reactions after NMES treatment. Provide clear instructions about what signs and symptoms to monitor, including both desirable and undesirable reactions, and advise when action should be taken.

Document the treatment parameters, electrode set-up, and patient positioning in enough detail that the treatment can be easily reproduced by another qualified clinician. Use valid outcome measures, and evaluate the measured outcomes (using minimum detectable change or minimal clinically important difference) to confirm treatment effectiveness.

Equipment care and maintenance

Electrode care

Carbon rubber electrodes should be rinsed with warm, soapy water after use and left to air dry, face up, or gently patted dry. They should not be aggressively rubbed

because that can damage or remove the embedded carbon, thereby decreasing electrode conductivity.

It is essential to wash the electrodes and follow decontamination protocols that are consistent with health and safety requirements; in addition, be sure to use products that do not compromise the conductivity of carbon rubber electrodes.

Equipment cleaning

Equipment, leads, and electrodes should always be cleaned between patients. Consider using antiseptic solutions that are known to kill a broad spectrum of microbes while preserving electrode conductivity and equipment integrity. High-alcohol-content solutions (>70%) can rapidly erode the conductive surface of carbon rubber electrodes. Discussion with infection control professionals is recommended when using NMES for patients who are colonized with resistant or virulent microorganisms or for patients who have compromised immune function and reduced capacity to deal with a microbial burden.

Equipment checks

It is strongly recommended, and in some provinces it is mandated by college regulations, to check all equipment and supplies intended for use on people (patients, volunteers, students) at least once a year. In some instances, more frequent equipment inspections are warranted. When equipment stands unused for long periods, electrical components can accumulate dust, which can affect conduction and insulation in the unit, resulting in current flow that does not adjust smoothly or is intermittent. Physical therapists should test equipment that has been unused for 3–6 months on themselves before using it on patients. Annual equipment checks should be conducted by qualified biomedical technicians who can evaluate the integrity and patency of electrical circuitry and calibrate the device (typically using an oscilloscope) to confirm the accuracy of electrical output. Safety checks of AC-powered stimulators should include a check of the insulation of electrical cords, the circuit grounding, and the measurement of leakage currents. Faulty equipment should always be taken out of service immediately.

Checking leads and electrodes

Leads and carbon electrodes need to be checked regularly to confirm that they are conducting electrical current consistently and evenly and with low resistance. The metal wire used in most leads is easily damaged, especially when leads are bent or stretched excessively or repeatedly. When a damaged lead wire moves during treatment, intermittent current flow can occur, and this can be uncomfortable and potentially harmful to the patient. Physical therapists should test that lead wires are patent by applying electrodes to themselves and gently moving the leads during the current ON cycle, noting any change in sensation.

Carbon rubber electrodes should be replaced when their impedance is more than 500 Ohms per centimetre. Impedance can be measured by an ohmmeter; for instructions on carrying out this measurement, visit http://cptbc.org/wp-content/uploads/2015/07/592107903-Practice-Standard-.pdf.

5. Terms and Definitions in NMES

A discussion of the NMES literature is confusing because of the inconsistency in electrotherapy terminology. A common set of terms to facilitate easy communication about EPAs is needed; however, the 2001 document most commonly cited by other authors[209,210] needs updating to bring it in line with changes in equipment and recent modifications to traditional waveforms (e.g., Russian current). In this section, we define and describe terms that are relevant to the discussion of NMES; clinicians working with electrical stimulators may find it helpful to use our standard set of terms to reconcile the variety of terms used in research and industry.

Neuromuscular electrical stimulation (NMES)

Repeated application of current to produce contraction of innervated muscle by depolarizing local motor nerves. Repeated application may produce effects—for example, muscle strengthening "that enhances function but that does not directly provide function."[42(p.412)]

Functional electrical stimulation (FES)

The use of electrical current to directly enable a functional movement.[42] FES systems are commonly designed for the limbs, such as UEs for activities of daily living (ADLs) or LEs for gait. FES might replace a completely lost movement, as in paralyzed muscles in individuals with spinal cord injury, or replace or augment orthotics. FES may require sophisticated microcircuitry, multiple channels, and creative triggering mechanisms (voice, intact muscles, switches) and might need to be applied long term and during all waking hours to achieve the objectives.

Transcutaneous electrical nerve stimulation (TENS)

Application of current using surface electrodes to activate peripheral nerves; TENS (sometimes abbreviated *TNS*) is typically used for the purpose of modulating pain. A variety of current waveforms and pulse frequencies are associated with TENS; customarily, the

approach produces sensory stimulation with or without small muscle twitches that are non-functional. Tetany is not normally required. TENS is not applied using the ON:OFF periods (measured in seconds) typical of NMES; rather, the current is delivered continuously for periods as short as 30 min or for many hours continuously.

Charge (coulombs)

A measure of how many electrons have been lost or gained by an object. Matter is either negatively or positively charged, or it has no net charge (neutral). One coulomb is the quantity of charge created when a current of 1 ampere flows for 1 second.

Current (amperes or milliamperes)

Movement of electrons or ions through a conductive medium. In human tissues and bodily fluids, this involves the flow of ions such as sodium, potassium, and chloride. A current flows according to Ohm's law (current = voltage/resistance) and is proportional to the magnitude of the electromotive force (voltage) divided by the opposition to current flow (resistance).

Voltage (volts or millivolts)

Electromotive force drives the movement of current from one location to another along a pathway or circuit. Current flow increases with an increase in voltage. Also known as the potential difference, voltage is created by the separation of negative and positive charges associated with two oppositely charged electrodes.

Resistance (ohms)

The opposition of a conductive material to the passage of an electrical current. Current flow increases with a decrease in the resistance of the conducting material. In the human body, high-resistance tissues (insulators) include skin, fat, and connective tissues, and low-resistance tissues (conductors) include muscles, blood, and other bodily fluids that have a high concentration of electrolytes.

Impedance (*Z*)

The opposition of a material to AC flow. It is also measured in ohms; however, it has the symbol *Z*. The relevance for clinicians is that impedance is lower for medium-frequency (1000 Hz) and high-frequency currents; therefore, they pass more easily through the skin layer than low-frequency currents.[28]

Resistance to ACs is complex because of the changing electrical and magnetic fields as pulse charge changes from positive to negative. Impedance factors into the resistance of capacitors in AC circuits. Skin is an insulator and stores an electrical charge on its outer surface—that is, it acts as a capacitor and resists current flow across it. Capacitor resistance is inversely dependent on frequency: As AC frequency increases, pulse duration decreases, allowing less time for a charge to be stored on the skin and, therefore, less impedance.

Constant voltage (CV) stimulator (current measured in milliamperes)

Maintains the voltage set by a clinician at the start of treatment. Current flow varies inversely with skin–electrode resistance, meaning that if the contact area between electrode and skin changes during treatment, the resistance, and therefore current flow, also change. A problem can arise when the initial skin–electrode contact is poor and full contact suddenly occurs: Resistance drops dramatically, current flow increases dramatically, and a patient feels a sudden surge of current, which could be uncomfortable or painful. In the reverse situation, when full skin–electrode contact changes to partial contact, voltage is maintained by the stimulator, but, because of higher resistance, the current flow drops. The drop could mean that current flow is below beneficial level.

Constant current (CC) stimulator (current measured in volts)

Delivers current to the electrodes at a constant amplitude by varying the voltage output whenever resistance changes. This means that if the contact area between skin and electrode is suddenly reduced during treatment, the same amount of current will flow through a smaller skin area, and the increased current density could be uncomfortable, even painful, for the patient. This type of stimulator has a built-in safety factor in that the maximum voltage adjustment is limited to a safe range. The advantage of CC stimulators is that they ensure that the current level is maintained at that set initially by the clinician. They may be more draining on battery-operated units.

Some stimulators permit selection of CV or CC. If a choice is not available, CC versus CV can be determined by slowly lifting an electrode corner off the skin while the stimulator is on. If the patient perceives that the current intensifies, the stimulator is delivering constant current; if the patient perceives that the current weakens, the stimulator is delivering constant voltage.

Cathode

The negatively charged electrode; it attracts positively charged cations. The cathode is considered more active because it can more readily depolarize a nerve; therefore, it is often placed over the muscle MP. The negative lead wire is typically coloured black at one end.

Anode

The positively charged electrode; it attracts negatively charged anions. The anode is often placed over the nerve innervating the target muscles or proximal or distal to the cathode. The positive lead wire is typically coloured red at one end.

Waveform

Diagrammatically represents a change in stimulus amplitude over time. This ''picture'' of an electrical event begins when the current flows and stops when the

current returns to zero. The amplitude and direction of the current flow is reflected in the shape of the waveform and depends on the polarity of the electrodes.

Many AC (plug-in) stimulators offer one or more different waveforms, which can be selected by a therapist (see monopolar and bipolar set-up, under ''Electrode Positioning''). Portable stimulators usually provide limited waveform choices.

Waveforms can be described as monophasic or biphasic, then further described by their shape (e.g., monophasic rectangular, symmetrical biphasic rectangular, asymmetrical biphasic rectangular, sinusoidal). More description follows under ''Pulsed Current.''

Please note that the terms *rectangular* and *square waves* are commonly used interchangeably. Both correctly describe a pulse with a rapid rise of amplitude and variable pulse duration. This article uses *rectangular*.

Types of current

Direct current (DC)

Current that flows in one direction continuously for a period of at least 1 second. It is also called *galvanic current*. Electrode polarity (positive or negative) remains constant until it is changed manually by the operator. This form of current results in an accumulation of charged particles (ions) under the electrodes, which, if excessive, will cause an electrochemical burn. DC has limited clinical application (e.g., iontophoresis and wound healing).

Alternating current (AC)

Continuous bidirectional current that changes in direction at least once every second. The most common type of AC is a sinusoidal wave, in which both phases are equal and opposite and no net charge accumulates. Unlike pulsed current, there is no OFF time between cycles or phases. AC is almost exclusively available on plug-in, multi-modal units and is not present on most portable devices.

Russian current as an example of burst-modulated AC (BMAC)

This classic waveform is a medium-frequency sinusoidal current that is balanced and switches polarity 2,500 times per second (2500 Hz). A type of BMAC, Russian current is interrupted (modulated) into 20-millisecond bursts, consisting of 10 milliseconds of AC current followed by 10 milliseconds of no AC current (50% duty cycle). This is repeated 50 times per second (burst rate of 50). The background 2500-Hertz AC is called the *carrier frequency*.

More recently,[211,212] devices have been designed to deliver different configurations of the traditional Russian current with adjustable levels of carrier frequency (1000–5000 Hz), burst frequency (50–75 bursts per second), or burst duration (2–10 ms). Modulated AC therapeutic currents are normally available only on wall-powered stimulators.

Some portable stimulators indicate that they offer Russian current, but the current characteristics show that it is a burst-modulated PC, which is distinct from true Russian current and BMAC. This current consists of three or more biphasic, balanced, rectangular wave pulses of 120- to 400-microsecond phase duration separated by a 100-microsecond interpulse interval. These bursts of three or more pulses are delivered 50 times a second.

Although these three forms of current would be indistinguishable to a patient, some research has suggested that the ability to elicit near-maximal force without considerable discomfort can be influenced by the waveform.[211,212]

Pulsed current (PC)

Pulsed current is a brief, intermittent current flow interrupted by periods of no current flow. Current can flow in one direction (monophasic) or both directions (biphasic). Each pulse is an isolated event described by waveform shape (e.g., rectangular, twin peaked), amplitude, and duration. With PC, the duration of the pulse is very short, typically only a few hundred microseconds (one-millionth of a second), and the total charge delivered using PC is extremely low. For example, during a 10-second muscle contraction with a pulse duration of 300 microseconds and pulse frequency of 50 Hertz, current would be delivered for a total of 0.15 seconds. PC is the type of current most commonly used for therapeutic purposes because the risk of tissue injury is minimal, and it can be delivered using small, battery-powered devices.

Monophasic pulsed current

Current flows in only one direction, and the polarity of the electrodes does not change. Most often, it appears as a rectangular waveform, with a range of pulse amplitude, pulse duration (commonly 100–400 μs), and pulse frequency (commonly 50–100Hz) that can be selected by the clinician. It is erroneous to describe monophasic PC as pulsed DC because current does not flow in one direction for periods of 1 second or longer. Because the pulse has a very short duration, very little charge accumulates under the electrode. Common types of monophasic PC include monophasic rectangular waveforms and high-voltage PC (twin-peaked monophasic PC).

High-voltage pulsed current (HVPC)

Pulses are characterized by high initial voltage, up to 500 volts, followed by a rapid, exponential fall in voltage. Pulses are delivered in pairs (so-called twin peaks), with minimal time between peaks. The duration of each phase is very short (20–60 μs), taking only 5–10 microseconds to reach 50% of peak amplitude. Because of the rapid decay in voltage, the total charge of individual pulses (about 15 μC) is lower than that of most other waveforms. During each pulse, current flows in only one

direction, resulting in a small accumulation of charge under each electrode. However, because of the very short pulse duration, this charge is negligible and does not change skin pH. This combination of high amplitude and brief pulse duration produces a relatively comfortable electrical stimulation. However, it is ineffective for activating muscles, other than small muscles (e.g., in the hand). HVPC is most commonly used to stimulate tissue repair and promote the closure of many types of chronic, open wounds.

Biphasic pulsed current

Bidirectional flow of current with two distinct phases. A current flows in one direction for a defined period, and then the polarity of the electrodes switches, causing the current to reverse and flow in the opposite direction.

Biphasic symmetrical pulsed current

A current with a waveform that has two identical phases; each has an equal and opposite current flow so that no net charge accumulates on the skin.

Biphasic asymmetrical pulsed current

A current in which the polarity of electrodes changes during each phase of the pulse, but the shape of each phase of the waveform is not the same. The two phases of the pulse may be balanced or unbalanced. If balanced, the charge in each phase is equal and opposite, resulting in no net charge accumulating on the skin. If unbalanced, the two phases of the pulse have different amounts of charge, leaving a net balance of charge on the skin. The waveform most often used in NMES stimulators has a leading phase that is rectangular, followed by a second phase with the current flowing in the opposite direction at a lower amplitude for a longer duration. In this way, the phase charge is balanced so that the pulse is electrochemically neutral—that is, there is no net charge.

Biphasic asymmetrical PC is the most common type used in portable TENS and NMES machines. The initial active phase behaves similarly to monophasic PC, in which there is one clearly defined, negatively charged electrode (cathode) and another positively charged electrode (anode).

NMES parameters

Frequency (pulse rate; Hertz or pulses per second [pps])

The number of pulses in 1 second (a biphasic pulse has two phases but still counts as a single pulse when considering pulses per second).

Phase and pulse duration (microseconds)

Pulse duration is the time elapsed from when the current (or voltage) leaves the isoelectric (zero) line until it returns to baseline. It includes both positive and negative phases when the pulse is biphasic as well as any interphase interval. Because pulse duration is measured in units of time, it is incorrectly, although commonly, referred to as *pulse width*.

Pulse amplitude (millivolts or milliamperes)

The magnitude of the current or voltage deviation from zero or isoelectric line (current or voltage, depending on whether the stimulator is a CV or CC device). Often described as peak or peak-to-peak amplitude, which is the maximum or largest deviation from zero.

ON time

The time over which a series of pulses is delivered. With NMES protocols, this time reflects the duration that the muscle will be activated (work cycle).

OFF time

The time over which the stimulator automatically cycles OFF and no current is delivered. With NMES protocols, this is the period between muscle contractions (rest cycle).

ON:OFF ratio

A ratio of the ON time of each cycle to the OFF time (e.g., ON:OFF 10:30 s = 1:3 ratio). Higher ratios (1:5) have more rest time between muscle contractions and cause less muscle fatigue.

Ramp-up time

The amount of time it takes for the stimulating current to reach the set amplitude of an ON cycle, commonly 1–2 seconds. Devices usually count the ramp-up time as part of the total ON time.

Ramp-down time

The amount of time it takes for the stimulating current to return to zero intensity at the end of an ON cycle, commonly 1–2 seconds. Devices commonly count the ramp-down time as part of the total OFF time.

CONCLUSION

The tables in this document provide data that have been extracted from a large body of evidence and critically analyzed to inform clinical practice. There is moderate to strong evidence that NMES is effective as a treatment for some UE and LE problems post-stroke, for weakness post-ACL repair and total knee replacement, for muscle weakness in knee OA, and for debilitation and weakness after critical illnesses. The benefit of NMES for PFPS is uncertain.

These data informed our recommendations for the key NMES parameters for effective treatment. For quads muscle strengthening, after knee surgery and in OA and PFPS, the optimal approach includes tolerance-level current amplitude and isometric contraction without voluntary assist, but with an additional voluntary strengthening programme performed at another time; also important are adequate pulse duration and a limited number of repetitions within a session, approximately 10–15

contractions three times a week. In contrast, for motor relearning and strengthening for patients post-stroke, the key factors are high levels of repetition within sessions applied on a daily basis at relatively lower current amplitudes and lower pulse frequency; shorter pulse durations are acceptable.

Optimal outcomes using EMG-NMES or NMES alone might be achieved when muscle stimulation is applied during functional activities post-stroke. For managing severe muscle weakness and atrophy and the deconditioning associated with critical illness and advanced cardiopulmonary disease, the optimal parameters are generally similar to those used post-stroke, although different outcomes are measured—namely, muscle strength and cardiopulmonary function, each of which has been reported to benefit from NMES treatment; relatively lower pulse frequency and amplitude and a high number of daily repetitions are indicated. For patients in the ICU, voluntary exercise is usually not an option, and patient positioning is determined by feasibility. For all these clinical conditions, an adequate total number of sessions is important to improve outcomes.

The authors of this article have clearly identified the positive effects of the use of NMES in a variety of clinical situations, and they have provided clinicians with appropriate information and parameters to promote the effective use of NMES on patients in these or similar clinical conditions.

ABBREVIATIONS

UNITS

cm – centimetre(s)
mm – millimetre(s)
mA – milliampere(s)
Hz – Hertz
μV – microvolts
AC – alternating current
HVPC – high-voltage pulsed current

MUSCLES

gastrocs – gastrocnemius muscle
hams – hamstring muscles (biceps femoris, semitendinosis, semimembranosis)
MP – motor point
quads – quadriceps muscle
VL – vastus lateralis muscle
VM – vastus medialis muscle

GENERAL

ACL – anterior cruciate ligament
CCT – controlled clinical trial
CHF – congestive heart failure
COPD – chronic obstructive pulmonary disease
EMG – electromyography
EPAs – electrophysical agents
Ex – exercise
FES – functional electrical stimulation
ICU – intensive care unit
LE – lower extremity
NMES – neuromuscular electrical nerve stimulation
OA – osteoarthritis
PFPS – patellofemoral pain syndrome
PT – physical therapy
QOL – quality of life
RCT – randomized controlled trial
SR – systematic review
sublux – subluxation
THA – total hip arthroplasty
TKA – total knee arthroplasty
UE – upper extremity

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