HOSPITAL CHRONICLES 2013, 8(3): 112–119

REVIEW

Therapeutic Applications of Neuromuscular Electrical Stimulation in Critical Care Patients

Manolis Papadopoulos, PT, PhD,[1] Irini Patsaki, PT, MSc,[1]
Anna Christakou, PT, PhD,[1] Vasiliki Gerovasili, MD,[2] Serafim Nanas, MD[3]

[1]Physiotherapy Section,
[2]Pulmonary Medicine Division,
[3]Department of Intensive Care, University of Athens, Evagelismos Hospital, Athens, Greece

KEY WORDS: *Neuromuscular electrical stimulation; intensive care unit acquired weakness; pressure ulcers; functional electrical stimulation*

ABBREVIATIONS

FES = functional electrical stimulation
HVES = high voltage electrical stimulation
HVPDC = high voltage pulsed direct current
ICU = intensive care unit
ICUAW= intensive care unit acquired weakness
LICD = low intensity direct currents
MRC = Medical Research Council
NMES = neuromuscular electrical stimulation
SCI = spinal cord injury
WMCS = wireless microcurrent stimulation

Correspondence to:
Manolis Papadopoulos, PhD,
Department of Intensive Care,
Evagelismos Hospital,
Athens, Greece;
E-mail: epapas2@gmail.com

Manuscript received March 5, 2013; Revised manuscript received May 15, 2013; Accepted June 9, 2013

Conflict of Interest: none declared

ABSTRACT

Neuromuscular electrical stimulation (NMES) is commonly used by physiotherapists for pain relief, stimulation of denervated or disused muscles, and the promotion of wound healing. The purpose of this review is to discuss the applications of NMES in intensive care unit (ICU) patients according to the current research evidence. The first application is the use of NMES in ICU acquired weakness with evidence indicating significant benefits, such as preservation of muscle mass, prevention of polyneuromyopathy and improvement of muscle performance. Secondly, NMES has been proved to be effective in preventing pressure ulcers and accelerating wound healing through mechanisms which are clearly demonstrated by many experimental and clinical studies. However, very few studies have examined the effect of electrical stimulation in pressure ulcers of long term hospitalized ICU patients. Lastly, NMES in ICU can be applied in the form of functional electrical stimulation (FES), a well known technique used to mobilize patients with permanent neurological deficits, such as stroke and spinal cord injury. Current evidence in this area is reviewed and future research is proposed.

INTRODUCTION

Physiotherapists are integral members of the multidisciplinary team in intensive care units (ICU). Apart from contributing in the prevention and treatment of various pathologies and complications of the respiratory system, they also play a very important role in the mobilization of patients soon after their admission. One of the physiotherapy treatment techniques that have recently attracted international attention in ICU research is neuromuscular electrical stimulation (NMES). The purpose of the present review is to describe the applications of NMES in the setting of the ICU in order to contribute to the improvement of physiotherapy clinical practice in this area. According to the literature, there are three main clinical applications of NMES in ICU:

- NMES in intensive care unit acquired weakness
- NMES for pressure ulcer healing
- Functional electrical stimulation

1. NMES IN INTENSIVE CARE UNIT ACQUIRED WEAKNESS

Intensive care unit acquired weakness (ICUAW) is the most common neuromuscular complication of critical illness which can be prevented and treated with NMES. It is mainly presented with generalized muscle weakness, diminished tendon reflexes, difficult weaning from mechanical ventilation[1,2] and is associated with prolonged ICU and hospital stay.[3] The incidence of ICUAW is reported to range from 23% to more than 50% depending on the diagnostic clinical and electrophysiological criteria and the patient population evaluated.[1,2] In afflicted patients muscular weakness may persist for months and in some of them it may never fully recover.[4]

According to the literature, early rehabilitation is one of the most effective physiotherapy strategies in order to prevent ICUAW. Several studies have shown that early mobilization techniques are safe and feasible[5] and contribute significantly to a shorter ICU and hospital stay[6] and a better rehabilitation outcome at ICU discharge.[5] Neuromuscular electrical stimulation (Figure 1) causes visible muscle contractions even at the acute patient care where critically ill patients cannot exercise actively due to sedation or cognitive impairment. NMES can be used in combination with other physiotherapy techniques, such as passive joint mobility, muscle stretching, passive bedside cycling, etc.

Neuromuscular electrical stimulation is a treatment tool which is widely used by physiotherapists for pain relief,[8] muscle training,[9] wound healing and other patient conditions,[10,11] as well as in healthy subjects.[4] NMES may be applied not only by clinicians but also by patients themselves in home-based rehabilitation programs.[11] According to the literature, each NMES session can last from 30 minutes[12] to 4 hours.[13] NMES is currently contraindicated in patients with implanted defibrillators and pacemakers for safety reasons although preliminary data indicate that it may be safe.[14]

FIGURE 1. Application of neuromuscular electrical stimulation (NMES) for quadriceps muscle contraction of ICU patients. ICU = intensive care unit.

The purpose of this section is to present the current available research evidence on the effect of NMES in ICUAW. Several clinical trials have assessed the effect of NMES on ICUAW.[16-21] Most patients included in these trials were severely ill, mechanically ventilated, and the majority were sedated during the acute phase of their care. Patient conditions included medical and surgical problems, trauma,[15-18,21] septic shock,[19,20] and chronic obstructive pulmonary disease.[12]

All studies that have investigated the effect of NMES in critically ill patients, mainly stimulated muscles of the lower extremities including the quadriceps muscle (Figure 1),[18,19,21] the peroneus longus,[12,15-17] and only one study stimulated the brachial biceps muscle of the upper limb.[20]

PARAMETERS OF NMES IN CRITICALLY ILL PATIENTS

According to the studies that have been carried out so far, there is no absolute agreement in the parameters of NMES application in ICU patients. In most studies, NMES sessions were delivered daily.[15-17,19-21] However, in two studies NMES was applied 5 days per week.[12,18] Each session may last from 30 minutes to one hour on a daily basis and the frequency of NMES stimulation also varies and ranges from 35 to 100 Hz. Table 1 summarizes the range of NMES parameters used in critically ill patients in the aforementioned studies.

CLINICAL EFFECTS OF NMES IN CRITICALLY ILL PATIENTS

The effect of NMES may not only be seen locally at the muscles applied, but NMES has also been observed to have a systemic effect. The first study conducted in the ICU[15] investigated the immediate effect of NMES on cardiovascular and microcirculatory parameters in 35 critically ill patients, who were mechanically ventilated (86%), sedated (50%) and under continuous vasopressor support (33%). NMES was applied bilaterally in 29 patients on the quadriceps and peroneus longus muscles, whereas 6 patients served as controls. Near infrared

TABLE 1. Parameters of Neuromuscular Electrical Stimulation (NMES) in ICU Acquired Weakness

Current type	Pulsed
Duration	5-7 days/week, 30-60 minutes
Frequency	35-100 Hz
Pulse duration	300-400 μsec
Duty cycle	12 sec on, 6 sec rest
Intensity	Maximum tolerance or visible contraction

spectroscopy of the thenar muscle of the hand, which did not receive any stimulation, showed that a single NMES session resulted in a statistically significant increase of the oxygen consumption rate and the reperfusion rate of the thenar, following vascular occlusion of the upper limb. Although this finding is indicative of the presence of factors induced by NMES that act in a systemic way, more studies are necessary before safe conclusions can be drawn. Neuromuscular electrical stimulation has also been shown to contribute to the prevention of intensive care unit acquired weakness (ICUAW). Specifically, a study was carried out in order to investigate the effect of daily NMES sessions on the prevention of ICUAW.[17] A total of 145 patients were randomly assigned to the NMES group or the control group and were assessed on awakening for the development of ICUAW by non blinded examiners. Patients assigned to the NMES group received daily sessions of both lower extremities from the second day after admission until ICU discharge. The results showed that daily NMES sessions of both lower extremities resulted in significantly lower incidence of ICUAW, 13% in the intervention group as compared to 39% in the control group. This is the first study to show that daily NMES sessions of lower extremities in critically ill patients may have a role in the prevention of ICUAW. More studies need to be carried out in order to confirm these findings.

In a secondary study, the same research group investigated the effect of NMES on muscle strength in 142 critically ill patients.[18] NEMS sessions were applied daily on vastus lateralis, vastus medialis, and peroneus longus of both lower extremities. Muscle strength was evaluated with the Medical Research Council (MRC) scale and handgrip strength. The results showed that patients treated with NMES, achieved higher MRC scores than the controls in wrist flexion, hip flexion, knee extension, and ankle dorsiflexion. Similar differences were also found in handgrip strength. The authors concluded that NMES has beneficial effects on muscle strength of critically ill patients, both in directly stimulated muscles as well as in distant muscle groups indicating a systemic effect which needs to be further investigated. The results of the above studies show that NMES may be a potential effective means of muscle strength preservation and early mobilization in critical care patients.

Despite the promising results of the above studies, another study showed that the application of NMES in 8 ICU patients daily for 60 minutes on the quadriceps muscle of one lower limb did not have a significant effect in muscle volume preservation as shown by computed tomography.[20] This finding necessitates the need for more studies before safe conclusions can be drawn.

CONCLUSION

NMES is an early ICU rehabilitation technique that can be used safely in critically ill, sedated patients, without requiring patient cooperation. Data in critically ill patients show that NMES sessions may preserve the muscle properties and prevent the development of ICU acquired weakness and even contribute to a faster weaning from mechanical ventilation. More studies however are necessary in order to establish the clinical role of NMES in critically ill ICU patients. Further studies are also needed to evaluate the systemic effect and the long term effect of NMES in ICU survivors.

2. EFFECT OF ELECTRICAL STIMULATION IN PRESSURE ULCER HEALING

Electrical stimulation has been shown to contribute to the prevention and treatment of pressure ulcers. However, limited evidence exists regarding the application of electrical stimulation in ICU for pressure ulcer healing. Electrical stimulation was firstly applied with electrostatically charged gold foil for wound healing 300 years ago and later in the sixties.[23,24] The theory behind that lies on the fact that the skin has intrinsic bio-electrical systems. Specifically, healthy skin has a negative

TABLE 2. Physiological effects of electrical stimulation

Inflammation phase	Proliferation phase	Regeneration phase
- Initiation of healing process	- Promotion of fibroblastic and epithelization process	- Promotion of epidermal cells production
- Increased blood flow	- Facilitation of DNA synthesis	- Production of fine scar tissue[28-32]
- Improved oxygenation	- Increase of ATP production	
- Promotion of phagocytosis	- Increase in cell membrane permeability	
- Edema reduction	- Formation of better collagen network	
- Pain relief	- Facilitation of wound contraction[29-31]	
- Galvanotaxis		
- Promotion of DNA synthesis		
- Antimicrobial effect[26-28,30,31]		

ATP = adenosine triphosphate ; DNA = deoxy-ribo-nucleic acid resting potential (skin battery) with a voltage ranging from 10 mV to 60 mV.

As soon as a skin lesion occurs, this potential is altered, creating a wound potential called "the current of injury" which promotes wound healing. The application of electrical stimulation may further enhance this process through a mechanism called 'Galvanotaxis'. Galvanotaxis can be defined as the directional migration of various types of cells, such as endothelial cells and keratinocytes, which facilitate re-epithelialization of the wound. The biological processes underlying galvanotaxis need further investigation. A proposed mechanism is the occurrence of lateral electrophoresis which causes changes in the plasma membrane and possibly affects protein redistribution and in turn may facilitate healing.[25]

PHYSIOLOGICAL EFFECTS OF ELECTRICAL STIMULATION

The physiological effects of electrical stimulation have been observed in all phases of healing and are outlined in Table 2.

PRESSURE ULCERS IN ICU

According to several epidemiological studies from Europe, South America, South Africa and Canada, the prevalence of pressure ulcers in ICU ranges widely from 5% to over 40%.[33] Additionally, over 31% of patients who are identified to be at high risk for pressure ulcers develop such ulcers.[33] Despite the fact that wound healing is mainly managed by nursing staff and plastic surgeons, several experimental and clinical studies show that physiotherapists can contribute significantly both in the prevention and the acceleration of wound closure.

EFFECT OF ELECTRICAL STIMULATION ON PRESSURE ULCER PREVENTION

Electrical stimulation has been shown to have a more functional role as it seems to contribute to the prevention of pressure ulcers, through the production of visible muscle contractions which result in equal distribution of skin pressures.[34] An experimental study showed that pulsed electrical stimulation which produced visible muscle contractions of the glutei muscles, mimicking movements of a healthy subject, significantly reduced the pressures around the ischial tuberosities and improved skin oxygenation, compared with the usual lifting techniques and decompression of the skin.[34]

Several investigators have studied the role of electrical stimulation in reducing ischial pressures and redistributing seating interface pressures, both of which might assist with pressure ulcer prevention.[35,36] In one study, it was shown that 8 weeks of chronic neuromuscular electrical stimulation delivered via an implanted neuroprosthesis significantly reduced interface pressure at the support/surface.[36] Electrical stimulation has been shown to change blood flow to skin and muscle, especially over bony prominences, where regional blood flow is adversely affected.[35,36] In a clinical study it was shown that 30 minutes of high-voltage pulsed galvanic stimulation (HVPGS) increased baseline transcutaneous oxygen tension ($TcPO_2$) levels by 35% in 29 subjects with spinal cord injury (SCI).[38] This finding is very important since maintaining skin oxygenation may prevent dermal breakdown. According to the above data there is evidence indicating that in patients with SCI, electrical stimulation may reduce ischial pressures, and increase blood flow at sacral and glutei areas. While the research data are optimistic, more randomized controlled clinical trials are necessary especially in ICU patient populations.

EFFECT OF ELECTRICAL STIMULATION IN PRESSURE ULCER HEALING

Electrical stimulation has been found to be effective in the promotion of wound healing and has been well documented since the 1940's, especially for wounds not responding to standard forms of treatment.[36,37,39] According to recently published clinical trials, systematic reviews and guidelines dealing with the healing of pressure ulcers (EPUAP) there is considerable first level documentation that electrical stimulation accelerates 3rd and 4th stage pressure ulcer healing, in conjunction with the usual ulcer care.[31,39-41] The possible mechanism which causes this effect is described above. Apart from facilitating healing time, increased collagen synthesis, increased wound tensile strength, increased rate of wound epithelization, and enhanced bactericidal effects,[36] electrical stimulation has also been shown to improve tissue perfusion and reduce edema formation, indirectly stimulating healing by improving oxygen delivery to the tissue.[42]

According to the literature, several types of electrical stimulation have been used for wound healing: low intensity direct currents (LICD) high voltage electrical stimulation (HVES), low frequency pulsed current (AS), interrupted direct current and other types. Low-intensity electric currents or micro currents are currents of an intensity less than or equal to 1 mA (1000 μA, μA = microampere). Because LIC resemble the current produced in wounds, several randomised clinical trials have been carried out to investigate whether this particular form of current may be beneficial for wound healing. A review paper revealed that both pulsed and continuous low intensity currents promote pressure sore and other wound type healing and appear to be effective in the range of 200–800 μA.[48] The authors conclude that further research is required in order to clarify the effects of LIDC on wound healing. HVPDC has also been used by the majority of studies with promising evidence. In a single blind study, it was found that high voltage electrical stimulation versus standard care that was applied in spinal cord injury patients with stage II to IV pressure ulcers resulted in a 50% greater healing proportion in the electrical stimulation group.[27] Similar results were reported in a retrospective case series study where high voltage electrical stimulation for 7-22 weeks resulted in complete healing of stage III-IV pressure ulcers in SCI patients.[42]

In a controlled clinical study,[31] it was found that HVPDC was effective in accelerating healing of pelvic pressure ulcers in subjects with SCI as compared with a placebo group. The subjects treated with HVPDC experienced a greater percentage reduction in wound surface area from day 5 to 20. In another study[32] it was found that the healing rate for wounds treated with low frequency pulsed current was significantly better from groups treated with direct current or standard treatment alone ($p=0.003$). Asymmetric biphasic stimulation[43] was found to be significantly more effective in ulcer healing than symmetrical biphasic electrical stimulation. Lastly, in another study[44] the application of interrupted direct current resulted in 22.6% decrease of stage IV pressure ulcer area compared to sham treatment.

Despite the differences of type and duration of current and the parameters used, it is obvious that electrical stimulation may accelerate the healing rate of pressure ulcers.[42] According to the currently available research data there is strong evidence to support the use of electrical stimulation of various types to accelerate the healing rate of stage III/IV pressure ulcers, when combined with standard wound management. However, more clinical studies are necessary in order to compare the efficacy of various types of electrical stimulation in pressure ulcer healing and determine the most effective form of treatment.

APPLICATION TECHNIQUE AND PARAMETERS OF ELECTRICAL STIMULATION

The types and parameters of electrical stimulation application vary from study to study. Despite the fact that there are a substantial number of research studies on wound healing, there is no comparison between types of electrical current in order to find which is the most effective one.[47] Still, various forms of currents, such as direct currents, pulsed direct currents, high or low voltage pulsed currents, alternative currents, and low-intensity currents (LIC) are available. It is therefore important to identify the most effective forms/parameters of currents, through randomized-controlled trials.[47] The most commonly used parameters of electrical stimulation for wound healing are outlined in Table 3.

Electrical stimulation is applied with surface electrodes. The negative electrode (active) is applied either at the side of the wound (Figure 2a) or directly on the wound surface in an impregnated gauze with normal saline (0.9% sodium chloride) (Figure 2b).

WIRELESS ELECTRICAL STIMULATION

Wireless micro current stimulation (WMCS) is a new type of electrical stimulation for wound healing where charged air gases are used to create and maintain the current to the wound, without any contact with the human tissue that may have advantages compared with conventional electrical stimulation devices (Fig. 3). In a recent study,[45] two case studies of diabetes-related wounds have been treated successfully using WMCS. The authors report that patients reported no discomfort during treatment, and the risk of infection was minimized because there was no direct contact with the device during the treatment course. In another case study, WMCS was applied to a patient with severe chronic leg ulcer, twice daily for 45 minutes, with an intensity of 1.5 μA, for a period of 6 weeks. Photography and wound area measurement were used in order to document wound healing progress. The ulcer was entirely healed after the 6-week period of therapy. Immuno-

TABLE 3. Parameters of Electrical Stimulation for Wound Healing.[48]

• Pulsed current
• Negative polarity
• Pulse duration: 100 μsec
• Frequency: 64-150 Hz
• Amplitude: 100-150 volts
• Duration: 60’
• Once daily, 5-7 times/week

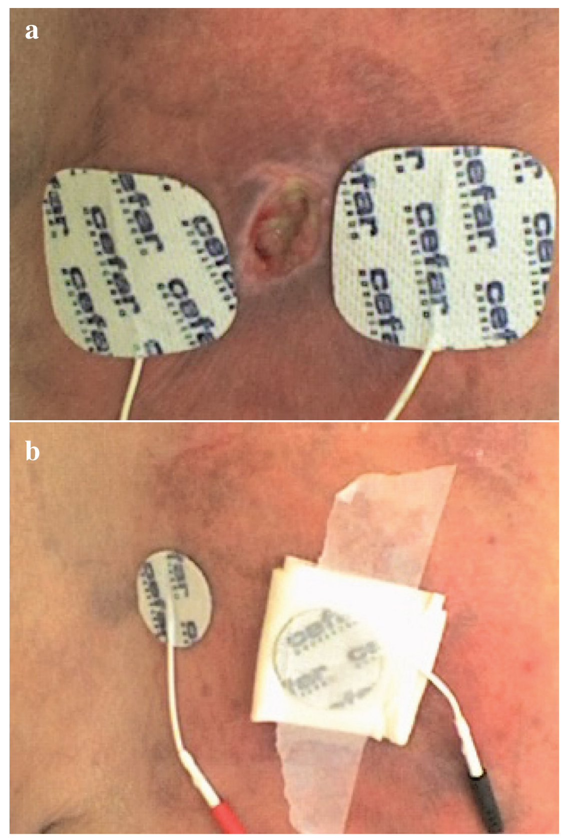

FIGURE 2. Application of electrical stimulation techniques a) adjacent of the wound, b) on the wound.

FIGURE 3. Application of wireless electrical stimulation in a sacral pressure sore.

histochemistry assays have illustrated abundance of thick collagen fibres and focal increase of mast cells. According to the authors, the rapid progress of wound healing in the above patient using WMCS seems very promising and the method indeed very effective.[46] According to the above data there is not enough evidence to substantiate the wide use of WMCS. However more research in this area is necessary.

3. FUNCTIONAL ELECTRICAL STIMULATION (FES)

Neuromuscular electrical stimulation creates passive contraction of skeletal muscles and can be used early after patient admission, without the need for patient participation in order to prevent skeletal muscle atrophy and ICU acquired weakness. Whereas there is need for further rigorous research on this area, functional electrical stimulation (FES) is just being introduced as an alternative form of NMES application in ICU early rehabilitation.[53] FES is different to NMES, as it recruits muscles in functional patterns (e.g., cycling, walking etc.) in order to stimulate them in a similar way to how the muscles would 'normally' contract under volitional control in healthy individuals. The majority of available literature on FES to date mainly involves neurological conditions, such as stroke[51] and spinal cord injury patients.[52] No research has been published so far investigating the effect of FES in ICU patients. Based on studies that have applied FES in a cycling activity in patients with SCI,[52] the published protocol of a randomized controlled trial[53] aims to investigate the effectiveness of functional electrical stimulation-assisted cycling and cycling alone compared to standard care, in 80 individuals with sepsis in the ICU. The aim of this trial is to examine the combined effect of FES-assisted cycling on muscle mass, strength, and physical function, and compare this with cycling alone, and standard physiotherapy in order to have a first indication of the effect of FES in ICU. The results of the study on muscle strength and physical function after ICU are expected in the near future.

CONCLUSIONS

NEMS has a clear role in ICU patients from their admission until their discharge from hospital. Firstly, there is strong evidence that NMES can prevent ICU acquired weakness as well as preserve muscle mass therefore preventing atrophy as presented above. Despite this promising research data more rigorous research must be carried out in order to investigate the long term effect of NMES on functional recovery of ICU survivors. Results from a trial in the USA are expected. [51] Secondly, according to the literature there is evidence to support the positive effectiveness of electrical stimulation of various types in the prevention and healing of pressure ulcers, not only by enhancing the endogenous mechanisms of wound closure, but also through muscle contractions that mediate skin pressure. Although these indications are promising, very few studies have been carried out to investigate the role of electrical stimulation in ICU pressure ulcers. Furthermore, since different types of electrical stimulation have been used by most studies, the optimum NMES parameters need to be clarified in future research. Despite that, it can be argued that NMES is a useful adjunct to standard care (e.g., positioning) for pressure ulcer healing and should be considered by physiotherapists during the daily treatment of their patients in ICU. Lastly, FES is a more functional NMES technique which has already been investigated in neurological patients (stroke, SCI, etc), has just merged in ICU research with results to be published and more studies to be conducted before firm conclusions can be drawn.

REFERENCES

1. Garnacho-Montero J, Madrazo-Osuna J, García-Garmendia JL, et al. Critical illness polyneuropathy: risk factors and clinical consequences. A cohort study in septic patients. *Intensive Care Med* 2001; 27:1288-1296.
2. Nanas S, Kritikos K, Angelopoulos E, et al. Predisposing factors for critical illness polyneuromyopathy in a multidisciplinary intensive care unit. *Acta Neurol Scand* 2008; 118:175-181.
3. De Jonghe B, Sharshar T, Lefaucheur JP, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. *JAMA* 2002; 288:2859-2867.
4. Fletcher SN, Kennedy DD, Ghosh IR, et al. Persistent neuromuscular and neurophysiologic abnormalities in long-term survivors of prolonged critical illness. *Crit Care Med* 2003; 31:1012-1016.
5. Bailey P, Thomsen GE, Spuhler VJ, et al. Early activity is feasi-

ble and safe in respiratory failure patients. *Crit Care Med* 2007; 35:139-145.
6. Morris PE, Goad A, Thompson C, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. *Crit Care Med* 2008; 36:2238-2243.
7. Bax L, Staes F, Verhagen A. Does neuromuscular electrical stimulation strengthen the quadriceps femoris? A systematic review of randomised controlled trials. *Sports Med* 2005; 35:191-212.
8. Celik EC, Erhan B, Gunduz B, Lakse E. The effect of low-frequency TENS in the treatment of neuropathic pain in patients with spinal cord injury. *Spinal Cord* 2013; 51:334-337.
9. de Oliveira Melo M, Aragão FA, Vaz MA. Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis - A systematic review. *Complement Ther Clin Pract* 2013; 19:27-31.
10. Vivodtzev I, Pepin JL, Vottero G, et al. Improvement in quadriceps strength and dyspnea in daily tasks after 1 month of electrical stimulation in severely deconditioned and malnourished COPD. *Chest* 2006; 129:1540-1548.
11. Quittan M, Wiesinger GF, Sturm B, et al. Improvement of thigh muscles by neuromuscular electrical stimulation in patients with refractory heart failure: a single- blinded, randomized, controlled trial. *Am J Phys Med Rehabil* 2001; 80:206-214.
12. Zanotti E, Felicetti C, Maini M, Fracchia C. Peripheral muscle strength training in bed-bound patients with COPD receiving mechanical ventilation: effect of electrical stimulation. *Chest* 2003; 142:292-296.
13. Nuhr MJ, Pette D, Berger R, et al. Beneficial effects of chronic low- frequency stimulation of thigh muscles in patients with advanced chronic heart failure. *Eur Heart J* 2004; 25:136-143.
14. Wiesinger GF, Crevenna R, Nuhr M, Huelsmann M, Fialka-Moser V, Quittan M. Neuromuscular electric stimulation in heart transplantation candidates with cardiac pacemakers. *Arch Phys Med Rehabil* 2001; 82:1476-1477.
15. Gerovasili V, Tripodaki E, Karatzanos E, et al. Short-term systemic effect of electrical muscle stimulation in critically ill patients. *Chest* 2009; 136:1249-1256.
16. Gerovasili V, Stefanidis K, Vitzilaios K, et al. Electrical muscle stimulation preserves the muscle mass of critically ill patients: a randomized study. *Crit Care* 2009; 13(5):R161.
17. Routsi C, Gerovasili V, Vasileiadis I, et al. Electrical muscle stimulation prevents critical illness polyneuromyopathy: a randomized parallel intervention trial. *Crit Care* 2010; 14(2):R74.
18. Karatzanos E, Gerovasili V, Zervakis D, et al. Electrical muscle stimulation: an effective form of exercise and early mobilization to preserve muscle strength in critically ill patients. *Crit Care Res Pract* 2012; 2012:432752.
19. Gruther W, Kainberger F, Fialka-Moser V, et al. Effects of neuromuscular electrical stimulation on muscle layer thickness of knee extensor muscles in intensive care unit patients: a pilot study. *J Rehabil Med* 2010; 42:593-597.
20. Poulsen JB, Moller K, Jensen CV, Weisdorf S, Kehlet H, Perner A. Effect of transcutaneous electrical muscle stimulation on muscle volume in patients with septic shock. *Crit Care Med* 2011; 39:456-461.
21. Rodriguez PO, Setten M, Maskin LP, et al. Muscle weakness in septic patients requiring mechanical ventilation: Protective effect of transcutaneous neuromuscular electrical stimulation. *J Crit Care* 2012; 27(3):319.e1-8.
22. Meesen RL, Dendale P, Cuypers K, et al. Neuromuscular electrical stimulation as a possible means to prevent muscle tissue wasting in artificially ventilated and sedated patients in the Intensive Care Unit: A Pilot Study. *Neuromodulation* 2010; 13:315-321.
23. Kanof N. Gold leaf in the treatment of cutaneous ulcers. *J Invest Dermatol* 964; 3:441-444.
24. Wolf M, Wheeler P, Wolcott L. Gold-leaf treatment of ischemic skin ulcers. *JAMA* 1966; 196:105-108.
25. Kloth LC. Electrical Stimulation for wound healing: A review of evidence from in vitro studies, animal experiments, and clinical trials. *Lower Extr Wounds* 2005; 4:23-44.
26. Huttenlocher A, Horwitz AR. Wound healing with electric potential. *N Engl J Med* 2007; 18; 356:303-304.
27. Houghton P, Campbell K, Fraser C, et al. Electrical stimulation therapy increases rate of healing of pressure ulcers in community-dwelling people with spinal cord injury. *Arch Phys Med Rehabil* 2010; l:91.
28. Woodbury MG, Houghton PE, Campbell KE, Keast DH. Pressure ulcer assessment instruments: a critical appraisal. *Ostomy Wound Manage* 1999; 45:42-5, 48-50, 53-5.
29. Ojingwa JC, Isseroff RR. Electrical stimulation of wound healing. *J Invest Dermatol* 2003; 121:1-12.
30. Sussman C. Managing wound care. Utilization management ensures optimal clinical outcomes. *Rehab Manag* 1998; 11:40-41.
31. Griffin JW, Tooms RE, Mendius R: Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. *Phys Ther* 1991; 71:433-444.
32. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2.Value of FES parameters for pressure sore treatment. *Med Biol Eng Comput* 1993; 31:213-220.
33. Reilly E, Karakousis G, Schrag S, Stawicki S, Pressure ulcers in the intensive care unit: The 'forgotten' enemy, *OPUS 12 Scientist* 2007; 1:17-30.
34. Solis L, Gyawali S, Seres P, et al. Effects of intermittent electrical stimulation on superficial pressure, tissue oxygenation, and discomfort levels for the prevention of deep tissue injury. *Ann Biomed Eng* 2011; 39:649-663.
35. Bogie KM, Wang X, Triolo RJ. Long-term prevention of pressure ulcers in high-risk patients: A single case study of the use of gluteal neuromuscular electric stimulation. *Arch Phys Med Rehabil* 2006; 87:585-591.
36. Bogie KM, Triolo RJ. Effects of regular use of neuromuscular electrical stimulation on tissue health. *J Rehabil Res Dev* 2003; 40:469-475.
37. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current. *Phys Ther* 1988; 68:503-508.
38. Mawson AR, Siddiqui FH, Connolly BJ, et al. Effect of high

voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. *Paraplegia* 1993; 31:311-319.
39. Bogie KM, Reger SI, Levine SP, Sahgal V. Electrical stimulation for pressure sore prevention and wound healing. *Assist Technol* 2000; 12:50-66.
40. Sosa IJ, Reyes O, Kuffler DP. Elimination of a pressure ulcer with electrical stimulation--a case study. *P R Health Sci J* 2008; 27:175-179.
41. Regan MA, Teasell RW, Wolfe DL, Keast D, Mortenson WB, Aubut J. A systematic review of therapeutic interventions for pressure ulcers following spinal cord injury. *Arch Phys Med Rehabil* 2009; 90:213-231.
42. Recio AC, Felter CE, Schneider AC, McDonald JW. High-voltage electrical stimulation for the management of stage III and IV pressure ulcers among adults with spinal cord injury: demonstration of its utility for recalcitrant wounds below the level of injury. *J Spinal Cord Med* 2012; 35:58-63.
43. Houghton PE, Campbell KE. Therapeutic Modalities in the treatment of chronic recalcitrant wounds. In: Krasner; Rodheaver; Sibbald, editors. *Chronic Wound Care: A clinical source book for health care professionals.* 3. Wayne, PA: Health Management Publications Inc; 2001.
44. Adegoke BO, Badmos KA. Acceleration of pressure ulcer healing in spinal cord injured patients using interrupted direct current. *Afr J Med Med Sci* 2001; 30:195-197.
45. Ramadhinara A, Poulas K. Use of wireless microcurrent stimulation for the treatment of diabetes-related wounds: 2 case reports. *Adv Skin Wound Care* 2013; 26:1-4.
46. Castana O, Dimitrouli OA, Stampolidis N, et al. Clinical Application of wireless microcurrent electrical stimulation for wound healing, *Wound Rep Reg* 2012; 20:A87-A121
47. Prentice WE. *Therapeutic Modalities in Rehabilitation*. 3rd ed. New York: McGraw Hill; 2005.
48. Balakatounis C, Angoules A. Low-intensity electrical stimulation in wound healing: review of the efficacy of externally applied currents resembling the current of injury. *Eplasty* 2008; 8:e28.
49. Franek A, Kostur R, Polak A, et al. Using high-voltage electrical stimulation in the treatment of recalcitrant pressure ulcers: results of a randomized, controlled clinical study. *Wound Manage* 2012; 58:30-44.
50. Kho ME, Truong AD, Brower RG, et al. Neuromuscular electrical stimulation for intensive care unit–acquired weakness: protocol and methodological implications for a randomized, Sham-controlled, phase II trial. *Phys Ther* 2012; 92:1564-1579.
51. Robbins SM, Houghton PE, Woodbury MG, et al. The therapeutic effect of functional and transcutaneous electrical stimulation on improving gait speed in stroke patients: a meta-analysis. *Arch Phys Med Rehabil* 2006; 87:853-859.
52. Hamzaid NA, Davis GM. Health and fitness benefits of functional electrical stimulation-evoked leg exercises for spinal cord injured individuals: a position review top spinal cord. *Inj Rehabil* 2009; 14:88-121.
53. Parry SM, Berney S, Koopman R, et al. Early rehabilitation in critical care (eRiCC): functional electrical stimulation with cycling protocol for a randomised controlled trial. *BMJ Open* 2012; 2:e001891. doi:10.1136/bmjopen-2012-001891