Chronic refractory myofascial pain: Characteristics of patients who self-select long-term management with Electrical Twitch-Obtaining Intramuscular Stimulation

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Chronic refractory myofascial pain: Characteristics of patients who self-select to undergo long-term management with Electrical Twitch-Obtaining Intramuscular Stimulation

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Abstract

Introduction: Noninvasive Electrical Twitch-Obtaining Intramuscular Stimulation (eToims) is safe and efficacious in long-term management of chronic refractory myofascial pain (CRMP).

Objective: To evaluate factors influencing patient self-selection for long-term eToims management of CRMP.

Methods and materials: Included were 133 consecutive CRMP patients (65 males, 68 females) who opted to pay for eToims treatments between 12/1/09 and 12/31/11. Each session involved treatment to large muscles of C3-C7 and L3-S1 myotomes. Outcome measures include immediate pre&post-treatment session visual analogue scale (VAS), symptomatic (**S**) and asymptomatic (**A**) side range-of-motion (ROM): for neck rotation (NR), shoulder external rotation (ER), shoulder internal rotation (IR), straight leg raising (SLR) and FABERE (FAB). Analysis performed by grouping results as follow: Group0: <=10 treatments and immediate reduction of VAS<2; Group1: <=10 treatments and immediate reduction of VAS>=2; Group2: >10 treatments and immediate reduction of VAS<2; and Group3: >10 treatments and immediate reduction of VAS>=2. Safety precautions include interval history and vital signs before and after treatment.

Results: Groups 0& 1 comparison showed no measured ROM difference. Group 3&Group 2 comparison demonstrated shorter interval between treatments (15$\pm$47 vs. 138$\pm$167 days respectively, $p<0.001$), longer treatment duration/session (52.0$\pm$26.0 vs. 49.0$\pm$22.0 minutes, respectively), and immediate improvement in all ROM measured. Group3 pain relief appears influenced by age, symptom duration, treatment duration/session, pulse reduction and improvement in ROM. No eToims-associated safety issues noted.

Conclusions: Safe and efficacious pain relief with concomitant immediate improvement in ROM and pulse rate reduction correlates with patient satisfaction and self-selection to return for multiple eToims treatments over time.

Keywords: chronic refractory myofascial pain, Electrical Twitch-Obtaining Intramuscular Stimulation (eToims), safety and efficacy, range of motion, pain relief, new non-invasive treatment for pain relief

INTRODUCTION

Patients with myofascial pain syndrome present with painful muscles, which tend to restrict the range of motion of the joint upon which they act. Tender points on palpable taut muscle bands, that when compressed produce stereotypical referred pain patterns, are named myofascial trigger points (MTrPs). On physical examination MTrPs are the main and pathognomonic finding of myofascial pain syndrome. Snapping palpation of the myofascial band also produces a local twitch response.[1] MTrPs merit special attention because eliciting local twitch response and referred pain requires skill and experience, with difficulty in reproducibility. Currently, meta-analysis suggests that physical examination cannot be recommended as a reliable test for the diagnosis of trigger points, based on limited number of available studies, along with concurrent problems in their design, reporting, statistical integrity, and clinical applicability.[2] Additionally, deeper MTrPs appear beyond the reach of manual palpation, especially those involving huge muscles of the pelvic girdle, such as gluteus maximus and adductor magnus, or in other similar deeply situated and/or large muscles.

With eToims, MTrPs are located and identified by electrical stimulation.[3] Classic motor point definition describe these points as areas requiring the shortest duration pulse widths with least stimulus intensity for muscle contraction, i.e., twitch elicitation. Consequently, using this principle, when twitches can be evoked, identification of MTrPs becomes more objective, enabling the twitch in myofascial pain syndrome to be diagnostic and, at the same time, therapeutic. Twitch force, firing pattern, characterization of elicitation (ease or difficulty) provide quantifiable and reproducible identification of MTrPs. MTrP identification and localization has become standardized as the area where the twitch force produces a palpable

recoil effect on the hand holding the twitch-eliciting probe. Deeper MTrPs are identified when twitches, from the stimulated muscle, produce on the joint upon which it acts, discernible movement, ranging from rocking/shaking to actual movement of the joint, even in an anti-gravity direction. Anti-gravity movement of the limb indicates full contraction of stimulated muscle(s) apposed to bone and joint, in contrast to partial or fractional contraction of said same muscle(s) from ineffective or distant stimulation of involved MTrPs.

With awareness of the high incidence of myofascial pain syndrome in the general population[4], to develop safe and efficacious methods for long-term management of chronic refractory myofascial pain, leads one to consider this pain's mediate cause.

The integrated hypothesis of Travell and Simons for MTrP formation suggests that muscle trauma, overload, or strain causes damage to the endplate, which results in release of excessive acetylcholine (Ach). This causes a local, partial contraction of a muscle fiber beneath the endplate. Muscle fiber contracture leads to ischemia and pain.

Myofascial pain, as postulated by Gunn, is caused by spondylotic radiculopathies in which pain arises from mechanical traction of muscle fibers, shortened by denervation, causing intramuscular entrapment of nerves and blood vessels and a tension effect on pain sensitive regions, such as annulus fibrosus, bones and joints.[5] Others have also found MTrPs in radiculopathies.[6] Intravertebral disc degeneration, with nerve root compression or angulation due to reduced intravertebral space, results in paraspinal muscle spasm. This causes a neuropathy, leading to distal muscle spasm in the distribution of the nerve root and contributes to another degenerative changes in tendons and ligaments within its distribution, that ongoing muscle shortening overall self-perpetuates.[7]

Gunn's postulated muscle traction effects, secondary to denervation, constitutes one instance and, possibly, the major instance of how, in the theory of Travell and Simons, initial muscle injury can result from excessive release of ACh. Another mechanism by which muscle fibers become shortened involves denervation supersensitivity to Ach, which develops within two weeks of denervation.[8] Increase in ACh receptors at extrajunctional areas and decrease in acetylcholinesterase activity contribute to the phenomenon of denervation supersensitivity.[9] Additionally, denervation supersensitivity can occur in muscles subjected to prolonged conduction block.[10] Muscle fiber shortening compresses small blood vessels and the tissue becomes ischemic. Ischemia leads to bradykinin release and sensitization or excitation of nociceptors.[11] Reflex spasm in a given muscle can be induced by nociceptive input from neighboring joints or muscles. If the force generated by a spasm is relatively high, it will compress large blood vessels supplying the involved muscle, causing more ischemia. This can lead to a drop in pH. The resulting acidic environment, as well as bradykinin and other neurochemical release in conditions attributed to hypoxia and ischemia, are known stimulants for muscle nociceptors, resulting in myofascial pain.[12] Impaired regulation of the microcirculation in a local muscle is of central importance in chronic trapezius myalgia, causing nociceptive pain, which can be objectively differentiated from neuralgic neck-shoulder pain.[13]

Hypothesized is that eToims, through twitch elicitation, stretches problematic tight and shortened muscle fibers, thereby reducing traction effects on pain sensitive structures, such as entrapped intramuscular nerves and blood vessels, bone surfaces and joint capsules. Within muscles, twitch-induced exercise effects promote local blood flow, improving microcirculation, tissue

oxygenation, and removing local accumulation of pain-producing neurochemicals, which either individually or taken together promote healing of MTrPs.

Receiving eToims at our facility involves fee-for-service in which a patient self-selects affordable treatment session duration, intersession interval (time between sessions), total number of sessions, determining time period over which treatments provided, that met the individual's need. Some become and stay pain-free or sufficiently pain-relieved to discontinue treatments and those who do not feel sufficient pain relief also do not return for more treatments early on. Other patients self-select treatment over significant periods of time. This latter group is the subject of this study. We aim to demonstrate that patients who self-select repeat eToims treatment sessions over prolonged periods of time, do so because of receiving pain-relieving results, indicating patient satisfaction. One common outcomes measure in chronic neck and lower back pain assessment is measurement of range of motion.[14,15] We intend to demonstrate that eToims effectiveness is partly due to reduction of muscle tightness and stiffness, related to internal stretching of problematic tight and shortened muscle fibers at MTrPs, shown by pain relief and improvement in range of motion.

METHODS AND MATERIALS

Longitudinal prospective observation was performed on consecutive outpatients with CRMP who gave informed consent and were treated between 12/1/09 to 12/31/11. Included patients had classical MTrPs. These patients requested eToims treatments and self select to pay for treatments since they had no appreciable pain relief from multiple treatments that involved medications including opioids, physical therapy and chiropractic treatments, psychological

support, spinal injections, neck and lower back surgeries. Patients were not excluded even when MRI scan studies showed various degrees of degenerative spinal conditions including central or foraminal spinal stenosis. Patients included also had symptoms and signs of chronic partial multiple spinal nerve root involvement documented on electromyography. The symptom durations ranged from 12-72 months. VAS levels range from 2-7/10 with a mean pain level of 3-4/10.

Treatments were performed using the CE approved ET127 constant current evoked response stimulator with bipolar probe (eToims Medical Technology LLC, PA, USA). The bipolar probe uses non-allergenic and biocompatible specially designed proprietary single use, disposable electrodes that are 100% cotton. The electrodes consist of a plug electrode (1.6 x 3.0 cm) placed inside each receptacle of the bipolar probe stem and covered with a pad electrode with a stimulating surface of 5 cm and draped over to be fastened to each probe stem with latex free Velcro straps. The electrodes are wetted with tap water for conduction purposes. The probe has an adjustable inter-electrode distance, up to 6". Treatments were performed with probe inter-electrode distance set at 6", stimulus rate of 1 Hz with 0.2-0.5 ms pulse width, with stimulus strength adjusted from 40-80 mA and titrated according to both the size of the muscle and patient tolerance to electrical stimulation, to elicit twitch force sufficient to enable therapeutic effect.

Routinely treated were muscles of bilateral cervical myotomes: levator scapulae (**C3**, C4), trapezius (C3, **C4**), rhomboid major (**C5**), deltoid (C5, **C6**), triceps (**C7**, C8) and latissimus dorsi (C6, **C7,** C8). Routinely treated for bilateral lumbosacral myotomes include: gluteus maximus (L5, **S1**), gluteus medius and tensor fascia latae **(L5**, S1), adductor magnus (L2-S1), and quadriceps (L3, **L4**). Also treated were bilateral paraspinal muscles from C4 - S1 levels. The

principle of treatment involves finding irritable MTrPs that, when stimulated, elicit brisk, rapid twitch contractions at a stimulus intensity tolerated by the patient, that cause, the joint upon which the stimulated muscle acts, to at least shake or rock. To locate such MTrPs, the least stimulus intensity with the shortest duration pulse, sufficient to stimulate the classic motor point definition for muscle contraction, i.e., twitch elicitation, was utilized and then titrated to obtain supramaximal stimulation, within patient tolerance, applied with its muscle positioned at a slight stretch.

Once an initial twitch is noted, the probe has to be carefully positioned with 0.5-1 cm movements to obtain the point that elicits the most forceful twitch. When the most brisk and vigorous twitch is elicited, repetitive re-stimulation is performed in that zone with 1-4 stimuli at each stimulus point to obtain at least 20 twitches in this affected zone. The twitches mobilize muscle tissues such that constant repositioning of the probe has to be done to recapture and focus the stimulation onto the MTrP. In chronic pain, the search for such twitch zones is very difficult and if other areas do not provide therapeutic twitches, the best zone is re-stimulated to elicit at least 100-200 twitches.

Muscles treated in all patients included the paraspinal muscles from the neck to the lumbosacral region. Trapezius and latissimus dorsi were always included in the treatment for those with cervical problems. For those with lower back problems, gluteus maximus and adductor magnus muscles were always included in the treatment. For those with total body pain, the spinal muscles and these four large muscles were always treated.

The total treatment time varies from 30-60 minutes depending on the session time requested by the patient. The time spent on each important muscle is dependent on the treatment session time requested. The clinician has to be skillful enough to be able to give pain relief with every treatment even when the treatment session time is short, by treating only the important muscles relevant to the patient's pain site.

A count-down timer in the ET127 system terminated the treatment session after sounding a warning audio signal during the last five seconds. Patients were usually positioned in supine, prone, side-lying and opposite side-lying positions during treatment to enable finding MTrPs. Search for these MTrPs was difficult in muscles that were chronically stiff or tight.

Outcomes data include pre- and immediate post-session patient VAS report (with maximum pain: 10/10), blood pressure (BP), pulse (P), symptomatic (**S**) and asymptomatic side (**A**) range of motion (ROM) measurement for neck, shoulders and lower limbs. We used ROM parameters measured in centimeters (cm) that include: NR (neck rotation) measured distance between middle of the chin to the ipsilateral acromioclavicular joint; ER (external rotation of shoulder) measured distance between tip of middle finger of tested side to contralateral angle of the mouth, when the tested upper limb is externally rotated, flexed at shoulder and elbow, and the patient places the tested limb behind the neck, with forearm in pronation (the examiner must keep the patient's head straight in the midline, with chin parallel to the floor); IR (internal rotation of the shoulder) measured distance between the tip of the middle finger of the tested side to the contralateral midpoint of the spine of the scapula, when the tested upper limb is extended and adducted at the shoulder, with elbow flexed behind the trunk and forearm in supination; and FAB

(for FABERE which tests patient's ability to flex, abduct and externally rotate each hip) measuring vertical distance between the most lateral knee flexion crease of the tested side to the surface of the bed, when the tested side heel is placed above the superior border of the contralateral patella. The other ROM parameter measured utilizes degrees, SLR (straight leg raising test), the angle between the surface of the bed and the plane bisecting the middle of the thigh and the leg.

Two medical assistants trained in eToims and supervised by the attending physician performed patient observation for untoward or adverse condition immediately pre-, during and post-treatment, obtained immediate pre- and post-treatment range of motion measurements, obtained patient determined VAS, obtained patient blood pressure (BP) pulse (P) measured with Omron Automatic BP Monitor (Kyoto, Japan), taken immediately pre- and post-treatment (three times each and then the mean determined by the device). Additionally, before beginning an eToims treatment session, a pertinent history of interval from last treatment was obtained. Pertaining to the interval between treatment sessions, patients were encouraged to contact us if anything that appeared medically aberrant and worrisome was experienced; otherwise, upon return for treatment, they were encouraged to bring to attention any health status change, change in symptom or sign that occurred. Pertaining to patient safety, decision to initiate, continue a given treatment session or provide following treatment sessions was supervising physician-based, utilizing the preceding information. If safe, while patients advised per condition/status to return weekly or longer for eToims treatments, as paying out-of-pocket, essentially the patients determined the treatment interval and total duration they chose to remain under treatment. Consequently, herein lies the traditional ethical medical relationship: physician advice, patient

consent. Regarding whatever prescription medications the patients were routinely taking before beginning a course of eToims treatment, they were advised to continue throughout the course of eToims therapy. Only two patients in Group 2 were on long-term opioids for pain control.

Data analysis was performed with patients' recorded data classified into Group 0 (those with <=10 treatments and immediate reduction of VAS<2); Group 1 (those with <=10 treatments and immediate reduction of VAS>=2); Group 2 (those with >10 treatments and immediate reduction of VAS<2 pain scales and Group 3 (>10 treatments and immediate reductions of VAS>=2). Analysis of pain reduction over the course of the treatment was performed by determining the average VAS gain by taking into account pre-treatment and post-treatment VAS levels throughout the course of the treatment to the VAS at the time when the patient decided not to return for further treatment or when the observational period was terminated.

RESULTS

Patients, who returned for multiple treatments over time, kept to a regular treatment schedule and rarely missed appointments they made. Patient characteristics are presented in Table 1. Of the 133 patients, 68.4% experienced trauma, 10.5% had spinal stenosis, 7.5% had previous spinal surgery, and 13.5% had miscellaneous causes of muscle pain. The primary site of pain in study patients with <=10 treatments was the neck in 46 patients and lower back in 47 patients. The primary site of pain in patients with >10 treatments was the neck in 19 and lower back in 21 patients. Of the 133 patients, 92 (69%) received <=10 treatments and 41 (31%) received >10 treatments.

Results showed no significant difference for all ROM between Groups 0 and 1 using analysis of variance (ANOVA). Comparing the means between Groups 2 and 3, all ROM parameters measured were significantly better for Group 3 (Table 2). VAS reduction over time as well as immediate treatment related VAS changes were significantly more for Group 1 than Group 0. Group 3 compared to Group 2 showed more immediate VAS reduction ($p=<0.01$), but no difference in VAS over time.

Multinomial logistic regression analysis showed that immediate VAS improvement was significantly influenced by age ($p<0.01$), duration of symptoms ($p<0.01$), treatment duration/session ($p<0.05$), pulse differences ($p<0.01$) and ROM improvement ($p<0.001$).

Pearson correlation (Table 3) showed that in Group 3, the number of treatments negatively correlates with immediate systolic BP and pulse reduction as well as improvement of ROM. In Group 2, negative correlation was found for immediate systolic and diastolic BP changes, SLR**A** and FAB**S**. No correlations were noted for Groups 0 and 1 with any of the ROMs or vital signs measured.

Mild reductions in systolic and diastolic BP were noted in Groups 2 and 3 and mild elevations of both systolic and diastolic BP were noted in Groups 0 & 1 (Figures 1 & 2 and Table 2). Pulse reduction was seen across all 4 Groups (Figure 3 and Table 2), especially in Group 3.

SPSS program for Windows (version 12) was used for statistical analyses.

There were no patient adverse events during, immediately after or between treatments.

DISCUSSION

As noted, despite being a new treatment, the eToims treatment model is based upon traditional medical ethics of physician advice-patient consent. As patients paid out-of-pocket, direct involvement of patient pocket appears to provide a direct, strong incentive for patient active involvement in this relationship. Yet, that relationship could not be maintained over time without patient perception of accruing benefit from consenting to treatment. This helps explain strong patient involvement, demonstrated by regularly keeping eToims treatment appointments. Essentially, the rest of this discussion helps put this patient gain in perspective.

Many methods are available to directly treat MTrPs. These involve needling methods, such as acupuncture, dry needling and local injections that involve water, saline, local anesthetics, steroids or Botox to inactivate, disrupt or suppress of MTrP activity. Meta-analysis has not shown treatments with Botox[16], acupuncture or dry needling of MTrPs[17] to be effective. Additionally, due to safety concerns none of these methods can be used repetitively or frequently to the same MTrPs, other MTrPs in the same vicinity or to multiple MTrPs, during the same session or with multiple treatment sessions applied throughout the body on a long-term basis during the lifetime of the chronic pain patient.

The common theme in physical therapy techniques used in treating MTrPs include stretching, yet little is known about effectiveness of stretching or ways to enhance its effectiveness. Methods that include stretching, such as spray and stretch technique, when used together with hot packs, active range of motion exercises and interferential current or TENS have been found helpful. Similarly found helpful in treating MTrPs is post-isometric relaxation technique that restores the full stretch length of the muscle; and a home program, consisting of ischemic pressure and

sustained stretching in individuals with neck and upper back pain. In athletes, stretching does reduce the incidence of new onset soreness, but does not appreciably reduce overall injury risk, although it may reduce the risk of some injuries.

On the contrary, stretching for three weeks has not demonstrated effectiveness in improving muscle extensibility in patients with chronic musculoskeletal pain, although it increases tolerance to the discomfort associated with stretch.[18] A meta-analysis of randomized studies suggests that muscle stretching, whether conducted before, after, or before and after exercise, does not produce clinically significant reduction in delayed-onset muscle soreness in healthy adults.[19] When muscles such as hamstrings are stiff and subjected to eccentric exercise, strength loss, pain, muscle tenderness, and increased creatine kinase activity occurs. This is consistent with the sarcomere strain theory of muscle damage showing experimental evidence of association between flexibility and tendency to muscle injury. [20]

These studies have shed light on the effects and limitations of mechanical stretching, confined to stretchable muscles, which usually are superficial. The solution to make stretching consistently more effective may lie in finding new methods that include non-invasive electrical stimulation procedures, such as eToims, to effectively exercise and mobilize deep muscle tissues at stretchable areas, particularly those with injured MTrPs. Morphologic and electromyographic studies have demonstrated atrophy and delayed activation of the deep muscles of the spine in patients with chronic neck pain [21] and chronic lower back pain.[22] Decrease in maximum force of the deep back muscles, such as multifidus, interspinales, intertransversarii, rotatores, iliocostalis, longissimus, psoas, and quadratus lumborum, increase resultant joint moments and reduce the stabilization function provided by these muscles to the lumbar spine.[23] This leads one to

postulate that strengthening deep muscles by electrical stimulation-evoked twitches that exercise muscles, might reduce the possibility of injury and pain in the lumbar spine.

eToims supports the hypothesis that spondylotic radiculopathy with denervation supersensitivity is the underlying cause of myofascial pain.[5] Consequently, denervation and/or conduction block leads to formation of MTrPs in many myotomes. eToims electrically excites MTrPs, eliciting twitches that not only mobilize deep muscles, but through this mechanism, simultaneously enable intramuscular stretch therapy to relax shortened deep muscles in spasm, that otherwise are not ordinarily able to be stretched or exercised, especially in the presence of pain. Ability of eToims to stretch individual deep muscles of limbs and spine leads to reduction of traction effects on pain sensitive structures, such as entrapped intramuscular nerves and blood vessels, bone surfaces and joint capsules. eToims also performs as a local, focused intramuscular exercise therapy that improves circulation to affected areas. Experiments on rat skeletal muscles have shown that twitch contractions from stimulation with 1 Hz increase muscle blood flow by 240%.[24]

Our prospective longitudinal study has shown eToims to be effective in reducing myofascial pain with concomitant improvement in range of motion. This appears related to its unique advantage, to cause intramuscular stretching at involved MTrPs, where spasm and/or muscle fiber shortening is most concentrated. This includes those MTrPs in the deepest muscles layers apposed to bone and joints. The eToims ability to perform internal stretch resulting in deep muscle relaxation provides increased capacity for these deep muscles to withstand activity-related pain-producing spasms/muscle shortening that occurs at various times of the day, on a daily basis in those with chronic pain.

Massage is reported to reduce myalgia symptoms and has been shown to reduce systolic and diastolic BP and pulse rate, attributed to the ability of massage to increase parasympathetic tone and inhibit sympathetic tone.[25] eToims provides state-of-the-art massage, with ability to mobilize deep tissues apposed to bone and joint that manual massage appears unable to mobilize. eToims has additional capacity to perform active exercise, through non-injurious twitch contraction and relaxation of muscles, through stimulation of MTrPs that elicit twitches, especially involving the deepest muscles.

With our present study, we have shown that >10 treatments and associated improvement in multiple range of motion measures is needed to consistently decrease systolic and diastolic BP, even if there is <=2 VAS pain reduction. When improvement in range of motion does not occur, pain during treatment may result in increase in augmenting sympathetic tone with mild increase in systolic and diastolic BP, as noted in Groups 0 & 1 (Fig 1, 2 and Table 2). Therefore, although pulse reduction is common with eToims treatment, the mild increase in systolic and diastolic BP in Groups 0 & 1 may not be a compensatory effect of pulse reduction, but rather related to stimulation of nociceptors in tight muscles, even though MTrP stimulation appears totally painless. The fact that Groups 2 & 3 exhibited greater pulse rate reduction and, yet, simultaneously showed systolic and diastolic BP reduction, are likely caused by inhibition of sympathetic tone.

Presented findings confirm our previous work that eToims reduces pulse rate, probably with most consistent underlying mechanism involving stimulation of the parasympathetic nervous system.[3] This may be related to simultaneous stimulation of the vagus nerve upon stimulating

trapezii and other neck muscles. Furthermore, vagus nerve stimulation has been known to reduce pain. [26,27] From a slightly different perspective, pain is a known physiologic stressor. Consequently, based on this, if increase in pain tends to increase pulse, then decrease in pain tends to decrease pulse, essentially consistent with pulse finding over time found with eToims treatment, regardless of whether a VAS reduction of equal to or greater than 2 levels was noted.

It is commonly accepted on a VAS pain scale, with maximum pain level reported up to 10/10, that VAS reduction of at least 2 levels is needed in order to adequately assess response to treatment and that caution should be exercised when applying these findings to studies with periods of observation longer than 12 weeks.[28] Consequently, with caution this method of assessment was used to analyze findings in this longitudinal study that recruited patients over 24 months. However, as treatment continued over long duration, this method of assessment requiring >=2 pain scale reductions was not found applicable, especially when assessing pain immediately after treatment, since a negative correlation with number of treatments appeared, as shown in Group 3 (Table 3). Over time we noted that the number of treatments appears important, in terms of patient satisfaction with treatment. As patients self-select to pay for ongoing treatment, then ultimately the patient determined the number of treatments, and, as a consequence, this led to adoption of this parameter as an important factor to analyze patient satisfaction with eToims treatment over time. Patients who returned for multiple treatments over time even though immediate pain reduction was < 2 grades as in Group 2, indicated that requiring VAS decrease at least 2 levels appears an arbitrary and subjective and possibly faulty indicator for measurement of pain relief and/or patient satisfaction with treatment for pain. The potential importance of number of treatments over time for demonstrating patient satisfaction

becomes clearer since there is no significant difference between VAS reduction over time between Groups 2 and 3, as shown in Table 3.

Chronic pain patients not only do not exhibit continued or incremental improvement in ROM and pain reduction with increasing number of treatments, they show less immediate improvement after a treatment. Among main reasons that Group 3 patients continue to return for ongoing treatment is because they do experience immediate pain reductions >=2 grade levels and immediate improvement in ROM results with each treatment, compared to their immediate pre-treatment status. Since eToims mainly provides painless, pleasant, pain relieving and active aerobic exercise, that concomitantly provides some improvement in ROM, the role of endorphin release associated with such exercise, from MTrP stimulation, may also explain why patients return for repeat treatment over prolonged duration.

The inability of chronic pain patients to continue to progressively improve with increasing number of treatments possibly appears related to difficulty in locating/stimulating all involved MTrPs. This is probably due to a combination of significant tightness or stiffness of overlying muscles in the presence of activity dependent hypo-excitability with axonal hyperpolarization. Activity related fluctuation of symptoms in CRMP is common. This may result from transient conduction block. Even natural activity results in substantial hyperpolarization of active axons and, for similar discharge rates, the degree of hyperpolarization is greater in motor axons than cutaneous afferents.[29]

There is potential for increased susceptibility of MTrPs in chronic pain patients for further trauma, induced by violent muscle contractions, as well as by new injuries that include falls, lifting injuries, auto accidents, exercise, or even repetitive contractions associated with activities of daily living. These injuries tend to keep chronic pain patients in a constant state of ongoing pain. The inability of chronic pain patients to continue to exhibit progressive, cumulative increase in immediate improvement in range of motion and progressive, cumulative immediate and/or dramatic pain reduction with increasing number of treatments may also be related to reduced efficiency of reciprocal inhibition. This results in delayed and incomplete muscle relaxation following exercise, disordered fine movement control, and unbalanced muscle activation.[30] Increased capacity for re-injury, need for pain relief and/or need for increased range of motion explains why patients self-select to remain in eToims therapy for long periods. At least, patient needs appear transiently met with repeat treatment, until patient self-selects next treatment. If the patient's condition is not severe, mild exercise under eToims supervision may be beneficial.

Although potential bias was inadvertently introduced in observations because treatments were not randomized, controlled or double blinded, our prospective longitudinal observations confirm that non-invasive eToims has pain relieving effects that appear safe and efficacious. Although observations were only made on patients who self-paid for their treatments, this cohort included patients in significant pain, unable to be alleviated by traditional methods, including physical therapy, multiple medications and spinal surgery. These patients self-paid for multiple treatments with eToims over time due to experience of therapeutic efficacy and safety, appearing

to obtain pain relief with demonstrated increase in mobility, associated with improvement in ROM, quality of life issues, which were improved. Herein, study patients perceived benefit from continued eToims treatment over time.

CONCLUSIONS

eToims is safe and efficacious with repeat use on a regular basis in many muscles throughout the body over time in chronic long-term care of patients with CRMP. There were no complications or adverse effects related to eToims in patients followed longitudinally over 24 months, similar to findings in our previous longitudinal study of over 18 months.[3] Immediate post-treatment pain relief, associated with some immediate post-treatment improvement in ROM and pulse rate reduction, appear to relate to patient satisfaction with subsequent self-selection to return for multiple treatment with eToims over time. Self-selection for repeat treatment for which one self-pays is consistent with experience of improvement in quality of life.

Further research, especially randomized controlled trials, should be carried out to ascertain effectiveness of eToims over other treatment modalities. In CRMP management, muscle twitches provide the local key to pain relief.

Addendum: Our experience with eToims in acute pain patients show that MTrPs are easy to locate for supramaximal stimulation and may result in fatigue of muscle even at 1 Hz repetition rate. Similar muscle fatigue phenomenon never occurs in chronic pain patients most likely due to inability to supramaximally stimulate MTrPs.

References

1. Simons DG, Travell J, Simon LS. Myofascial pain and dysfunction. The Trigger Point Manual. Volume1, 2nd ed. Baltimore, MD. Williams & Wilkins;1999.
2. Myburgh C, Larsen AH. Hartvigsen J. A systematic, critical review of manual palpation for identifying myofascial trigger points: evidence and clinical significance. Arch Phys Med Rehabil 2008; 89(6):1169-76.
3. Chu J, Schwartz I. eToims twitch relief method in chronic refractory myofascial pain (CRMP). Electromyogr Clin Neurophysiol 2008; 48: 311-320.
4. Skootsky SA, Jaeger B, Oye RK. Prevalence of myofascial pain in general internal medicine practice. West J Med 1989; 151 (2): 157-60.
5. Gunn CC: Treatment of Chronic Pain: Intramuscular Stimulation for Myofascial Pain of Radiculopathic Origin. London, UK.Churchill Livingston; 1996.
6. Sari H., Akarirmak U., Uludag M. Active myofascial trigger points might be more frequent in patients with cervical radiculopathy. European Journal of Physical and Rehabilitation Medicine (Europa Medicophysica) 2012; 48(2):237-44.
7. Huguenin LK. Myofascial trigger points: Current evidence. Phys Ther Sport 2004; 5:2-12.
8. Antony MT, Tonge DA. Effects of denervation and botulinum toxin on muscle sensitivity to acetylcholine and acceptance of foreign innervation in the frog. J Physiol 1980; 303:23-31.
9. McConnell MG, Simpson LL. The role of acetylcholine receptors and acetylcholinesterase activity in the development of denervation supersensitivity. J Pharm Exp Therap 1976; 198(3):507-17.

10. Lorkovic H. Supersensitivity to ACh in muscles after prolonged nerve block. Arch Internat Physiol Biochimie 1975; 83(4):771-81.
11. Mense S, Simons DG, Hoheisel U, Quenzer B. Lesions of rat skeletal muscle after local block of acetylcholinesterase and neuromuscular stimulation. J Appl Physiol 2003; 94(6):2494-501.
12. Shah JP, Phillips TM, Danoff JV, Gerber LH. An in vivo microanalytical technique for measuring the local biochemical milieu of human skeletal muscle. J Appl Physiol 2005; 99:1977–1984.
13. Larsson R, Oberg PA, Larsson SE. Changes of trapezius muscle blood flow and electromyography in chronic neck pain due to trapezius myalgia. Pain 1999; 79(1):45-50.
14. Rudolfsson T, Bjorklund M, Djupsjobacka M. Range of motion in the upper and lower cervical spine in people with chronic neck pain. Manual Therapy 2012; 17(1):53-9, 2012
15. Chapman JR, Norvell DC, Hermsmeyer JT, Bransford RJ, DeVine J, McGirt MJ, Lee MJ. Evaluating common outcomes for measuring treatment success for chronic low back pain. Spine 2011; 36(21 Suppl):S54-68.
16. Ho KY, Tan KH. Botulinum toxin A for myofascial trigger point injection: a qualitative systematic review. European Journal of Pain 2007; 11(5):519-27.
17. Tough EA, White AR, Cummings TM, Richards SH, Campbell JL. Acupuncture and dry needling in the management of myofascial trigger point pain: a systematic review and meta-analysis of randomised controlled trials. European Journal of Pain 2009; 3(1):3-10.
18. Law RY, Harvey LA, Nicholas MK, Tonkin L, De Sousa M, Finniss DG. Stretch exercises increase tolerance to stretch in patients with chronic musculoskeletal pain: a randomized controlled trial. Physical Therapy 2009; 89(10):1016-2.

19. Herbert RD, de Noronha M, Kamper SJ. Stretching to prevent or reduce muscle soreness after exercise. [Update of Cochrane Database Syst Rev. 2007;(4):CD004577; PMID: 17943822] Cochrane Database of Systematic Reviews 2011; (7):CD004577.
20. McHugh MP, Connolly DA, Eston RG, Kremenic IJ, Nicholas SJ, Gleim GW. The role of passive muscle stiffness in symptoms of exercise-induced muscle damage. American Journal of Sports Medicine 1999; 27(5):594-9.
21. Falla D, Jull G, Hodges PW. Feedforward activity of the cervical flexor muscles during voluntary arm movements is delayed in chronic neck pain. Exp Brain Res 2004; 157:43–8.
22. Hides JA, Stokes IA, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. Spine 1994;19:165–72.
23. Kim K, Lee SK, Kim YH. The biomechanical effects of variation in the maximum forces exerted by trunk muscles on the joint forces and moments in the lumbar spine: a finite element analysis. Proceedings of the Institution of Mechanical Engineers. Part H - Journal of Engineering in Medicine 2010; 224(10):1165-74.
24. Behnke BJ, Kindig CA, Musch TI, Koga S, Poole DC. Dynamics of microvascular oxygen pressure across the rest-exercise transition in rat skeletal muscle. Respiration Physiology 2001; 126(1):53-63
25. Delaney JP, Leong KS, Watkins A, Brodie D. The short-term effects of myofascial trigger point massage therapy on cardiac autonomic tone in healthy subjects. Journal of Advanced Nursing 2002; 37(4):364-71.

26. Hord ED, Evans MS, Mueed S, Adamolekun B, Naritoku DK.The effect of vagus nerve stimulation on migraines. Journal of Pain 2003; 4(9):530-4.

27. Kirchner A, Birklein F, Stefan H, Handwerker HO. Left vagus nerve stimulation suppresses experimentally induced pain. Neurology 2000; 55(8):1167-71.

28. Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 2001; 94(2):149-58.

29. Vagg R, Mogyoros I, Kiernan MC, Burke D. Activity-dependent hyperpolarization of human motor axons produced by natural activity. J Physiol 1998; 507 (Pt 3):919-25.

30. Ibarra JM, Ge HY, Wang C, Martinez Vizcaino V, Graven-Nielsen T, Arendt-Nielsen L. Latent myofascial trigger points are associated with an increased antagonistic muscle activity during agonist muscle contraction. Journal of Pain 2011; 12(12):1282-8.

Table 1. Cause of pain in patients undergoing eToims (N=133)

Cause of pain	No trauma history (N=18)	Trauma history (N=115)	> 10 txs (N=38)	<= 10 txs (N=95)
Auto accident		**30**	**11**	**19**
Repetitive stress injury		**23**	**8**	**15**
Falls		**16**	**3**	**13**
Sports		**11**	**1**	**10**
Lifting		**11**	**2**	**9**
Failed back or neck surgery		**10**	**4**	**6**
Spinal stenosis		**14**	**4**	**10**
Others	**18**		**5**	**13**

Table 2. Differences in immediate changes in ROM of the 4 groups receiving eToims

	Group 0 <=10 txs & Pain Δ<2	Group 1 <=10 txs & Pain Δ>=2	P levels	Group 2 >10 txs & Pain Δ<2	Group 3 >10 txs & Pain Δ>=2	P levels
Treatment observations (no)	97	138		1186	812	
Age (years)	50.6± 14.5	49.7± 15.9	**0.019**	51.4±12.4	52.0±12.0	**<0.001**
Symptom duration (months)	75.7± 90.4	81.7± 116.9	**0.046**	146.3±119.1	92.3±66.5	**<0.001**
Session time/treatment (minutes)	48.0± 22.0	48.0± 22.0	0.303	52.0±24.0	56.0±25.0	**<0.001**
Treatment interval (days)	20.0± 50.0	42.0± 87.0	0.951	12.0±43.0	14.0±29.0	0.999
VAS Δ over time	2.4±1.9	3.2±1.5	**0.002**	3.5± 2.5	4.9± 2.3	0.168
Treatment related immediate Δ						
VAS Δ (no)	0.6± 0.5	2.7± 1.0	**<0.001**	0.7±0.4	2.6±1.3	**<0.001**
Systolic BP Δ (mm Hg)	1.6± 8.0	0.4± 9.5	0.915	-1.1± 9.0	- 0.6± 9.0	0.176
Diastolic BP Δ (mm Hg)	0.6± 5.0	0.7± 5.0	0.555	- 0.5± 6.0	- 0.6± 6.0	0.771
Pulse Δ (no/min)	- 6.0± 7.0	- 7.0± 7.0	0.195	- 7.0± 7.0	- 9.0± 10.0	**0.026**
NR**S** Δ (cm)	1.2± 1.2	1.5± 1.3	0.507	1.2±1.1	1.4±1.3	**0.012**
NR**A** Δ (cm)	1.2± 1.3	1.6± 1.3	0.305	1.3±1.0	1.4±2.1	**<0.001**
ER**S** Δ (cm)	1.2± 1.4	1.7± 2.2	0.643	1.3± 1.0	1.4± 2.1	**<0.001**
ER**A** Δ (cm)	1.1± 1.8	1.3± 1.8	0.779	1.1±1.2	1.2± 1.5	**0.017**
IR**S** Δ (cm)	2.0± 3.0	2.6± 3.8	0.815	2.0±2.3	2.4±3.0	**0.027**
IR**A** Δ (cm)	1.8± 3.0	1.5± 2.3	0.261	1.7±2.0	1.8±2.4	**<0.001**
SLR**S** Δ (degrees)	7.0± 6.0	6.0± 7.0	0.289	4.0±5.0	6.0±9.0	**<0.001**
SLR**A** Δ (degrees)	6.0± 7.0	6.0± 7.0	0.417	4.0±5.0	6.0±9.0	**<0.001**
FAB**S** Δ (cm)	2.5± 2.0	3.1± 3.3	0.913	2.3±2.1	2.5±3.6	**<0.001**
FAB**A** Δ (cm)	2.3± 2.0	2.6± 3.3	0.479	2.2±2.2	2.2±2.5	**<0.001**

Abbreviations:
No= number, N=number, txs = treatments, BP=blood pressure, ROM = range of motion

NR**S**= Neck rotation to symptomatic side, NR**A**= Neck rotation to asymptomatic side, ER**S**= external rotation of shoulder on symptomatic side, ER**A**= external rotation of shoulder on asymptomatic side, IR**S**= internal rotation of shoulder on symptomatic side, IR**A** = internal rotation of shoulder on asymptomatic side, SLR**S**= straight leg raising on symptomatic side, SLR**A**=straight leg raising on asymptomatic side, FAB**S**= FABERE on symptomatic side, FAB**A**= FABERE on asymptomatic side.

Table 3. Correlations between number of treatments and eToims induced immediate changes in VAS, BP, pulse and ROM measured

	Group0 N= 97	**P levels**	**Group1 N= 138**	**P levels**	**Group2 N= 1186**	**P levels**	**Group3 N= 812**	**P levels**
SBPΔ (mmHg)	0.128	0.181	-0.066	0.432	**-0.098**	**0.001**	**-0.080**	**0.03**
DBPΔ (mmHg)	0.128	0.179	0.078	0.353	**-0.073**	**0.012**	-0.027	0.452
Pulse Δ (no)	-0.027	0.780	-0.008	0.923	-0.009	0.758	**-0.367**	**<0.001**
Pain Δ	-0.016	0.869	0.073	0.381	**0.167**	**<0.001**	**-0.257**	**<0.001**
NR**S** Δ (cm)	0.164	0.088	-0.022	0.795	0.048	0.101	**-0.152**	**<0.001**
NR**A** Δ (cm)	-0.025	0.796	-0.029	0.729	-0.050	0.090	**-0.204**	**<0.001**
ER**S** Δ (cm)	-0.017	0.862	**-0.211**	**0.010**	-0.053	0.074	**-0.251**	**<0.001**
ER**A** Δ (cm)	-0.078	0.420	-0.139	0.092	-0.016	0.610	**-0.260**	**<0.001**
IR**S** Δ (cm)	-0.030	0.759	-0.029	0.728	0.045	0.128	**-0.173**	**<0.001**
IR**A** Δ (cm)	0.032	0.743	-0.040	0.634	0.019	0. 520	**-0.230**	**<0.001**
SLR**S** Δ (degrees)	0.032	0.755	-0.062	0.476	**0.137**	**<0.001**	**-0.142**	**<0.001**
SLR**A** Δ (degrees)	-0.032	0.760	0.013	0.884	**-0.104**	**0.001**	**-0.166**	**<0.001**
FAB**S** Δ (cm)	-0.090	0.384	**-0.181**	**0.03**	**-0.063**	**0.040**	**-0.237**	**<0.001**
FAB**A** Δ (cm)	0.059	0.574	-0.072	0.405	-0.034	0.261	**-0.293**	**<0.001**

Abbreviations:
Δ =changes. Refer to Table 2 for other abbreviations.

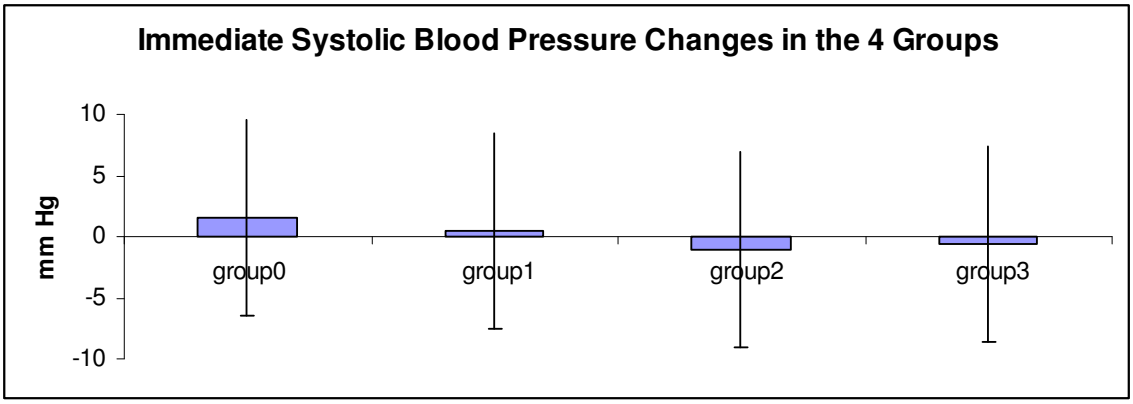

Figure 1. Immediate increase in systolic blood pressure noted in Group 0 and Group 1 patients; with immediate systolic blood pressure reduction noted in Group 2 and Group 3 patients.

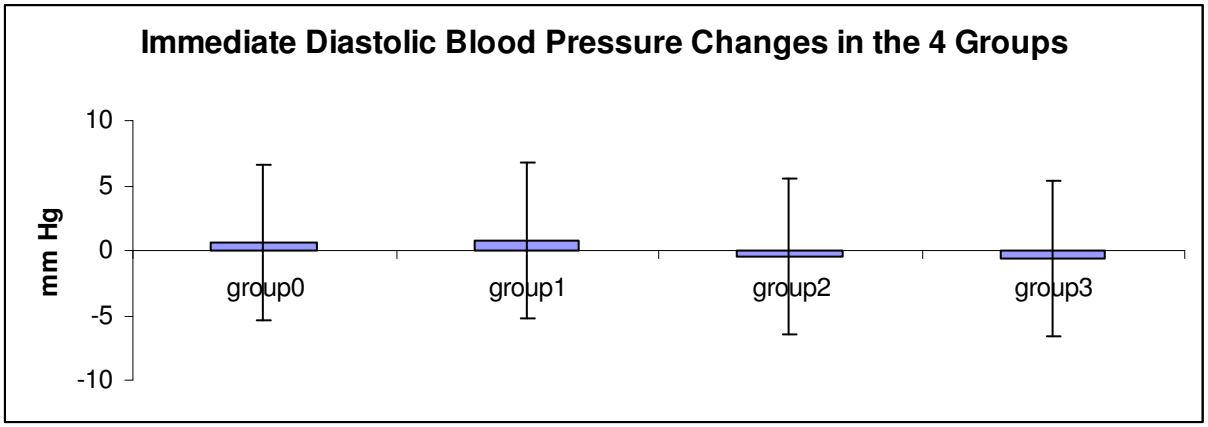

Figure 2. Immediate increase in diastolic blood pressure noted in Group 0 and Group 1 patients; with immediate diastolic blood pressure reduction noted in Group 2 and Group 3 patients.

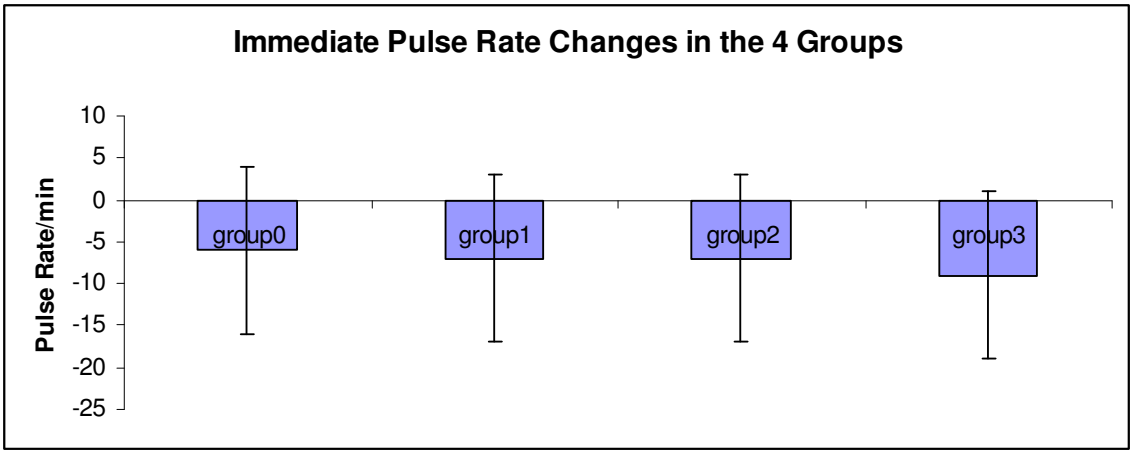

Figure 3. Immediate reduction in pulse rate noted in all four groups, especially those in group 3.