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## Effects of pulsed electromagnetic field therapy on symptoms associated with eccentric exercise-induced muscle damage

Henry Banyard  
*Edith Cowan University*

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**Master of Science (Sports Science) Thesis**

**Effects of Pulsed Electromagnetic Field Therapy on  
Symptoms Associated with Eccentric Exercise-Induced  
Muscle Damage**

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**Co-Supervisor: Associate Professor Michael Newton**

**Date of Submission: 16<sup>th</sup> December 2013**



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## ABSTRACT

Unaccustomed exercise consisting of eccentric contractions induces muscle damage that is characterised by muscle weakness, soreness, swelling and increased muscle stiffness. These symptoms affect daily activities and athletic performance; therefore, interventions to attenuate the symptoms and enhance recovery from muscle damage are necessary. Pulsed electromagnetic field therapy (PEMFT) is anecdotally reported to increase muscle blood flow and oxygenation to enhance tissue healing. One previous study showed that PEMFT was effective for alleviating muscle soreness and losses in range of motion after exercise. However, studies investigating the effect of PEMFT on recovery of muscle strength following eccentric exercise are lacking. The purposes of this study were to investigate the effects of PEMFT treatment on muscle temperature, blood flow and oxygenation (Study 1), and on the symptoms associated with eccentric exercise-induced muscle damage (Study 2).

In Study 1, the effects of 30 min PEMFT on muscle temperature, blood flow and oxygenation were examined using nine healthy men ( $23.6 \pm 3.7$  years). A device called e-cell<sup>™</sup> was used for PEMFT in this study, which is the size and shape of a computer mouse weighing approximately 140 g, and sham treatment used a visually identical device without pulsed electromagnetic field production. PEMFT was applied over the bicep brachii of one arm for 30 min, and the other arm received sham treatment, while each subject was lying supine on a massage table. The device was marked A or B; thus, both the investigator and subjects were blinded as to which device was active e-cell<sup>™</sup> or sham, and the use of dominant or non-dominant arm for device A or B was randomised and counterbalanced among subjects. Pre-treatment muscle temperature was measured by a thermistor needle (22 gauge, 70 mm) inserted to a depth of 20 mm at 10 mm laterally adjacent to a near infrared spectroscopy (NIRS) probe unit that was attached to the skin at the mid-belly of the biceps brachii, and the post-treatment measurement was taken at 5 mm proximal to the first site.

The NIRS was used to measure tissue oxygenation index (TOI), a measure of muscle oxygenation, and total haemoglobin content (tHb), an indirect measure of blood flow, which were recorded throughout the treatment period. Changes in muscle temperature from before to immediately post-treatment were compared between e-cell™ and sham conditions using a paired t-test, and changes in TOI and tHb from baseline to 30 min of treatment (0, 10, 20 and 30 min) were compared between conditions by a two-way repeated measures analysis of variance (ANOVA). Muscle temperature significantly ( $p<0.05$ ) increased after e-cell™ treatment only and was  $0.55 \pm 0.22^{\circ}\text{C}$  higher ( $p=0.033$ ) for the arm that received e-cell™ than sham treatment. No significant changes in TOI and tHb were evident for either condition.

In Study 2, eight men and eight women ( $24.8 \pm 6.2$  years) performed two bouts of 60 maximal isokinetic ( $30^{\circ}\cdot\text{s}^{-1}$ ) eccentric contractions of the elbow flexors on each arm separated by 4 weeks. In each eccentric contraction, the elbow joint was forcibly extended from a flexed ( $90^{\circ}$ ) to a fully extended position ( $0^{\circ}$ ). At immediately after, and 1-4 days following the exercise, the exercised arm received 30 min of either e-cell™ or sham treatment described above. The arm dominance and the order of treatment conditions were randomised and counterbalanced among the subjects, and the study was conducted in a double-blinded manner. Dependant variables included maximal voluntary contraction (MVC) strength, range of motion (ROM), upper arm circumference (CIR), muscle soreness by a visual analogue scale, muscle tenderness measured by pressure pain threshold (PPT) and plasma CK activity. Changes in these variables for 7 days following the exercise were compared between e-cell™ and sham treatment conditions, men and women, and the first and second bouts of exercise by a two-way repeated measures ANOVA. The changes in the variables from pre- to post-treatment were also analysed by a two-way repeated measures ANOVA. All variables changed significantly ( $p<0.05$ ) following eccentric exercise; however, the changes in the variables over time were not significantly different between men and women. Thus, men and women were combined for subsequent analyses. For the acute changes in the variables from pre- to post-treatment, no significant differences in any variables were evident between e-cell™ and sham

conditions. A significant ( $p<0.05$ ) reduction in MVC by 8% was observed for both conditions, but no significant changes were found for other variables. Regarding the changes in the variables 1-7 days following exercise, the rate of recovery for MVC strength and ROM was significantly enhanced, and increases in muscle soreness, CIR and plasma CK activity were significantly attenuated for the e-cell™ compared with sham condition. When comparing the first and second bouts by ignoring the treatment, MVC strength and ROM recovered significantly faster, and increases in CIR and muscle soreness were significantly smaller for bout 2 compared with bout 1, and these effects were similar or greater than those produced by e-cell™. It was concluded that e-cell™ treatment enhanced the recovery of muscle damage; however, the magnitude of recovery following e-cell™ and sham treatment was influenced in the second bout of exercise by the contralateral repeated bout effect. Furthermore, pre-conditioning the muscle with non-damaging exercise could be more effective for attenuating symptoms associated with exercise-induced muscle damage compared to e-cell™ treatment.

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# **CHAPTER ONE**

## **INTRODUCTION**

### **1.1 Background**

Muscle damage occurs when receiving harmful physical, chemical or biological stimulus. In exercise and sports or daily activities, muscle damage induced by eccentric contractions is most common. Downhill running (Byrnes et al., 1985) or walking (Balnave & Thompson, 1993) and bench stepping (Gleeson, Blannin, Walsh, Field, & Pritchard, 1998) are used to experimentally induce muscle damage in humans. Other frequently used eccentric exercise models include maximal or sub-maximal eccentric exercise of the knee extensors (Kellis & Baltzopoulos, 1998) and flexors (Johansson, Lindstrom, Sundelin, & Lindstrom, 1999) as well as the elbow flexors (Chapman, Newton, Sacco, & Nosaka, 2006). Among them, the elbow flexor model is most often used in many previous studies (e.g. Chen et al., 2011; Clarkson & Tremblay, 1988; Cleak & Eston, 1992; Jones, Newham, & Clarkson, 1987).

After performing “unaccustomed” eccentric exercise, muscles become weak, sore, swollen and stiff for several days (Chen, Lin, Chen, Lin, & Nosaka, 2011; Cleak & Eston, 1992; Nosaka & Clarkson, 1995; Nosaka, Newton, & Sacco, 2002). To quantify these symptoms, maximal voluntary contraction (MVC) strength, pain scale, limb circumference or muscle thickness, and range of motion (ROM) are often used. Other markers of muscle damage include muscle proteins (e.g. creatine kinase: CK, myoglobin) in the blood, and abnormality detected by ultrasound or magnetic resonance images (Clarkson & Hubal, 2002; Fleckenstein & Shellock, 1992; Nosaka, Muthalib, Lavender, & Laursen, 2007). It is important to note that these markers do not necessarily correlate with one another. For example, muscle soreness does not develop immediately following eccentric exercise of the elbow flexors but at the same time the greatest decreases in muscle strength loss are



apparent (Nosaka, 2008). Nosaka et al. (2002) reported that the magnitude of muscle soreness did not correlate with the magnitude of decrease in maximal isometric strength and range of motion, increases in upper arm circumference and plasma CK activity. Consequently, it appears that there are several aspects to eccentric exercise-induced muscle damage (EIMD).

The magnitude of muscle damage incurred after eccentric exercise depends on the training status of an individual, the force and velocity of contractions, number of repetitions and range of movement (Chapman, et al., 2006; Cheung, Hume, & Maxwell, 2003; Connolly, Sayers, & McHugh, 2003; Nosaka & Sakamoto, 2001). Nosaka and Clarkson (1996) reported that it took more than two months for muscle strength to fully return to baseline levels when untrained individuals performed maximal eccentric exercise of the elbow flexors. In contrast, Newton and colleagues (2008) demonstrated that resistance trained men had smaller decreases in muscle strength after exercise compared with men who had little experience in resistance training, and muscle strength fully recovered by 3 days following 60 maximal eccentric contractions of the elbow flexors. Previous studies have demonstrated that the magnitude of muscle damage is greater when greater force is produced (Nosaka & Newton, 2002), a larger number of contractions are performed (Chapman, et al., 2006), muscle is stretched more (Nosaka & Sakamoto, 2001) and contraction velocity is faster (Chapman, Newton, McGuigan, & Nosaka, 2008).

There are also studies that report gender differences exist for the changes in muscle damage markers. For example, Seawright et al. (2008) compared the muscle damage markers between 58 women and 42 men after 50 maximal eccentric contractions of the elbow flexors, and reported that women showed greater relative strength losses than men immediately after exercise, but men had significantly higher peak CK activity than women. In contrast, Rinard and associates (2000) showed that gender had no significant effect on muscle damage markers following 70 maximal eccentric contractions of the elbow flexors performed by 83 women and 82 men. Therefore, it remains unclear as to whether gender affects the magnitude of eccentric exercise-induced muscle damage.

Since muscle damage is often inevitable, therapeutic interventions are needed to alleviate the symptoms of muscle damage and facilitate the recovery process. Several different types of interventions have been investigated for their efficacy on the symptoms and markers of muscle damage experimentally induced by various eccentric exercises. Some examples of interventions include eccentric contractions, cryotherapy (ice massage, ice packs), electrotherapies (ultrasound, transcutaneous electrical nerve stimulation: TENS, diathermy), physical therapies (stretching, massage, compression), nutritional supplements and non-steroidal anti-inflammatory drugs among others (Allen, Mattacola, & Perrin, 1999; Burgess & Lambert, 2010; Cheung, et al., 2003; Connolly, et al., 2003; Howatson & van Someren, 2008). As explained previously, symptoms associated with EIMD are dissimilar in that they typically peak on separate days; nevertheless, therapeutic modalities should primarily focus on attenuate delayed onset muscle soreness (DOMS) and enhancing the recovery of muscle function after exercise, since these aspects of EIMD can directly affect daily activities and athletic performance.

The effect of therapeutic interventions in the treatment of EIMD of the elbow flexors has previously been investigated. Some examples include, deeply applied sport massage (10 minutes effleurage and petrissage) that was performed at 3 hours post exercise and reported to alleviate muscle soreness and swelling but had no effect on enhancing the recovery of muscle function after maximal eccentric exercise of the elbow flexors (Zainuddin, Newton, Sacco, & Nosaka, 2005). Similarly, Denegar and Perrin (1992) compared 5 treatment groups (8 untrained women per group) consisting of TENS, ice pack, a combination of TENS and ice pack, sham TENS and control in which the therapeutic treatment was performed 48 hours after elbow flexor exercise with a dumbbell. Their study showed that the combination of TENS and ice pack and the ice pack treatments had a significant analgesic effect, but no significant effect on recovery of muscle strength. Weber and colleagues (1994) compared therapeutic massage (2 min light effleurage, 5 min petrissage followed by 1 min effleurage), microcurrent stimulation and upper body ergometry (60 rpm for a workload of 400 kgm/min) applied immediately and 24 hours after exercise, and reported

that none of the treatments had a significant effect on alleviating muscle soreness and maximal isometric contraction strength following dumbbell exercise of the elbow flexors until exhaustion. Considering the above and other studies (e.g. Allen, et al., 1999; Bonacci & Higbie, 1997; Tourville, Connolly, & Reed, 2006), it appears that most of the interventions tested in the previous studies were not strongly effective for attenuating DOMS and enhancing muscle function recovery. Therefore it is necessary to establish an improved therapeutic treatment for EIMD.

Pulsed electromagnetic field therapy (PEMFT) is an electrotherapy that uses an alternating current through a copper coil to produce a magnetic field that penetrates deeply through tissues and is believed to enhance cellular repair, reduce pain, oedema and inflammation (Markov, 2007; Robertson, Ward, Low, & Reed, 2006). There is significant evidence to suggest that PEMFT can treat non-union fractures, avascular necrosis, and alleviate pain in chronic musculoskeletal injuries such as osteoarthritis (Trock et al., 1993), carpal tunnel syndrome (Weintraub & Cole, 2008), and post operative pain following breast augmentation (Hedan & Pilla, 2008). Trock et al. (1993) used low frequency (less than 30 Hz) PEMFT consisting of 18 treatment sessions (30 minutes / session) in comparison to sham treatment (applied treatment by not energizing the magnetic coil) to treat patients with osteoarthritic pain, and reported that the PEMFT treatment group had significant pain relief from baseline measurements (up to 50% reduction on 10 cm VAS) compared with sham treatment group (10% reduction). An in vivo study demonstrated that PEMFT treatment augments angiogenesis, which can assist in the repair of injured tissue (Tepper et al., 2004). The supply of oxygen and nutrients via the blood vessels is known to be essential for tissue repair (Zampetaki, Kirton, & Xu, 2008), thus if PEMFT treatment can increase blood flow and muscle oxygenation, a more rapid recovery of injured tissue could follow. However, experimental studies measuring the changes in blood flow following PEMFT treatment are lacking.

To the best of our knowledge only one study has investigated the effects of PEMFT on the signs and symptoms of muscle damage. Spodaryk (2002) had 36 healthy men perform exhaustive eccentric exercise of the elbow flexors using a dumbbell and then applied either 20 minutes of

PEMFT or sham treatment for 5 days starting from immediately post-exercise and found significant attenuation of muscle soreness (VAS) and smaller decreases in ROM in PEMFT treatment group only but no enhanced recovery of muscle strength.

A portable low frequency PEMFT device called e-cell™ (Global Energy Medicine, Western Australia, see Appendix A), which has been cleared by the Australian Register of Therapeutic Goods, is anecdotally reported to increase blood flow and cellular proliferation, reduce inflammation and enhance the healing of muscle strain injuries, tendonitis and contusions. Furthermore, swelling that occurs with the movement of inflammatory cells and fluids to an injured area following strenuous unaccustomed eccentric exercise is known to contribute to the sensation of pain (Connolly, et al., 2003). As a consequence, if the e-cell™ treatment was to reduce oedema, the associated DOMS could be eased. As mentioned earlier PEMFT treatment has been shown in vivo studies to stimulate cellular repair. If e-cell™ treatment is effective for regeneration of skeletal muscle fibres and connective tissue surrounding the fibres, it is possible that the treatment could enhance muscle function recovery after eccentric exercise. Therefore, it seems reasonable to assume that e-cell™ treatment could be effective for alleviating DOMS and enhancing recovery of losses in muscle function after EIMD. However, no experimental studies have yet examined the effects of e-cell™ treatment on markers of muscle damage induced by eccentric exercise.

## **1.2 Purpose**

The purposes of the present study were to investigate whether 30 minutes of e-cell™ treatment would effect muscle temperature, blood flow and oxygenation compared to sham treatment when it was applied to the elbow flexors (Study 1). To compare changes in the dependent variables of muscle damage of the elbow flexors seen in e-cell™ and sham treatment arms when applied 30 minutes, 1, 2, 3 and 4 days after eccentric exercise of the elbow flexors (Study 2).

### **1.3 Research Questions**

- 1) Does 30 minutes of e-cell™ treatment increase biceps brachii temperature? (Study 1)
- 2) Does 30 minutes of e-cell™ treatment increase muscle oxygenation and blood flow in the biceps brachii? (Study 1)
- 3) Does e-cell™ treatment improve MVC torque, ROM, upper arm circumference, muscle soreness and tenderness acutely? (Study 2)
- 4) Does e-cell™ treatment influence muscle damage markers (MVC torque, ROM, upper arm circumference, muscle soreness, tenderness and plasma CK activity) following eccentric exercise of the elbow flexors, and do these differ between genders? (Study 2)

# **CHAPTER TWO**

## **LITERATURE REVIEW**

### **Electrotherapy Treatment of Exercise-Induced Muscle Damage**

#### **2.1 Introduction**

Exercise-induced muscle damage (EIMD) results in symptoms such as prolonged losses of muscle function, increased passive stiffness, muscle soreness and swelling (Chen, et al., 2011; Nosaka & Clarkson, 1995; Nosaka, et al., 2002). EIMD is repairable, but could increase the risk of musculoskeletal injuries, and impair exercise performance and activities of daily living (Cheung, et al., 2003). Therefore, interventions are needed to attenuate the symptoms of EIMD.

There are many modalities used as interventions for soft tissue injuries. These interventions can be classified as prophylactic or therapeutic based on the timing of their application. A prophylactic intervention is characterised by its application prior to an injury. Conversely, therapeutic interventions are typically applied once the primary damage has already occurred. However, many of the interventions are used both prophylactically and therapeutically. Some prevalent prophylactic and/or therapeutic interventions include pre-exercise isometric (Chen, Chen, Pearce, & Nosaka, 2012) and eccentric contractions (Nosaka, Newton, Sacco, Chapman, & Lavender, 2005; Nosaka, Newton, & Sacco, 2005), pre- and post-exercise concentric contractions (Nosaka & Clarkson, 1997; Zainuddin, Sacco, Newton, & Nosaka, 2006), stretching (Chen, et al., 2011; Pizza, Koh, McGregor, & Brooks, 2002), nutritional supplements (Bryer & Goldfarb, 2006; Maxwell, Jakeman, Thomason, Leguen, & Thorpe, 1993), non-steroidal anti-inflammatory drugs (Baldwin, Stevenson, & Dudley, 2001; Hasson et al., 1993), cryotherapy (Howatson & Van Someren, 2003; Yanagisawa et al., 2003), hot cold contrast baths (Vaile, Gill, & Blazeovich, 2007), massage therapy (Mancinelli et al., 2006; Zainuddin, et al., 2005), compression garments

(Jakeman, Byrne, & Eston, 2010; Kraemer et al., 2001) and electrotherapies (Bougie, 1997; Denegar & Perrin, 1992).

Among these, electrotherapies are popular interventions used by medical practitioners for the treatment of musculoskeletal injuries in conjunction with other therapeutic interventions such as transcutaneous electrical nerve stimulation (TENS), microcurrent electrical neuromuscular stimulation (MENS), ultrasound, vibration, pulsed electromagnetic field therapy (PEMFT), light amplification by stimulated emission of radiation (laser) and diathermy (Brukner & Khan, 2002; Watson, 2008). An electrotherapy refers to any form of treatment modality that incorporates an electro-physical component that can be applied externally to the human body to stimulate or enhance physiological processes to restore normal function (Robertson, et al., 2006; Watson, 2008). Electrotherapies can be categorised into electrical (e.g. TENS and MENS), mechanical (e.g. ultrasound, vibration), electromagnetic (e.g. PEMFT and laser) and thermal (diathermy) (Brukner & Khan, 2002; Robertson, et al., 2006).

It has been reported that electrotherapies are effective for enhancing recovery from musculoskeletal injuries. For example, Trock et al., (1993) applied 30 minutes of PEMFT for 18 sessions to treat patients with osteoarthritic pain, and reported significantly greater pain relief from baseline measurements in the PEMFT group (up to 50% reduction on 10 cm visual analogue scale) compared to sham treatment group (10% reduction). Furthermore, it was reported that 56 patients suffering from chronic leg ulcers received pulsating ultrasound and had a 20% greater healing rate than traditional bandaging treatment group (Callam, Harper, Dale, Ruckley, & Prescott, 1987). Similarly, the healing of other musculoskeletal conditions such as non-union bone fractures and calcific tendonitis were enhanced after electrotherapy treatment (Ebenbichler et al., 1998; Mollon, da Silva, Busse, Einhorn, & Bhandari, 2008).

Given that electrotherapies can enhance the healing from musculoskeletal injuries, it seems reasonable to assume that they could also enhance the recovery from EIMD. Several studies have investigated the effects of electrotherapies on the treatment of symptoms associated with EIMD.

However, he reported effects vary considerably among the types of electrotherapy employed, frequency of application, muscle group utilised and their overall effectiveness. This brief literature review aims to describe some of electrotherapies and potential mechanisms underpinning the effects of electrotherapies on soft tissue injuries, and to examine the potential efficacy of electrotherapies in the attenuation of muscle damage symptoms.

## **2.2 Possible Mechanisms for Electrotherapies to Enhance Recovery from Muscle Injury**

Understanding the physiological changes during electrotherapy treatment is necessary to validate the efficacy of electrotherapies. To elicit a physiologically favourable response, the target tissues must absorb the energy emitted from the modalities. For example, dense tissues such as bone or tendons will elicit favourable responses to higher energy devices compared to lower energy devices that will benefit less dense tissues such as muscle, nerves and cell membrane activity (Robertson, et al., 2006). This section provides a brief summation of the theorised physiological mechanisms affected by electrotherapy modalities (Figure 1).

### **2.2.1 Mechanical Therapy**

#### **2.2.1.1 Ultrasound**

Therapeutic ultrasound is a mechanical therapy resulting from the conversion of electrical energy into soundwaves, employed at frequencies between 0.7 and 3.3MHz, which can penetrate through the epidermis and be absorbed into the target tissue (Brukner & Khan, 2002; Robertson, et al., 2006). Clinicians use both continuous (thermal) and pulsed (athermal) ultrasound to treat various musculoskeletal conditions. Continuous ultrasound involves an uninterrupted stream of ultrasound waves that are reported to increase muscle blood flow and tissue metabolism (Dyson, 1987). It is traditionally employed during the remodelling phase of wound healing to improve scar formation (Young & Dyson, 1990). However, during the acute phase of an injury (~the first 72



hours post-injurious stimuli), thermal ultrasound is not applied since it will significantly increase muscle temperature (2 - 4C°) and further exacerbate acute inflammation. Pulsed ultrasound involves a regularly alternating stream of ultrasound waves thought to stimulate cavitation and streaming. The soundwaves (frequencies of 0.85 – 3MHz) are believed to penetrate the skin and generate micron-sized bubbles in the blood or tissue fluids which are then streamed in the direction of the mechanical force which is thought to influence cell membrane permeability, facilitate tissue metabolism, diffusion of cellular metabolites and influence the sensation of pain (Brukner & Khan, 2002; Dyson, 1987).

#### **2.2.1.2 Vibration**

Vibration therapy is also a mechanical electrotherapy often employed by clinicians at frequencies between 30 and 50Hz to reduce oedema and alleviate pain from acute and chronic musculoskeletal injuries (Broadbent et al., 2010; Lundeberg, Nordemar, & Ottoson, 1984; Yarnitskya, Kunin, Brik, & Sprecher, 1997). When applied to the skin of the target area, it is believed to modulate the afferent input from sensory units within skeletal muscle, which may influence the sensation of pain associated with group III and IV afferent nerve fibres (Robertson, et al., 2006).

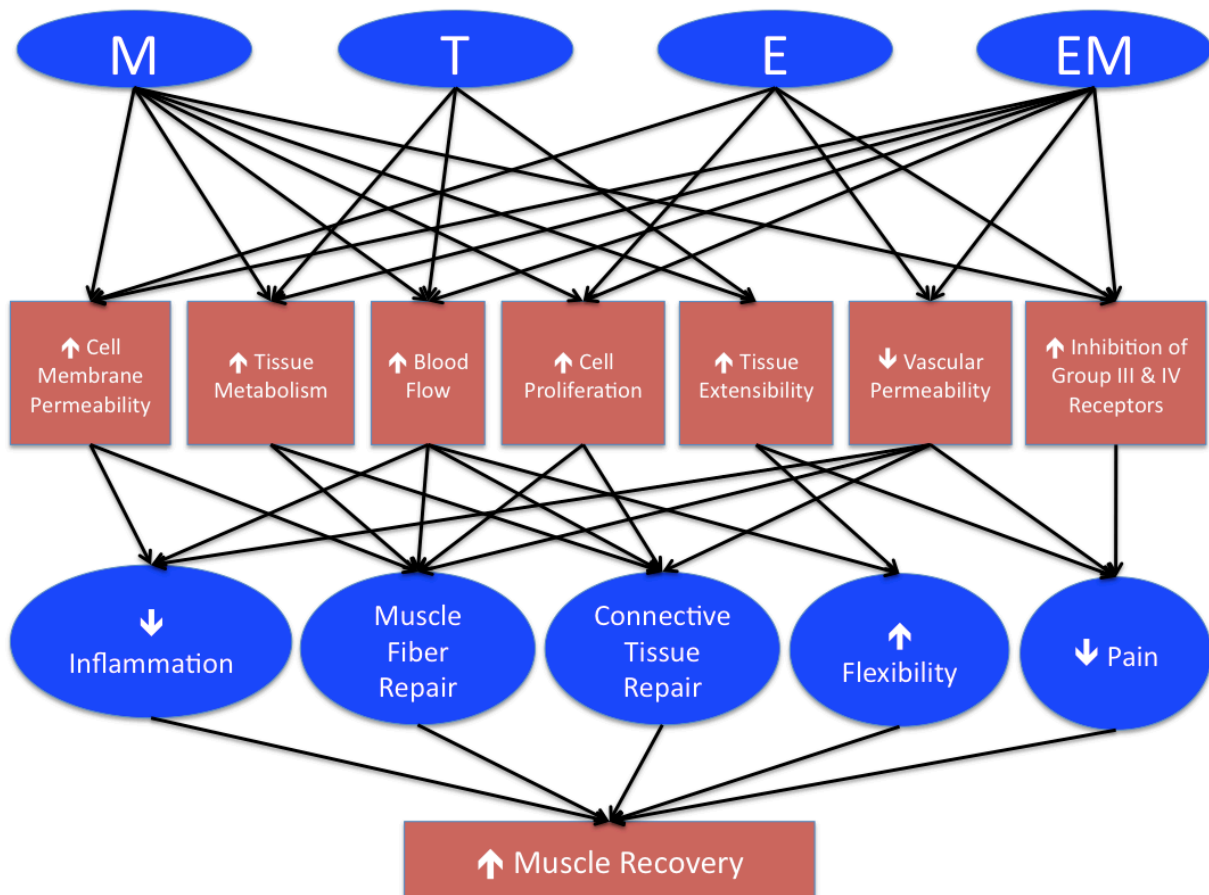


Figure 1: Potential mechanisms leading to the recovery of soft tissue injuries by electrotherapies. Each electrotherapy has been categorised into groups, where M = mechanical; T = thermal; E = electrical; EM = electromagnetic. It is then proposed that these electrotherapies may modify various physiological mechanisms within the body; for example enhanced blood flow or cell membrane permeability, which can possibly influence factors that affect the rate of muscle recovery; such as muscle fibre or connective tissue repair. ↓ indicates decrease; ↑ indicates increase.

## 2.2.2 Thermal Therapy

### 2.2.2.1 Diathermy

Diathermy (Shortwave and Microwave) treatment is a thermal electrotherapy that passively increases muscle temperature via high oscillating electromagnetic frequencies (Brukner & Khan, 2002). Shortwave diathermy for example is typically applied at a frequency of 27.12MHz compared to the higher frequencies of Microwave diathermy at 434MHz, 915MHz or 2450MHz (Robertson, et al., 2006). Higher frequency modalities utilising 1MHz or greater are designed to enhance tissue heating which is believed to influence metabolic processes, enhance muscle blood flow and

extensibility in collagen containing tissues (Robertson, et al., 2006). Diathermy is not utilised immediately post-injury since it will enhance acute inflammation; however, for the treatment of musculoskeletal injuries, heating tissues is thought to reduce joint stiffness by increasing extensibility of connective and muscle tissues (Szymanski, 2001), accelerate the removal of oedema associated with inflammatory processes via enhanced blood and lymph flow and potentially affect cell membrane permeability (Brukner & Khan, 2002; Collis & Segal, 1988).

### **2.2.3 Electrical Therapy**

#### **2.2.3.1 Transcutaneous Electrical Nerve Stimulation**

There is evidence to suggest TENS treatment is effective for pain relief, and in clinical practice is often the modality of choice for pain control (Johnson, Ashton, & Thompson, 1991). TENS is an electrical therapy believed to modify sensory stimulation and enhance pain thresholds facilitating a temporary analgesic response (Robertson, et al., 2006). The frequency, intensity and duration of TENS modalities can have differing analgesic effects. High frequency, short pulse duration TENS (80 – 120 Hz; 50  $\mu$ s) is believed to engage the ‘Pain Gate Control Theory’, which suggests that stimulating a large area of sensory nerve fibres in the muscle can inhibit afferent signals sent from a smaller number of sensory nerve fibres and diminish the perception of pain (Melzack & Wall, 1967). Conversely, low frequency, long pulse duration TENS (2 – 5 Hz; >300  $\mu$ s) is thought to activate endogenous opioid pathways that aid to inhibit the sensation of pain (Sluka, Deacon, Stibal, Strissel, & Terpstra, 1999).

#### **2.2.3.2 Microcurrent Electrical Neuromuscular Stimulation**

Microcurrent electrical neuromuscular stimulation (MENS) is an electrical therapy similar to TENS that produces extremely low intensity (100 $\mu$ A - 200 $\mu$ A) and frequency (0.3 – 300Hz) direct electrical currents believed to attenuate symptoms of musculoskeletal injuries such as pain, swelling and losses in muscle function (Allen, et al., 1999; Robertson, et al., 2006). Clinically, MENS has

been used in the treatment of non-union bone fractures (Bertolucci & Grey, 1995) and tissue healing (Brighton & Friedenberg, 1974). At a cellular level, MENS is believed to influence the bioelectricity involved with the transport of ions through the cell membrane in order to maintain membrane permeability, which can facilitate cell proliferation and protein synthesis (Cheng et al., 1982).

## **2.2.4 Electromagnetic Therapy**

### **2.2.4.1 Laser**

Low-level laser therapy has been advocated as an effective therapeutic treatment for various musculoskeletal conditions such as the relief of pain (Chow, Heller, & Barnsley, 2006) and accelerating wound healing (Gur et al., 2002). Clinically, lasers are used at two wavelengths, with the helium neon (HeNe) laser at 632.8nm and the gallium arsenide (GaAs) laser at 904nm (Brukner & Khan, 2002; Enwemeka, 2001); however, other wavelengths of 655nm (Junior et al., 2008) and 830nm (Junior et al., 2009) have also been reported. It is proposed that the light energy absorbed by the target tissues can modulate intracellular processes and reduce pain, oedema, improve mitochondrial function and vascularisation (Brukner & Khan, 2002).

### **2.2.4.2 Pulsed Electromagnetic Field**

Pulsed electromagnetic field therapy (PEMFT) transmits an alternating current through a copper coil to produce a magnetic field that penetrates deeply through tissues and is believed to enhance blood flow and cellular repair, reduce pain, oedema and inflammation (Robertson, et al., 2006). PEMFT is typically applied to treat non-union fractures (Mooney, 1990; Sharrard, 1990), avascular necrosis (Aaron, Lennox, Bunce, & Ebert, 1989), and alleviate pain in chronic musculoskeletal injuries such as osteoarthritis (Trock, et al., 1993), carpal tunnel syndrome (Weintraub & Cole, 2008), and post operative pain following breast augmentation (Hedan & Pilla, 2008).

## **2.3 Electrotherapy Interventions for Exercise-Induced Muscle Damage**

Many studies have investigated the effects of various interventions on EIMD, but only a limited number of studies have examined the effects of electrotherapies on the treatment of symptoms associated with EIMD. This review introduces the studies in which interventions categorised as electrotherapy were used for the treatment of EIMD. The interventions include ultrasound and vibration therapy (both mechanical therapies), TENS and MENS (electrical therapies), pulsed electromagnetic field therapy, diathermy (thermal therapy) and laser therapy (electromagnetic therapy).

### **2.3.1 Mechanical Therapy**

#### **2.3.1.1 Ultrasound**

Many studies have examined the efficacy of ultrasound as an intervention for the recovery of EIMD, but there is limited evidence validating its effectiveness. For example, a study by Tiidus et al., (2002) found that 11 subjects who received 8 minutes of daily-pulsed ultrasound after 50 maximal eccentric contractions of the elbow flexors had no significant attenuation of any indirect markers of muscle damage. Similar findings have also been reported in other elbow flexor studies (Aytar et al., 2008; Craig, Bradley, Walsh, Baxter, & Allen, 1999; Stay, Richard, Draper, Schulthies, & Durrant, 1998). Contrastingly, Hasson et al. (1990) found that a single 20-minute application of pulsed ultrasound significantly enhanced the recovery of muscle soreness and muscle strength of the quadriceps one-day post-EIMD. Whilst there is some evidence to suggest that therapeutic ultrasound can enhance the recovery of EIMD, it appears the large majority of literature indicates that ultrasound has little or no effect in attenuating the signs and symptoms of muscle damage.

### **2.3.1.2 Vibration**

With regards to the attenuation of symptoms associated with EIMD, Lau et al. (2011) found that 30-minutes of vibration treatment for 5 consecutive days applied to 15 subjects after performing after 60 maximal eccentric contractions of the elbow flexors was effective at attenuating muscle soreness and losses in ROM but did not affect the recovery of muscle strength, swelling or plasma CK activity. Similarly, Bakhtiary and colleagues (2007) found that 1-minute of vibration treatment applied to the knee flexors and extensors of 25 subjects prior to 30 minutes of downhill walking at 4-km per hour on a 10° incline resulted in smaller increases of muscle soreness and plasma CK activity but no affect on muscle strength recovery. This was also in accordance with the findings from Ayles, Graveson-Nielsen and Gibson (2011). It appears that like TENS, vibration treatment can be effective in the treatment of DOMS but has little effect on other markers of EIMD.

### **2.3.2 Thermal Therapy**

#### **2.3.2.1 Diathermy**

In the treatment of EIMD, Diathermy is typically applied prophylactically because its application immediately post-exercise is contraindicated. Nosaka et al. (2004) found that 10 female subjects who received 10 minutes of microwave diathermy (27.12MHz, 100W) immediately after performing 12 maximal eccentric contractions of the elbow flexors had no significant attenuation of muscle damage symptoms. Conversely, Nosaka and colleagues (2007) reported that 15 males who received 20 minutes of microwave diathermy treatment (150 W)  $18 \pm 0.4$  hours prior to performing 24 maximal eccentric contractions of the elbow flexors had significant attenuation of muscle soreness, faster recovery of muscle strength, as well smaller decreases in range of motion compared to control. Thus, it appears that the muscle temperature, time duration, and time of application prior to EIMD may influence the effectiveness of diathermy treatment.

### **2.3.3 Electrical Therapy**

#### **2.3.3.1 Transcutaneous Electrical Nerve Stimulation**

A study by Denegar and Perrin (1992) compared 5 treatment groups (8 untrained women per group) consisting of TENS, ice pack, a combination of TENS and ice pack, sham TENS and control in which the therapeutic treatment was performed 48 hours after elbow flexor exercise with a dumbbell. They reported the combination of TENS and ice pack treatment had a significant analgesic effect, but no significant effect on the recovery of muscle strength and other markers. Conversely, Craig et al. (1996) found that low and high frequency pulsating TENS applied for 20 minutes to 24 subjects (n=12 per group) after performing 24 maximal eccentric contractions had no significant effect on the recovery of muscle damage symptoms. Thus, given the aforementioned studies, TENS may have a small influence on the perception of pain in relation to muscle soreness, but it appears that TENS has little or no influence on other muscle damage markers. Given that the recovery of muscle function, most notably muscle strength, is perhaps the most important muscle damage variable (Warren, Lowe, & Armstrong, 1999), TENS appears limited as an effective electrotherapy for the treatment of muscle damage.

#### **2.3.3.2 Microcurrent Electrical Neuromuscular Stimulation**

Studies investigating the effects of MENS on the symptoms of EIMD appear to have conflicting results. Curtis and colleagues (2010) found that 20-minutes of MENS treatment employed at varying frequencies (18 - 191Hz) and an intensities (100 - 200 $\mu$ A) applied after 75 maximal voluntary eccentric contractions of the knee flexors provided significantly less soreness compared to control. Conversely, Allen et al., (1999) found that 20-minutes of MENS treatment (10 minutes at 30Hz, 200 $\mu$ A and 10 minutes at 0.3Hz, 100 $\mu$ A) had no significant effect on reducing pain or losses in ROM compared to sham treatment after exhaustive eccentric exercise of the elbow flexors using a dumbbell. In addition, Weber et al., (1994) compared between MENS, therapeutic massage and upper body ergometry groups with 8 minutes of the treatments applied immediately

after and 24 hours after maximal exhaustive eccentric contractions of the elbow flexors, and reported that none of the interventions had a significant effect on alleviating muscle soreness and maximal isometric contraction strength.

### **2.3.4 Electromagnetic Therapy**

#### **2.3.4.1 Laser**

Studies evaluating the effectiveness of laser therapy on muscle damage symptoms have been conflicting. Baroni et al., (2010) found that when 18 males (36 total) were exposed to laser therapy (810 nm, 200mW) for 3 minutes (30 seconds in each of 6 points of the quadriceps) and applied 24 ± 1 hours prior to 75 maximal eccentric contractions of the knee extensors, they had significantly smaller increases in plasma CK activity and lactate dehydrogenase, smaller decreases and faster recovery of isometric strength but no change in the recovery of muscle soreness (VAS) compared to placebo treatment. Conversely, Craig et al., (1999) showed that 4 minutes of combined low intensity laser therapy/phototherapy (660-950nm, 534mW) applied after 18 males and 18 females performed 3 sets of maximal exhaustive eccentric contractions of the elbow flexors using a dumbbell had no significant attenuating effect on any signs of muscle damage compared to placebo and control conditions. Since the exercise and laser therapy treatment protocols were different in the aforementioned studies, it is difficult to make a direct comparison between the two. However, it appears that laser therapy can provide prophylactic effects when applied approximately one day prior to EIMD of the knee extensors. Given that only one study has demonstrated the efficacy of laser therapy, further evidence is required to determine whether this therapy is an effective treatment for EIMD.



#### **2.3.4.2 Pulsed Electromagnetic Field**

To the best of our knowledge, only one study that has investigated the effects of PEMFT treatment on the signs and symptoms of muscle damage. The study by Spodaryk (2002) had 36 healthy men perform exhaustive eccentric exercise of the elbow flexors using a dumbbell, and were treated for 20 minutes of PEMFT for 5 days, starting from immediately post-exercise, had significant attenuation of muscle soreness (VAS) and smaller decreases in ROM. However, they did not report on the recovery of strength or plasma CK activity. Consequently, it remains unclear as to whether PEMFT affects the recovery of muscle function following eccentric exercise.

### **2.4 Conclusion**

The limited evidence suggests that the majority of electrotherapies are strongly effective for attenuating DOMS, enhancing the recovery of muscle function or other symptoms of EIMD. Of the electrotherapy studies reviewed, several found some effect on reductions in muscle soreness and swelling, but very few studies have found any significant effect on muscle function recovery. The recovery of muscle function, particularly the ability to generate force, is regarded as the most critical marker of muscle damage due to its impact on exercise performance and its requirement to complete activities of daily living. Given that the recovery of muscle strength is the most important marker of muscle damage, only one electrotherapy study, employing pulsed ultrasound, has reported a significant effect on the recovery of muscle strength following EIMD. This suggests that existing electrotherapies have not been particularly effective in the treatment of EIMD and a more effective electrotherapy must be established for the treatment of symptoms associated with EIMD. The electrotherapy PEMFT is believed to influence a number of physiological mechanisms including enhanced blood flow and cell membrane permeability and may have the greatest potential to enhance the healing of soft tissue injury and attenuate the symptoms associated with EIMD.

## **CHAPTER THREE**

### **METHODS**

#### **3.1 STUDY 1 – The effects of 30 minutes of e-cell and sham treatment on muscle temperature, muscle blood flow and oxygenation of the biceps brachii**

##### **3.1.1 Participants**

Nine healthy male volunteers ( $23.6 \pm 3.7$  years,  $176.5 \pm 4.5$  cm,  $74.6 \pm 5.9$  kg) were recruited from the staff and students of Edith Cowan University for this study following approval from the Human Research Ethics Committee. Participants were free from musculoskeletal injuries to the upper body and none were taking medication or dietary supplementation before participating. All participants completed an informed written consent form and a medical questionnaire prior to testing.

##### **3.1.2 Experimental Design**

A company (Global Energy Medicine, WA, Australia) provided two identical e-cell™ devices; one being the actual e-cell™ and the other a sham device that did not generate electromagnetic pulses. The investigator and participants were blinded to the devices (only informed as Device A and Device B). Participants were required to attend one testing session where one arm received e-cell™ treatment and the other arm received sham treatment. The treatment device used and the choice of arm (dominant arm versus non-dominant arm) were chosen at random and counterbalanced among the participants.

The dependant variables measured were muscle temperature, blood flow (total haemoglobin volume) and muscle oxygenation (tissue oxygenation index). Changes in the measures after treatment were compared between the e-cell™ and sham treatment.

### 3.1.3 e-cell™ and Sham Treatments

Each subject lay supine on a massage table and requested to keep both arms as still as possible until the treatment period had concluded to minimise changes in blood flow and muscle temperature due to movement. The devices (similar in shape and size to a computer mouse, powered by a rechargeable internal battery and weighing approximately 140 g) were placed longitudinally along the lateral aspect of the biceps brachii and held in place with adhesive tape, aligning the midpoint of the device with the mid-belly of the biceps brachii (Figure 2). The e-cell™ and sham treatments were applied for 30 min. When the devices were switched on, green and red lights would flash to indicate they were operating and then turned off after 30 min of treatment indicated by the sound of a double beep. A stopwatch was also used to ensure the 30 min treatment time was adhered to.



*Figure 2: e-cell™ and sham treatments applied to the subjects arm.*

### 3.1.4 Muscle Temperature

Changes in muscle temperature was measured by a thermometer (model N550; Nikkiso- YSI Co., Ltd, Tokyo Japan), with a needle thermistor probe as shown in figure 3 (model N451; Nikkiso- YSI Co., Ltd, Tokyo Japan) inserted to a depth of 20mm, corrected for skin thickness, at a 45° angle into the biceps brachii, and the muscle temperature was recorded after stabilisation. The thermometer and thermistor was calibrated according to the manufacturers specifications before testing each subject. The sterilised thermistor probe (22 gauge, 70mm) was then inserted at 4 sites (2 measurements for each arm). The first site was standardised at 10mm laterally adjacent to the NIRS probe determined as one-third the distance from the lateral epicondyle of the humerus to the lateral aspect of the acromion process, and the second site was 5 mm above the first site. Measurements were taken 5 min before and 30 min (immediately after) after treatment. The temperature measures were counterbalanced between participants as to whether e-cell or sham arm was recorded first.



*Figure 3: Muscle temperature thermistor probe needle (a) and 2 insertion sites (b).*

### 3.1.5 Muscle Oxygenation and Blood Flow

Changes in muscle oxygenation and blood flow in the biceps brachii was measured using a NIRO-200 (Hamamatsu Photonics, Japan) NIRS system (Figure 4). The NIRO-200 optical probe unit consists of one emitter (laser emitting diodes of 775, 810 and 850 nm) and one detector (two silicon photodiodes separated by a 6 mm centre-centre distance) that measures changes in oxygenated-haemoglobin ( $O_2Hb$ ), deoxygenated-haemoglobin ( $HHb$ ) and the total haemoglobin volume ( $tHb = O_2Hb + HHb$ ). The tissue oxygenation index (TOI) can then be expressed as a percentage ( $TOI = O_2Hb / tHb \times 100$ ). Thus changes observed in  $tHb$  can be considered as an indirect measure of changes in blood flow and changes in TOI reflect the percentage of  $O_2$  remaining in the bloodstream. The NIRS system was calibrated prior to each testing session according to the manufacturers standard procedures. The probe unit was firmly attached to the skin at the mid-belly of the biceps brachii with double-sided adhesive tape to ensure no sliding of the probe on the skin. The NIRS probe in relation to the treatment device was aligned adjacently with minimal direct contact between the two (less than 140 g of weight), and the midpoint of both was aligned with the mid-belly of the biceps brachii. The NIRO-200 system recorded TOI and  $tHb$  levels from 5 min prior to the onset of treatment and continued until the treatment concluded (30 min). Baseline measures of TOI and  $tHb$  were determined as the mean value over 1 min before the onset of treatment following 4 min of complete rest. TOI and  $tHb$  were also continuously recorded using the PowerLab (Australia) and then averaged for every 10 mins (0, 10, 20 and 30 min) and used for further analysis.



*Figure 4: NIRS probe located on the biceps brachii.*

### 3.1.6 Statistical Analysis

Changes in muscle temperature from baseline to 30 min (immediately post-treatment) were analysed using a paired t-test and changes in TOI and tHb from baseline to 30 min (0, 10, 20 and 30 minutes) were compared between the e-cell™ and sham treatments using a two-way repeated measures analysis of variance (ANOVA) using SPSS for Mac (Version 19, SPSS Corp, Chicago, Illinois). Data analysis was performed by a statistical significance set at  $P < 0.05$ .

## 3.2 STUDY 2 – The effects of e-cell and sham treatment on muscle damage symptoms

### 3.2.1 Participants

A total of 16 volunteers, 8 men ( $26.1 \pm 6.1$  years;  $177.1 \pm 7.8$  cm;  $80.1 \pm 13.4$  kg) and 8 women ( $23.4 \pm 4.2$  years;  $170.1 \pm 10.4$  cm;  $67.1 \pm 9.6$  kg), were recruited for this study. The sample size was calculated by the equation “ $N=2+C(s/d)^2$ ” where “N” is the number of participants, “C” is a constant that depends on values chosen for  $\alpha$  and  $\beta$  (when  $\alpha=0.05$ ,  $\beta=0.8$ ,  $C=7.85$ ), “s” is the standard deviation of the population means and “d” is the difference to be detected. Based on the data from a previous study using the same eccentric exercise (Zainuddin, et al., 2006), muscle soreness measures are expected to be around 50 with a standard deviation of 20 ( $50 \pm 20$ mm). It is assumed that 30% reduction in muscle soreness is physiologically significant and the e-cell™ treatment could result in 15mm reduction in muscle soreness over all with a power of 80% and a significance level of 5%. Therefore, “s” is 20 and “d” is equal to 15 for the equation.

$$N = 2 + C(s/d)^2 = 2 + (7.85)(20/15)^2 = 15.95$$

Thus, 16 participants were recruited for this study, which was divided into 8 men and 8 women. All participants completed an informed written consent form and medical questionnaire prior to the onset of the study. Female participants were also required to complete a menstrual history questionnaire. Ethical approval from the Human Research Ethics Committee was ensured

prior to commencing the study. The participants had not performed resistance training of the upper limbs for at least six months prior to the study. They did not have any current or previous injury of the elbow joints, elbow flexors, tendons and other tissue around the joints, had no neuromuscular disorders and were not taking any medications. Participants were requested not to change their lifestyle and diet, not to take any anti-inflammatory drugs or nutritional supplements and not to perform unaccustomed exercise during the experimental period.

### **3.2.2 Experimental Design**

This was a double-blinded, randomised, crossover design study. As previously mentioned, the company provided two identical e-cell™ devices; one being the actual e-cell™ and another that did not generate electromagnetic pulses (sham). Participants performed a bout of maximal eccentric exercise of the elbow flexors of each arm 4 weeks apart. Female participants performed the exercise during the mid-follicular phase (lowest oestrogen and progesterone levels) of their menstrual cycle, since oestrogen may have a protective effect on skeletal muscle and may therefore reduce the markers of eccentric exercise-induced muscle damage (Kendall & Eston, 2002). One arm received e-cell™ treatments and the other arm received sham treatments on five occasions such as 30 minutes after the exercise, and 1, 2, 3 and 4 days following the exercise. The treatment duration was 30 minutes for each occasion, which is normally used in the e-cell™ treatment. The experiment period included one block of 9 days for the first bout (familiarisation session, reliability testing session 3 days before exercise, before and immediately after exercise, 1, 2, 3, 4, 5, and 7 days post-exercise) and one block of 7 days of testing for the second bout (before and immediately after exercise, 1, 2, 3, 4, 5, and 7 days post-exercise). In the testing session, maximal voluntary isometric contraction (MVC) torque of the elbow flexors, range of motion (ROM) of the elbow joint, upper arm circumference, muscle soreness and pressure pain threshold (PPT) of the elbow flexors, and blood samples to assess plasma creatine kinase (CK) activity were taken. Changes in these measures over time were compared between the conditions. To examine the acute effects of the

treatment, MVC torque, ROM, upper arm circumference, muscle soreness and PPT measurements were taken immediately after the treatments performed 30 min, and 1, 2, 3 and 4 days post-exercise, and were also compared between conditions.

### **3.2.3 Familiarisation Session**

Participants participated in a familiarisation session before they participated in the study. Participants were restricted to performing 2 maximal isometric contractions at  $60^\circ$  and 2 maximal isokinetic concentric contractions at  $30^\circ \cdot s^{-1}$  and  $210^\circ \cdot s^{-1}$  during this session on the lever arm of the isokinetic dynamometer (Cybex 6000, Lumex Inc. Runkonkoma, USA). No eccentric contractions were performed to minimise any muscle damage to the elbow flexors. However the participants were shown and briefed on the eccentric exercise protocol. Measurements including ROM, upper arm circumference, muscle soreness and PPT, and plasma CK activity were also demonstrated.

### **3.2.4 Eccentric Exercise**

The exercise protocol consisted of 10 sets of 6 maximum voluntary eccentric contractions of the elbow flexors against the lever arm of the isokinetic dynamometer moving at a constant velocity of  $30^\circ \cdot s^{-1}$ . This protocol has been shown to induce muscle damage in previous studies (Chapman, et al., 2006; Chen, Nosaka, & Sacco, 2007; Saka et al., 2009). Participants were randomly chosen to perform the initial bout of exercise with either their dominant or non-dominant arm and they were individually positioned on a seated preacher arm curl bench with a supinated forearm position and the elbow aligned with the axis of rotation of the dynamometer. The elbow joint was forcibly extended from a flexed position ( $90^\circ$ ) to a fully extended position ( $0^\circ$ ) in 3 seconds (Figure 5). Participants were verbally encouraged to generate a maximal isometric force at the starting position and to maximally resist against the elbow extending action throughout the full range of motion. After each eccentric action, the isokinetic dynamometer returned the arm to the flexed position at a constant velocity of  $9^\circ \cdot s^{-1}$  while participants were asked to relax the arm, creating a 10 second



passive recovery between contractions. The rest period between sets was 3 minutes. Torque and displacement signals were obtained directly from the dynamometer output and captured using a data acquisition hardware and software system (Power Lab, Australia). Average peak torque (Nm) was determined as the mean peak torque for 6 eccentric contractions over 10 sets and work during exercise (J) was calculated as the average peak work of the 6 repetitions over 10 sets of the eccentric exercise bout.



*Figure 5: Eccentric exercise protocol. Each eccentric contraction commenced at an elbow joint of  $90^{\circ}$  (a) and finished at  $0^{\circ}$  (b).*

### 3.2.5 e-cell™ and sham Treatments

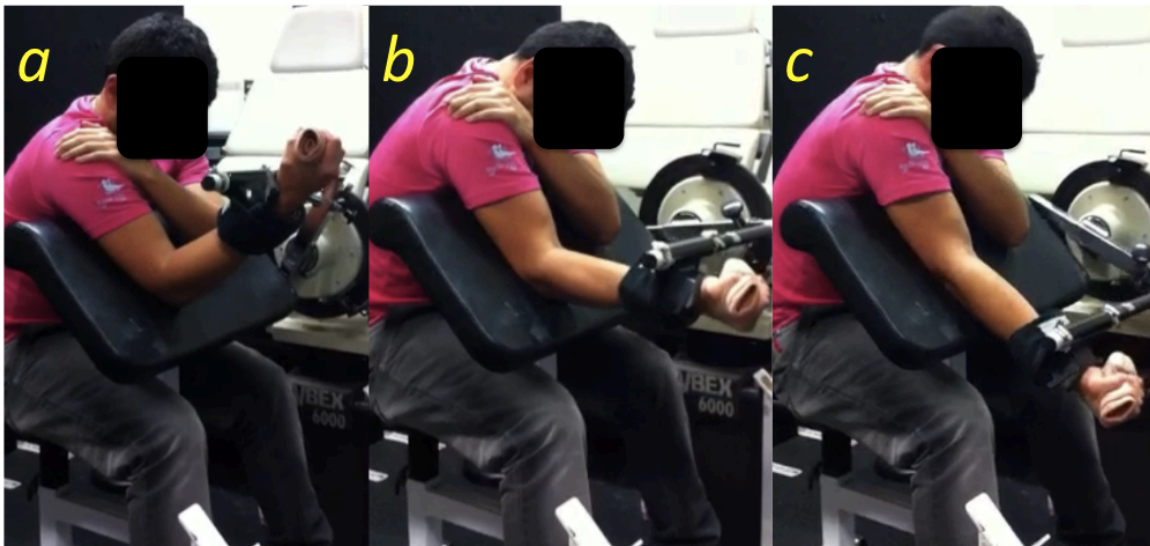
The e-cell™ (Global Energy Medicine, Australia) was applied to a randomly assigned exercise arm and the other exercised arm received sham treatment (the device was applied without electromagnetic pulses). The order of the conditions (e-cell™, sham) as well as the arm dominance was counterbalanced amongst the participants. The device (similar in shape and size to a computer mouse, is powered by a rechargeable internal battery and weighs approximately 140 g) was placed longitudinally along the lateral aspect of the biceps brachii and held in place with a specially designed Velcro strap, aligning the midpoint of the device with the mid-belly of the biceps brachii (Figure 6). The Velcro strap (containing the device) was secured on the upper arm so that the position of the device would not alter throughout the entire treatment period, while also ensuring the strap was not too tight as to induce the enhanced recovery effects of compression. The subject was seated in a chair during the entire treatment period. The e-cell™ treatment had a pulse duration of 380  $\mu$ s, frequency of 75 Hz with the intensity of the electromagnetic pulse set at 10 mT.



*Figure 6: e-cell™ and sham treatments applied to a subject and held in place with a specially designed Velcro strap.*

### 3.2.6 Maximal Voluntary Isometric Contraction (MVC) Torque

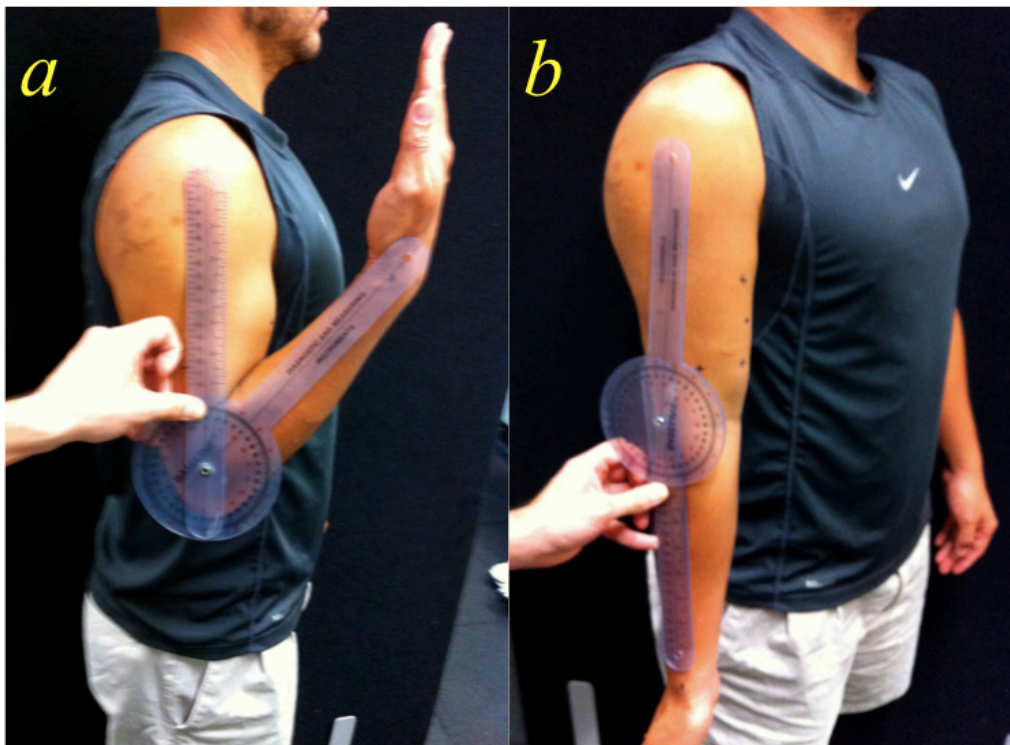
MVC torque was measured on a Cybex isokinetic dynamometer with a HUMAC system (CSMI Medical Solutions, Massachusetts, USA) that was connected to a power lab system (Powerlab, ADInstruments, Castle Hill, Australia). The participants were positioned as they were for the eccentric exercise protocol. As shown in Figure 7, participants performed two 3-s maximal isometric contractions at elbow joint angles of  $90^\circ$ ,  $60^\circ$  and  $30^\circ$  (where  $0^\circ$  represents a fully extended elbow joint angle) in this order with 30 seconds rest between contractions at the same joint angle and 60 seconds rest between contractions at different joint angles. Participants were asked to generate maximal force as fast as possible when a signal was given. Verbal encouragements were given during all muscle strength testing. The higher torque of the two measures was used for further analysis.



*Figure 7: Measurements of MVC torque at  $90^\circ$  (a),  $60^\circ$  (b), and  $30^\circ$  (c) on the preacher arm curl bench and isokinetic dynamometer.*

### 3.2.7 Range of Motion (ROM)

A plastic goniometer was used to measure ROM of the elbow joint. The ROM was calculated as the difference between two types of joint angles; extended elbow joint angle (EANG) and flexed elbow joint angle (FANG) (Figure 8). The EANG was determined when the subject attempted to fully extend the elbow joint as much as possible in the same setting as that of RANG. The FANG was determined when the subject attempted to fully flex the elbow joint to touch the shoulder of the same side with the palm. To measure these, a semi-permanent ink pen was used to create a mark on the skin to achieve a consistent measurement. The landmarks where the marks were placed included the lateral epicondyle of the humerus, the acromion process and the mid point of the styloid process of the ulna and radius. Measurements were taken twice for each type of joint angle and the mean value of the two measurements was used for ROM by subtracting FANG from EANG.



*Figure 8: Measurements of FANG (a) and EANG (b) using a goniometer.*



### 3.2.8 Upper Arm Circumference (CIR)

A constant tension tape was used to measure the CIR of the exercise limb while the arm was hanging relaxed by the subject's side. The measurements were taken from three sites, the mid-belly of the biceps brachii determined as half way between the lateral aspect of the acromion process and lateral epicondyle (Deighan, De Ste Croix, Grant, & Armstrong, 2006), and 3 cm above and below the mid-belly. Each site was marked with a semi-permanent ink marker to obtain consistent measures. Measurements were taken twice at each site with the mean of the two measurements being recorded. The mean measurement from the three sites were summated and averaged to produce a CIR measure used for further analysis.



*Figure 9: Measurements of upper arm circumference with constant tension tape.*

### 3.2.9 Muscle Soreness

The level of muscle soreness was assessed using a 100 mm visual analogue scale (VAS), in which 0 mm indicated no pain and 100 mm represented extreme pain. The participants were asked to mark their level of perceived soreness on the VAS while the corresponding joint was extended by the investigator with the resulting extension soreness measure used for further analysis. Palpation was also applied using the index and middle fingers slowly in a circular motion 5 times on three sites of the upper arm including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly. One measurement was taken from each site, which was used for further analysis.



*Figure 10: The investigator assessed extension soreness (a) and muscle soreness upon palpation of the upper arm (b) on the preacher arm curl bench.*

### 3.2.10 Pressure Pain Threshold (PPT)

PPT is a measure that corresponds with muscle tenderness. It was recorded using an electronic algometer (Somedic AB, Sweden) with a stimulation area of 1.0 cm<sup>2</sup>. The probe head of the algometer was placed perpendicular to the measurement sites, which included the mid-belly of the biceps brachii, 3 cm above and below the mid-belly. Force was gradually applied until the subject reported the first feeling of noticeable pain. The PPT was performed twice with a 30-s interval between measures. The absolute value (in kPa) corresponding to the amount of force applied was noted and the mean of the two measures for each site was recorded. The recorded absolute value (kPa) was then converted into a percentage with pre-exercise values set at 100%.



*Figure 11: Measurements of pressure pain threshold using an electronic algometer.*

### 3.2.11 Plasma CK Activity

Blood samples were collected from the participants by making a small prick on the end of a finger and 30  $\mu$ l of blood was loaded onto a CK test strip (Reflotron CK, Inverness Medical, Cheshire, UK) and measured by a Reflotron (Roche Diagnosis, Germany). If the plasma CK value exceeded 1500 U/L, the blood sample was diluted with saline solution.



*Figure 12: Measurement of plasma CK activity using a Reflotron.*



### 3.2.12 Statistical Analysis

Data analyses were performed by a statistical software package (SPSS version 19.0) with a statistical significance set at  $p < 0.05$ . Intra-class correlation coefficient (ICC) and coefficient of variation (CV) statistics were used to calculate the test-retest reliability of all the dependent variables (Table 1). The comparison between male and female participants for the changes in the dependent variables over time (pre-, immediately post-, 60 minutes, 1-5 and 7 days post) was performed using a two-way repeated measures ANOVA. To analyse the acute effects, changes in measures before and after treatment for days 1-4 were compared between arms by a two-way repeated measures ANOVA. Changes in the dependent variables over time were also compared between arms by two-way repeated measures ANOVA. If the ANOVA showed a significant difference between conditions for main or interaction effect, a LSD post hoc test was applied to find significant differences between pairs of observations. To examine the magnitude of effect between exercise and treatment, an independent  $t$ -test was performed. Data are presented as means  $\pm$  SEM, unless otherwise stated.

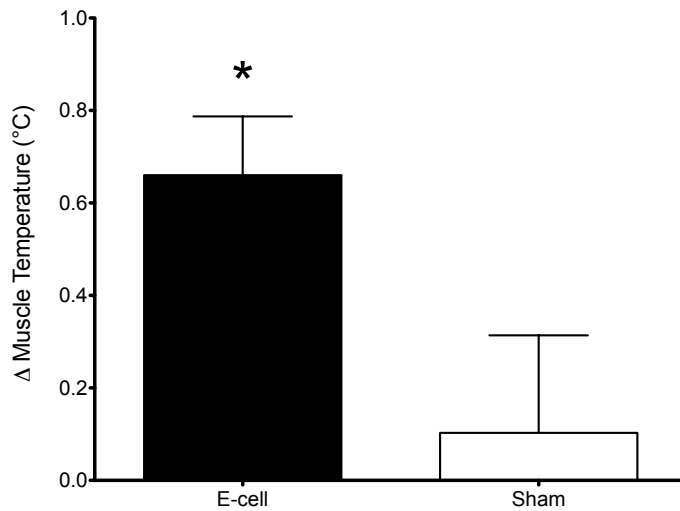
## CHAPTER FOUR

### RESULTS

#### 4.1 STUDY 1

##### 4.1.1 Muscle Temperature

There were no significant differences ( $t=2.974$ ,  $df=8$ ,  $p=0.324$ ) in pre-exercise measures between e-cell™ ( $33.64 \pm 0.38^{\circ}\text{C}$ ) and sham ( $33.97 \pm 0.20^{\circ}\text{C}$ ) treatment arms. Figure 13 shows the changes in biceps brachii muscle temperature, which increased ( $p<0.05$ ) after e-cell™ treatment only and was  $0.55 \pm 0.22^{\circ}\text{C}$  higher ( $t=2.751$ ,  $df=8$ ,  $p=0.033$ ) than after sham treatment.



*Figure 13: Changes in Biceps Brachii muscle temperature after 30 mins of e-cell™ and Sham treatment. \*Indicates significant difference ( $p<0.05$ ) between e-cell™ and sham treatments.*

#### 4.1.2 Total Haemoglobin Concentration (tHb)

The mean changes in tHb during e-cell and sham treatment are shown in Figure 14. No significant differences ( $F_{1,8}=0.324$ ,  $p=0.808$ ) in the changes in tHb over time were evident between e-cell™ and sham treatments.

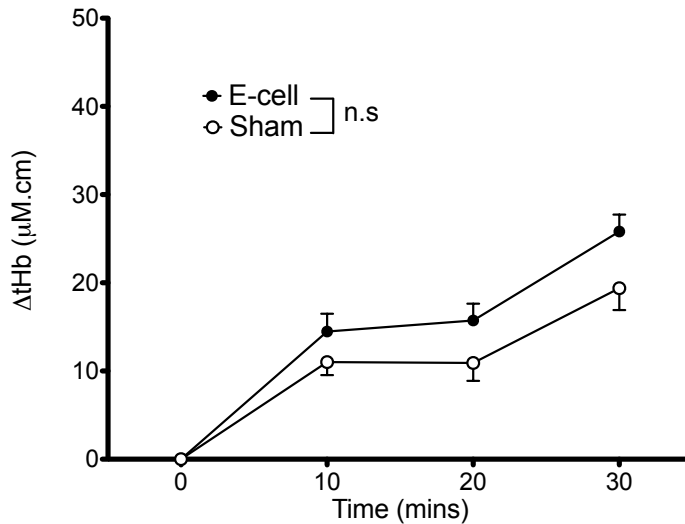


Figure 14: Changes in total haemoglobin concentration at 10, 20 and 30 mins after e-cell™ and sham treatment. n.s. No significant difference was seen between treatment conditions.

#### 4.1.3 Tissue Oxygenation Index (TOI)

There were no significant ( $F_{1,8}=0.148$ ,  $p=0.710$ ) changes in TOI from baseline to the end of treatment for both conditions (Figure 15). Similarly no significant differences ( $F_{1,8}=2.038$ ,  $p=0.191$ ) in the mean changes of TOI over time were evident between e-cell™ and sham treatments.

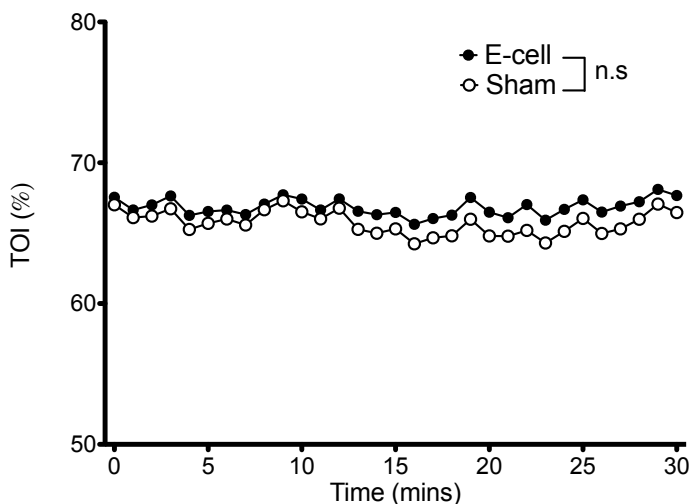


Figure 15: Mean tissue oxygenation during 30 minutes of e-cell™ and sham treatments.

## 4.2 STUDY 2

### 4.2.1 Reliability of Measurements

Intraclass correlations (ICC) and coefficient of variation (CV) were used to assess the test-retest reliability over the reliability and pre-exercise testing sessions for the dependant variables (Table 1). Muscle soreness was not determined as all participants recorded scores of zero on the VAS for extension and palpation soreness. Values of 0.89 – 1.0 for ICC showed substantial reliability of the measures. Additionally, all CV values were less than 10% indicating good reliability.

**Table 1:** Test-retest reliability of dependent variables using intraclass correlation coefficient (ICC) and coefficient of variation (CV; 95% CI)

Variable	ICC	CV
MVC torque at 30°	0.95	4.2%
MVC torque at 60°	0.96	4.0%
MVC torque 90°	0.98	3.7%
ROM	0.97	0.6%
CIR	0.95	0.5%
PPT	0.89	8.4%
Plasma CK Activity	0.93	8.4%

#### 4.2.2 Gender Effects

A comparison was made for the changes in muscle damage markers, regardless of treatment condition, between male (n=8) and female (n=8) participants post-eccentric exercise (Table 2). This was done to establish whether gender specific differences existed for any of the criterion measures. No significant gender differences were found for the dependent variables except for upper arm PPT (average of 3 bicep sites), with male participants recovering to baseline values by day 5 compared to females that were still 9% below baseline values but had recovered by day 7. Even if there was a gender effect for PPT, the counterbalanced arm-to-arm experimental design allows us to combine the data so that a comparison can still be made between e-cell™ and sham conditions, regardless of gender.

**Table 2:** Interaction effect between Male and Female groups

Variable	Group		Time		Interaction	
	<i>F</i> value	<i>p</i> value	<i>F</i> value	<i>p</i> value	<i>F</i> value	<i>p</i> value
<b>Peak Torque (Nm)</b>	0.546	0.472	390.000	<0.000	1.639	0.110
<b>Total Work (Nm)</b>	0.826	0.378	299.662	<0.000	1.748	0.084
<b>MVC 30° (Nm)</b>	0.177	0.680	67.184	<0.000	2.006	0.061
<b>MVC 60° (Nm)</b>	0.594	0.453	115.064	<0.000	2.051	0.055
<b>MVC 90° (Nm)</b>	0.165	0.691	116.473	<0.000	1.892	0.078
<b>ROM (degrees)</b>	3.775	0.071	47.427	<0.000	1.727	0.099
<b>CIR (mm)</b>	3.583	0.065	14.817	<0.000	1.295	0.253
<b>SOR-Pal (mm)</b>	3.413	0.071	81.282	<0.000	1.605	0.122
<b>SOR-Ext (mm)</b>	0.011	0.918	16.476	<0.000	0.490	0.861
<b>PPT (kPa)</b>	8.615	0.005	91.940	<0.000	5.670	<0.000
<b>CK activity (U/L)</b>	0.010	0.920	11.772	<0.000	0.386	0.886

*Note: No significant interaction effect exists between Male and Female participants*

#### 4.2.3 Baseline Values comparing between e-cell™ and sham Conditions

There were no significant differences ( $p>0.05$ ) for any of the pre-exercise values between e-cell™ and sham treatment groups (Table 3) for MVC torque, ROM, CIR, palpation (average of 3 sites) and extension soreness, PPT (average of 3 sites) and plasma CK activity.

**Table 3:** Absolute baseline values for e-cell™ and sham treatment groups

Variable	E-cell	Sham	<i>F</i> value	<i>df</i>	<i>p</i> value
MVC torque at 30° (Nm)	33.8 ± 3.9	35.3 ± 4.7	1.524	1,15	0.236
MVC torque at 60° (Nm)	43.5 ± 6.7	44.3 ± 8.5	0.474	1,15	0.502
MVC torque 90° (Nm)	51.4 ± 4.5	53.6 ± 5.2	2.478	1,15	0.136
ROM (degrees)	136.1 ± 2.2	136.9 ± 2.9	0.218	1,15	0.668
CIR (mm)	282.3 ± 6.4	283.6 ± 2.5	0.521	1,15	0.459
Palpation Soreness (mm)	0.1 ± 0.1	0.1 ± 0.1	0.000	1,15	1.000
Extension Soreness (mm)	0.1 ± 0.1	0.1 ± 0.1	0.000	1,15	1.000
PPT (kPa)	376.4 ± 12.6	384.1 ± 16.7	0.325	1,15	0.612
Plasma CK Activity (U/L)	121.5 ± 47.6	131.7 ± 66.0	0.243	1,15	0.629

*Note: No significant baseline differences between e-cell™ and sham treatments*

#### 4.2.4 Peak Torque during Exercise

There were no significant differences ( $F_{1,15}=0.093$ ,  $p=0.765$ ) for the changes in mean peak torque (mean of 6 contractions for each set over 10 sets) during the eccentric exercise between e-cell™ and sham treatment arms (Figure 16). The average peak torque decreased significantly by approximately 40% over the 10 sets for both treatment conditions.

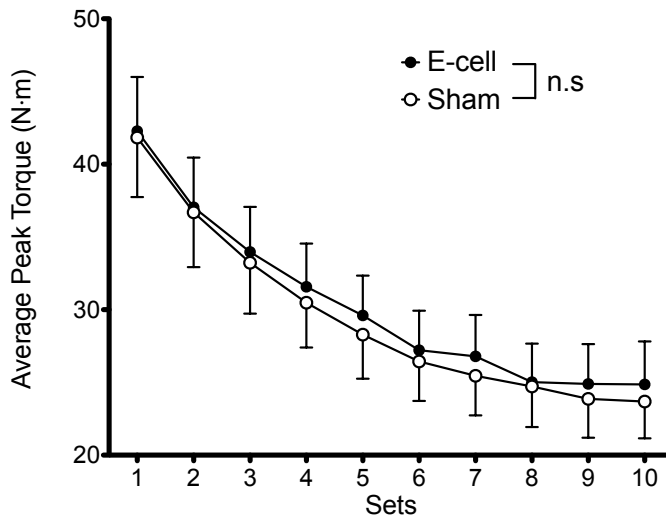


Figure 16: Changes in average peak torque for 6 contractions over 10 sets for e-cell™ and sham treatment conditions. N.s: No significant difference was seen between the arms.

#### 4.2.5 Work During Exercise

There were no significant differences ( $F_{1,15}=0.543$ ,  $p=0.473$ ) in the total work completed for each of the ten sets of eccentric exercise between arms for both e-cell™ and sham treatment conditions (Figure 17). Total work completed for the first set was approximately 540 J, which then decreased significantly by almost 44% from the first to the final set. The total work over the 10 sets was  $3875 \pm 79.8$  J and  $3799 \pm 75.4$  J for the e-cell™ and sham treatment conditions respectively.

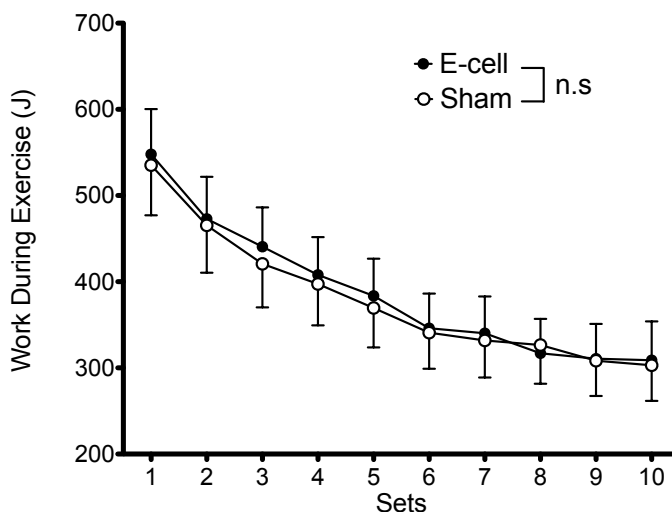


Figure 17: Changes in total work for 6 eccentric contractions over 10 sets for e-cell™ and sham treatment conditions. N.s: No significant difference was seen between the arms.

#### 4.2.6 Acute Effects of e-cell™ and sham treatments

Changes in criterion measures after exercise were compared between the e-cell™ and sham treatment to evaluate the efficacy of e-cell™ treatment. There were no significant differences between conditions for any of the pre-exercise criterion measures however all criterion variables changed significantly ( $p<0.05$ ) following the eccentric exercise. There was no significant acute effect ( $p<0.05$ ) for the time course changes (days 1 – 4) between e-cell™ and sham conditions for any of the dependent variables (Figures 18 – 22).

##### 4.2.6.1 MVC torque

No significant differences ( $F_{1,15}=0.059-1.692$ ,  $p=0.213-0.811$ ) were found for the changes in MVC torque between e-cell™ and sham treatments for days 1 to 4, and for any of the elbow joint angles. However, MVC torque decreased significantly ( $p<0.05$ ) after the 30 minutes of treatment for both conditions (Figure 18). The average magnitude of decrease in strength among participants from pre- to post-treatment was  $7.5 \pm 1.0\%$  for e-cell™ and  $7.9 \pm 1.3\%$  for sham conditions.

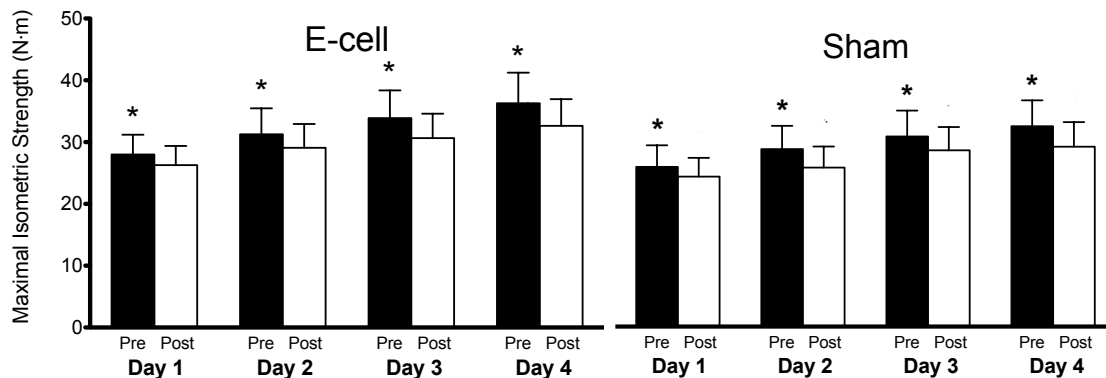


Figure 18: Changes in MVC torque at 60° before (Pre) and immediately after (Post) treatments for days 1 – 4 after eccentric exercise for e-cell™ and sham treatment conditions. \* Indicates significant difference ( $p<0.05$ ) between Pre and Post.



#### 4.2.6.2 ROM

There were no significant changes ( $F_{1,15}=0.546$ ,  $p=0.471$ ) in ROM measures from pre- to post-treatment for days 1 to 4 for both treatment conditions (Figure 19).

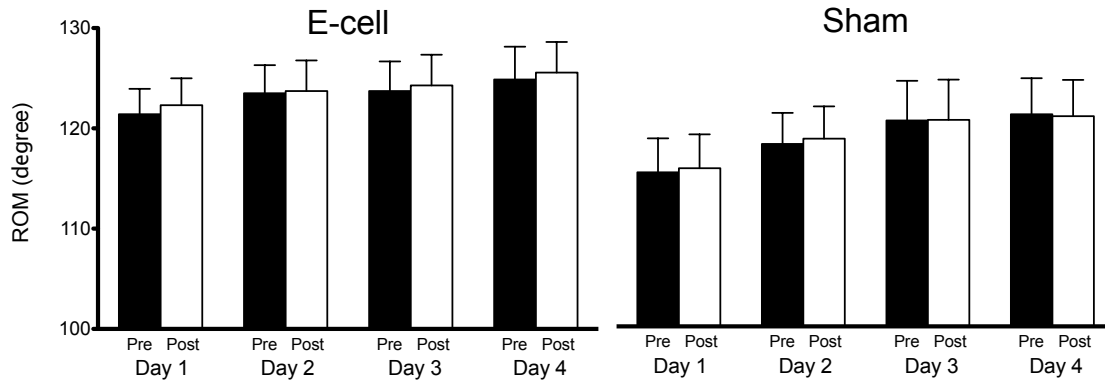


Figure 19: Changes in range of motion from before (Pre) and immediately after (Post) treatment for days 1 – 4 after eccentric exercise for e-cell™ and sham treatment conditions.

#### 4.2.6.3 CIR

No significant changes ( $F_{1,15}=1.911$ ,  $p=0.144$ ) in CIR were evident from pre- to post-treatment for days 1 to 4 for both e-cell™ and sham treatments (Figure 20).

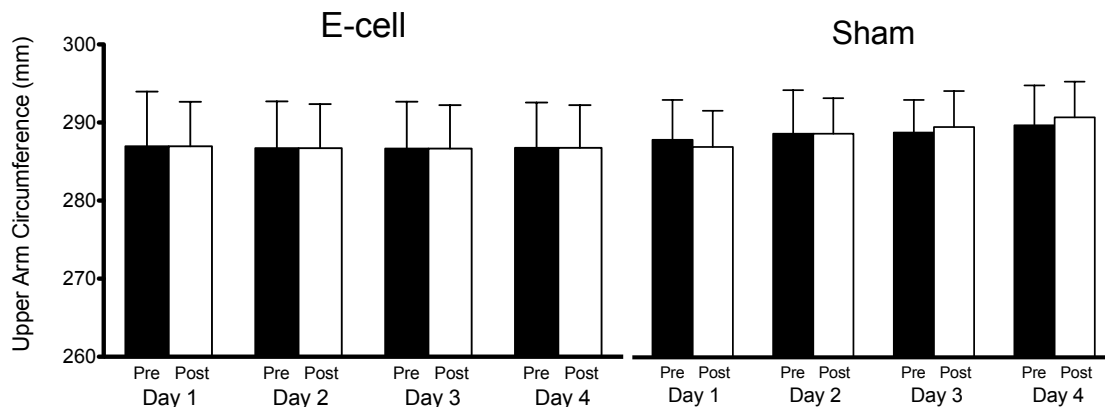


Figure 20: Changes in CIR (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) from before (Pre) and immediately after (Post) treatment for days 1 – 4 after eccentric exercise for e-cell™ and sham treatment conditions.

#### 4.2.6.4 Muscle Soreness

Muscle soreness with palpation ( $F_{1,15}=0.647, p=0.434$ ) and extension ( $F_{1,15}=0.148, p=0.706$ ) was not changed from pre- to post-treatment for days 1 to 4 for e-cell™ and sham conditions. Figure 21 represents the muscle soreness measures during palpation, which was similar for extension muscle soreness.

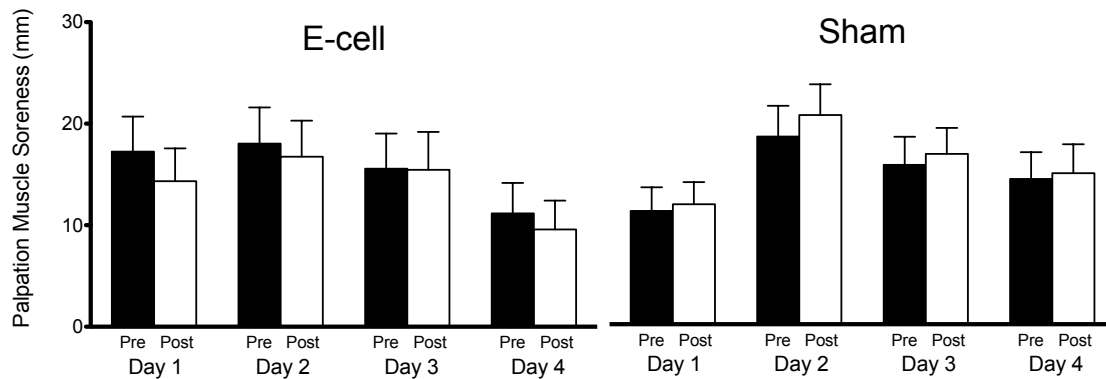


Figure 21: Changes in palpation muscle soreness (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) from before (Pre) and immediately after (Post) treatment for days 1 – 4 after eccentric exercise for e-cell™ and sham treatment conditions.

#### 4.2.6.5 PPT

Upper arm PPT ( $F_{1,15}=1.431, p=0.247$ ) did not show any significant changes from pre- to post-treatment for days 1 to 4 for either e-cell™ and sham conditions. Figure 22 represents PPT of the upper arm (average of 3 biceps sites).

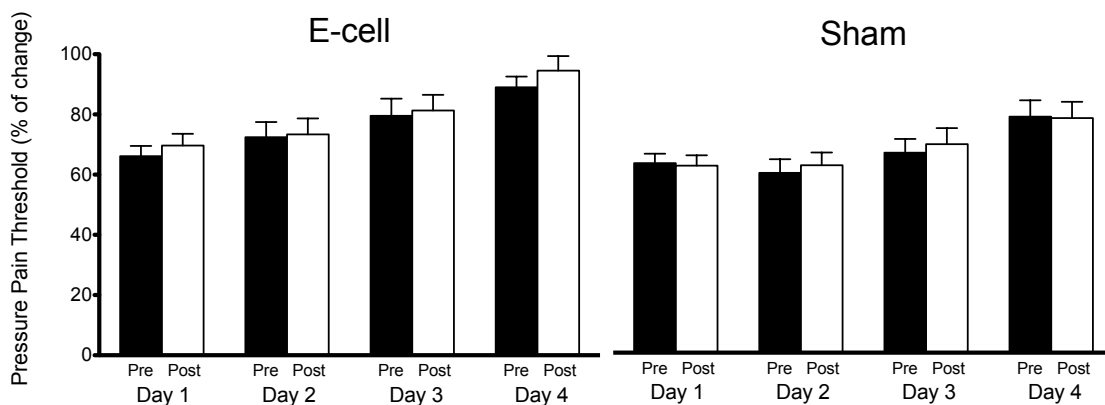


Figure 22: Changes in acute upper arm PPT (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) from before (Pre) and immediately after (Post) treatment for days 1 – 4 after eccentric exercise for e-cell™ and sham treatment conditions.

#### 4.2.7 Effect of Treatments on Recovery after Eccentric Exercise

Changes in the criterion measures post exercise were compared between e-cell™ and sham treatments to examine the therapeutic effect of the treatment.

##### 4.2.7.1 MVC torque

Figure 23 shows the changes in MVC torque at 60°, and the changes at other angles were similar to that shown. MVC torque decreased significantly ( $p<0.05$ ) immediately post-exercise by approximately 55% from baseline but there was no significant difference ( $F_{1,15}=0.731$ ,  $p=0.406$ ) between conditions. However, there was a significant ( $F_{1,15}=8.903$ ,  $p=0.009$ ) interaction effect between conditions, such that following e-cell™ treatment MVC torque had recovered to 91% of baseline measures compared to only 81% for sham condition after 7 days. This recovery was similar for elbow joint angles 30° (97% cf. 82%) and 90° (90% cf. 81%) for e-cell™ and sham treatments respectively. Following post-hoc tests, significant differences were found at days 2, 5 and 7 between conditions. This was similar for other elbow joint angles that reported significant differences between conditions on days 5 and 7.

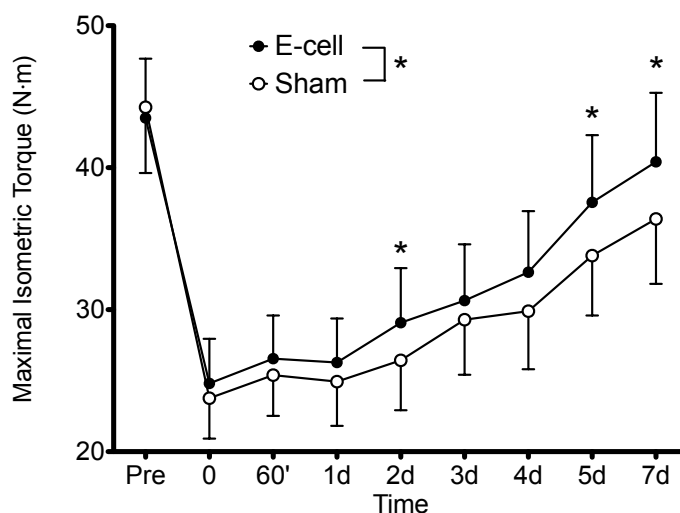


Figure 23: Changes in MVC-60° torque at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise between e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.7.2 ROM

Figure 24 shows the changes in ROM over 7 days. Immediately post-exercise, ROM decreased significantly ( $p<0.05$ ) by 16% from baseline and there were no significant differences ( $F_{1,15}=0.147$ ,  $p=0.707$ ) between conditions. However, a significant ( $F_{1,15}=2.546$ ,  $p=0.013$ ) interaction effect was found between conditions, with a faster rate of ROM recovery seen in the e-cell™ (97%) compared with sham (94%) treatment after 7 days. Post-hoc tests revealed a significant difference on day 1 between conditions.

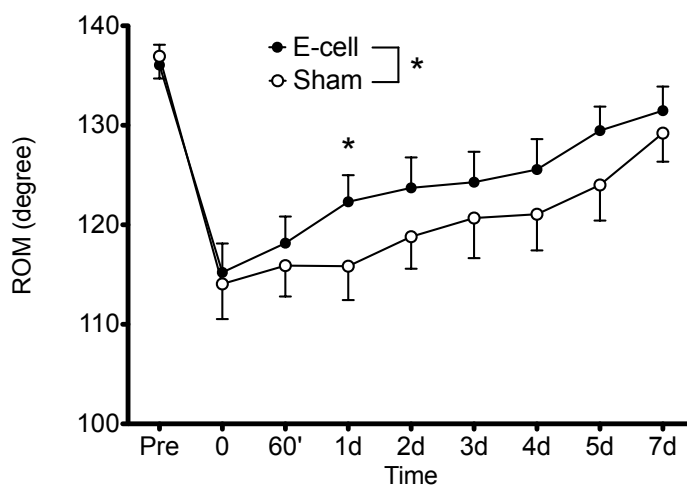


Figure 24: Changes in range of motion at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise for e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.7.3 CIR

Figure 25 shows the changes in CIR (average of 3 sites) from baseline, which was similar for each of the three sites that were combined for the CIR measures. CIR increased significantly ( $p<0.05$ ) immediately post-exercise for both conditions compared to baseline but there was no significant difference ( $F_{1,15}=0.057$ ,  $p=0.871$ ) between conditions. However, there was a significant difference ( $F_{1,15}=10.225$ ,  $p<0.000$ ) between conditions over 7 days, such that following sham treatment, CIR increased ( $p<0.05$ ) from immediately post-exercise compared to e-cell™ treatment where there was no increase in CIR from immediately post-exercise to day 7. CIR peaked on day 5 for both conditions with  $54.1 \pm 8.4\%$  less swelling after e-cell™ ( $5.0 \pm 0.8\text{mm}$ ) compared to sham treatment ( $10.9 \pm 1.3\text{mm}$ ). Significant differences in CIR were seen at 60 minutes, 2 – 5 and 7 days post exercise between conditions following post-hoc tests.

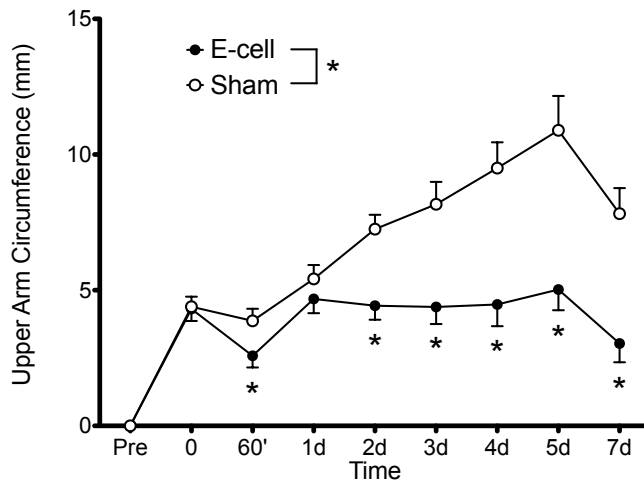


Figure 25: Changes in CIR at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise for e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p < 0.05$ ).

#### 4.2.7.4 Muscle Soreness

Figure 26 shows the changes in palpation muscle soreness based on VAS upon palpation for the arm. Muscle soreness developed from 1-day post-exercise for both conditions; however, there was significantly ( $F_{1,15} = 6.158$ ,  $p = 0.010$ ) less palpation soreness of the upper arm (average of 3 bicep sites) after e-cell™ compared to sham treatment over 7 days. For example, when soreness peaked on day 2 there was a 19% reduction in soreness for e-cell™ ( $16.8 \pm 2.1\text{mm}$ ) compared to sham ( $20.6 \pm 2.0\text{mm}$ ) condition. Significant differences were observed 2, 4 and 7 days post-exercise between conditions following post-hoc tests. There was no significant difference for extension ( $F_{1,15} = 2.145$ ,  $p = 0.165$ ) muscle soreness between conditions.

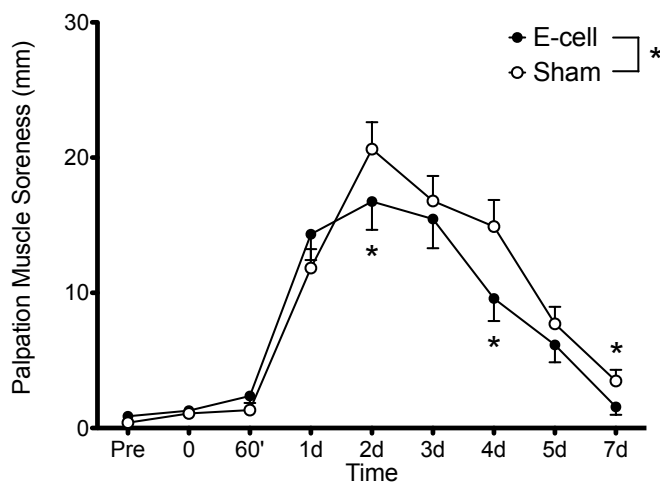


Figure 26: Changes in palpation muscle soreness (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise for e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p < 0.05$ ).

#### 4.2.7.5 Peak Muscle Soreness

Peak muscle soreness (Figure 27) post-exercise upon palpation of the upper arm (the average of the 3 bicep sites) occurred between days 1 and 3 and was 14% ( $t= 2.751, df=15, p=0.041$ ) lower after e-cell™ ( $21.1 \pm 2.2\text{mm}$ ) treatment compared with sham ( $24.5 \pm 2.1\text{mm}$ ) treatment.

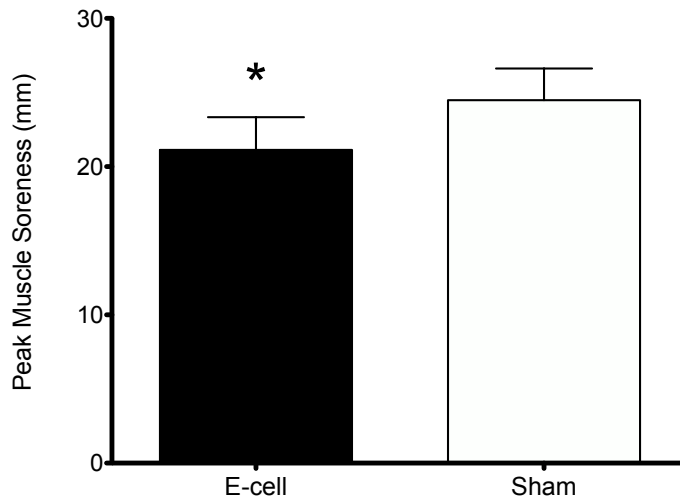


Figure 27: Peak muscle soreness upon palpation of the upper arm (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) after eccentric exercise between e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.7.6 PPT

Muscle tenderness developed ( $p<0.05$ ) at 1 day post-exercise for both conditions but there was no difference between treatments. However, there was a significant difference ( $F_{1,15}=9.754, p<0.000$ ) in upper arm PPT (average of 3 bicep sites) between e-cell™ and sham treatments (Figure 28), with the e-cell™ treatment arm recovering to baseline values by 5 days compared to sham treatment which was still 10% below baseline values ( $p<0.05$ ). Post hoc tests showed significant differences at 2 – 5 days and 7 days post-exercise between conditions.

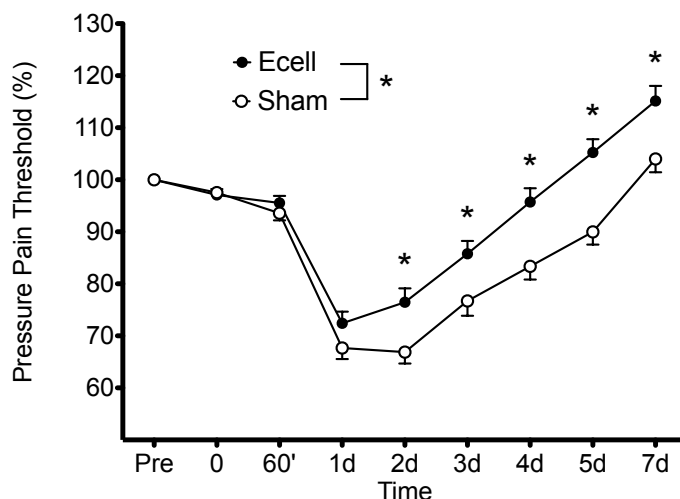


Figure 28: Normalised changes in PPT of the upper arm (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise between e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.7.7 Plasma CK Activity

Plasma CK activity was significantly higher after day 3 in both conditions; however, there was significantly lower ( $F_{1,15}=4.080$ ,  $p=0.010$ ) increases in plasma CK activity for e-cell™ compared to sham treatment over 7 days (Figure 29). For example when plasma CK activity peaked on day 5, there was a 49% reduction after e-cell™ ( $1316.9 \pm 536.5$ mm) compared to sham treatment ( $2576.2 \pm 681.5$ mm). Based on post-hoc tests, there were significant differences on days 5 and 7 post-exercise between conditions.

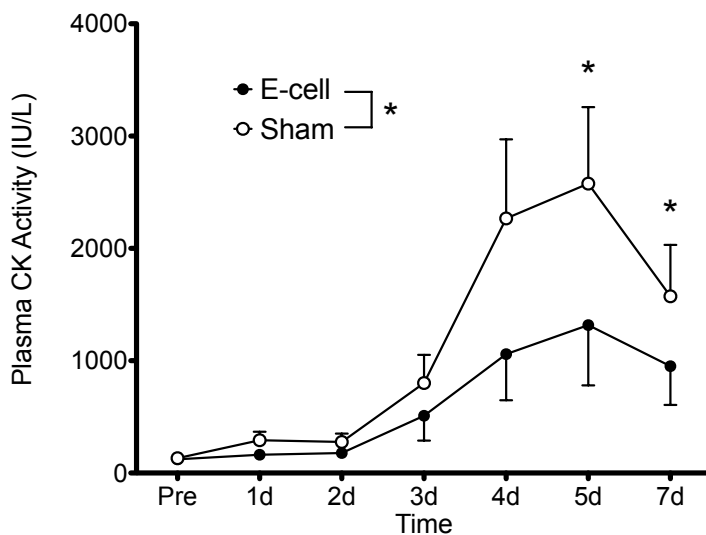


Figure 29: Changes in plasma CK activity at baseline (Pre), immediately Post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise between e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.7.8 Peak Plasma CK Activity

Peak plasma CK activity (Figure 30) post-exercise occurred between days 4 and 5 and was 43% ( $t=3.852$ ,  $df=15$ ,  $p=0.035$ ) lower after e-cell™ ( $1504 \pm 542$ IU/L) treatment compared with sham ( $2629 \pm 742$ IU/L) treatment.

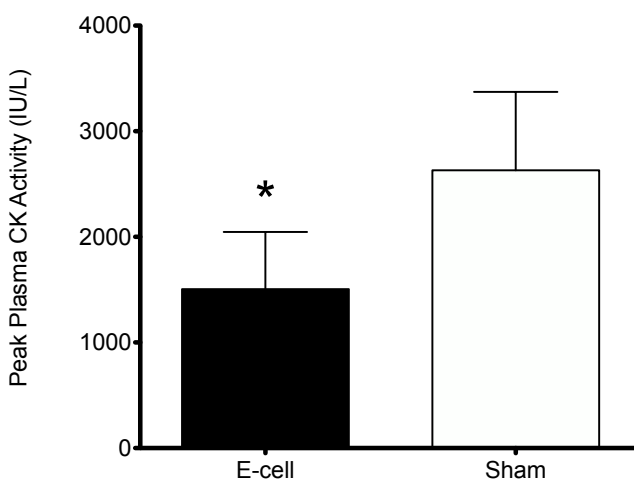


Figure 30: Peak plasma CK activity after eccentric exercise between e-cell™ and sham treatment conditions. \* Indicates a significant difference between treatment conditions ( $p<0.05$ ).

#### 4.2.8 Effects of a Contralateral Repeated Bout of Eccentric Exercise

A comparison was made for the changes in muscle damage markers, regardless of gender or treatment condition, between the first and second bouts of eccentric exercise when the second bout was performed on the contralateral arm 4 weeks apart.

##### 4.2.8.1 Pre Exercise Values between the First and Second Bouts of Eccentric Exercise

There were no significant differences in the pre exercise absolute values for any of the criterion measures between the first and second bouts of eccentric exercise (Table 4).

**Table 4:** Absolute baseline values for bout 1 and bout 2 groups

Variable	Bout 1	Bout 2	<i>F</i> value	<i>df</i>	<i>p</i> value
MVC torque at 30° (Nm)	35.2 ± 4.6	33.0 ± 4.0	2.761	1,15	0.117
MVC torque at 60° (Nm)	44.9 ± 4.5	43.1 ± 4.4	2.729	1,15	0.119
MVC torque at 90° (Nm)	53.0 ± 4.9	51.4 ± 4.5	2.317	1,15	0.149
Range of Motion (degree)	136.6 ± 2.2	136.3 ± 2.1	0.027	1,15	0.877
Upper Arm Circumference (mm)	283.1 ± 6.1	283.5 ± 2.5	0.078	1,15	0.789
Palpation Soreness (mm)	0.1 ± 0.1	0.1 ± 0.1	0.000	1,15	1.000
Extension Soreness (mm)	0.1 ± 0.1	0.1 ± 0.1	0.000	1,15	1.000
Pressure Pain Threshold (kPa)	378.5 ± 12.2	386.8 ± 14.7	0.010	1,15	0.921
Plasma CK Activity (IU/L)	119.2 ± 11.8	134.0 ± 16.4	0.517	1,15	0.483

**Note:** No significant baseline differences exist between first and second bouts of eccentric exercise ( $p>0.05$ )



#### 4.2.8.2 MVC torque

Figure 31 shows the changes in MVC torque at 60°, and the changes at other angles were similar. MVC torque decreased significantly ( $p<0.05$ ) immediately post-exercise by approximately 55% from baseline but there was no significant difference ( $F_{1,15}=0.297$ ,  $p=0.594$ ) between bouts. However, recovery of MVC torque was significantly different ( $F_{1,15}=16.159$ ,  $p<0.000$ ) between first and second bouts such that 7 days following the second bout, MVC torque had recovered to 94% of baseline but the recovery was only 79% for the first bout. This was a similar case for elbow joint angles at 30° (98% and 80%) and 90° (91% and 80%) between second and first bouts respectively. Following post-hoc tests, significant differences were found on days 2 – 5 and 7 days post-exercise between bouts. Interestingly, the magnitude of difference for the recovery of MVC torque between first and second bouts after 7 days was 5% greater than the magnitude of difference between e-cell™ and sham treatment.

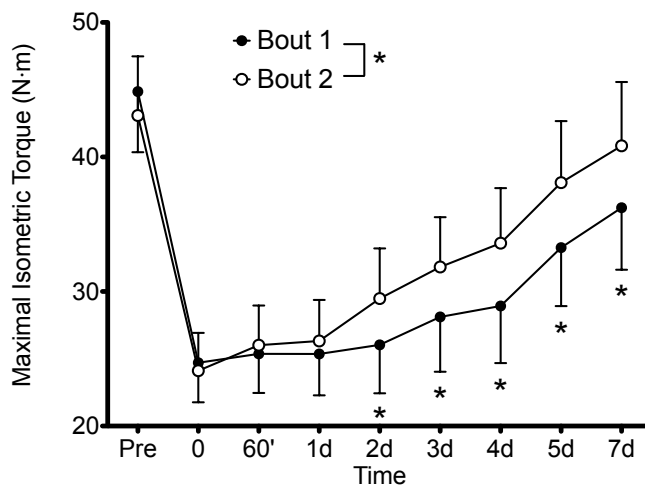


Figure 31: Comparison between the first (Bout 1) and second (Bout 2) bouts for the changes in MVC-60° torque at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).

#### 4.2.8.3 ROM

Figure 32 shows the changes in ROM over 7 days. Immediately post-exercise ROM decreased significantly ( $p<0.05$ ) by 16% from baseline but there was no significant difference ( $F_{1,15}=1.433$   $p=0.250$ ) in ROM measures between bouts. There was significantly ( $F_{1,15}=5.144$ ,  $p<0.000$ ) faster recovery of ROM seen in the second bout (97%) compared to the first bout (93%) after 7 days. Post-hoc tests revealed significant differences on days 1 – 5 between bouts. Similarly, the magnitude of difference in the recovery of ROM between first and second bouts was only 1% greater than the magnitude of difference between and e-cell™ and sham treatment.

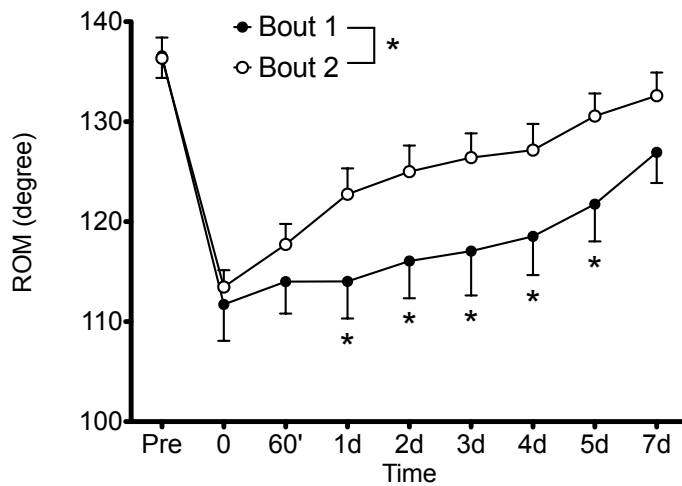
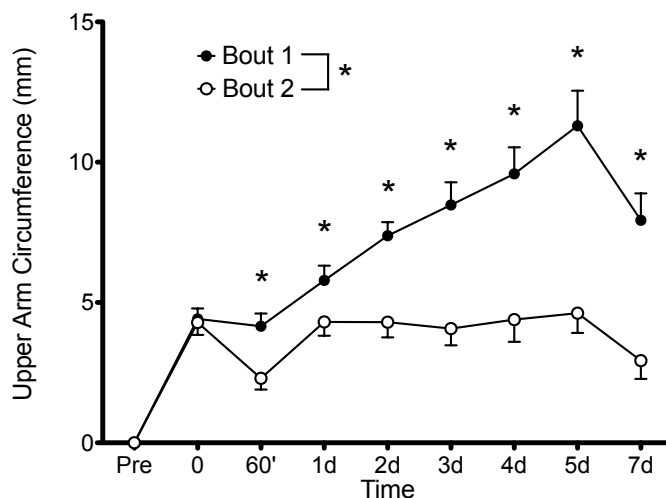


Figure 32: Comparison between the first (Bout 1) and second (Bout 2) bouts for the changes in range of motion at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).

#### 4.2.8.4 CIR

Figure 33 shows the changes in CIR (average of 3 sites), which was similar for all circumference measures. CIR increased ( $p<0.05$ ) immediately post-exercise for both bouts compared to baseline; but there was no significant difference ( $F_{1,15}=0.066$ ,  $p=0.799$ ) between bouts. However, there was a significant difference ( $F_{1,15}=15.201$ ,  $p<0.000$ ) between bouts over 7 days, such that following the first bout of exercise, CIR increased ( $p<0.05$ ) from day 1 post-exercise compared to the second bout of exercise where there was no significant increase in CIR from immediately post-exercise to day 7. CIR peaked on day 5 for both bouts with 60% less swelling after the second bout ( $4.6 \pm 0.7\text{mm}$ ) compared to the first bout ( $11.3 \pm 1.2\text{mm}$ ). Significant differences in CIR were seen at 60 minutes, 1 – 5 days and 7 days post-exercise between bouts following post-hoc tests. Interestingly, the magnitude of difference in CIR on day 5 post-exercise between the first and second bouts was 6% greater than the magnitude of difference on day 5 between e-cell™ and sham treatment.



*Figure 33: Comparison between the first (Bout 1) and second (Bout 2) bouts for the changes in CIR at baseline (Pre), immediately post (0), 60 minutes post (60'), and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).*

#### 4.2.8.5 Muscle Soreness

Figure 34 shows the changes in palpation muscle soreness based on VAS upon palpation for the arm. Muscle soreness developed from day 1 post-exercise for both bouts; however, there was significantly ( $F_{1,15}=9.108$ ,  $p<0.000$ ) less palpation soreness of the upper arm (average of 3 bicep sites) after the second bout compared to the first. For example when soreness peaked on day 2, there was a 26% reduction in soreness after the second bout ( $15.9 \pm 1.9\text{mm}$ ) compared to the first bout ( $21.4 \pm 2.1\text{mm}$ ). Significant differences were found 2 – 5 days post-exercise following post-hoc

tests. Comparatively, the magnitude of difference for soreness of the upper arm on day 2 between the first and second bouts of exercise was 7% greater than the magnitude of difference between e-cell™ and sham treatment. A significant difference ( $F_{1,15}=4.433$ ,  $p<0.000$ ) was also found for extension muscle soreness between bouts.

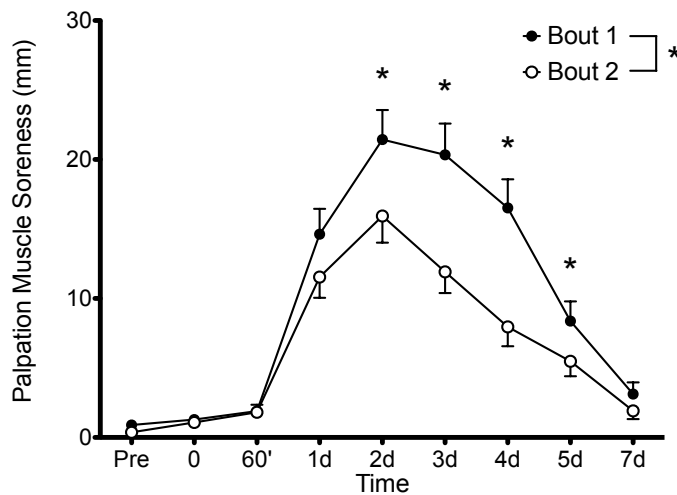


Figure 34: Comparison between the first (Bout 1) and second (Bout 2) bouts for the changes in palpation muscle soreness (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).

#### 4.2.8.6 Peak Muscle Soreness

Peak muscle soreness (Figure 35) post-exercise upon palpation of the upper arm (the average of the 3 bicep sites) occurred between days 1 and 3 and was 33% lower ( $F_{1,15}=5.348$ ,  $p<0.000$ ) after the second bout ( $18.3 \pm 2.0\text{mm}$ ) compared with the first ( $27.2 \pm 2.2\text{mm}$ ). Additionally, the magnitude of difference for peak soreness upon palpation between the first and second bouts was 19% greater than the magnitude of difference between e-cell™ and sham treatment.

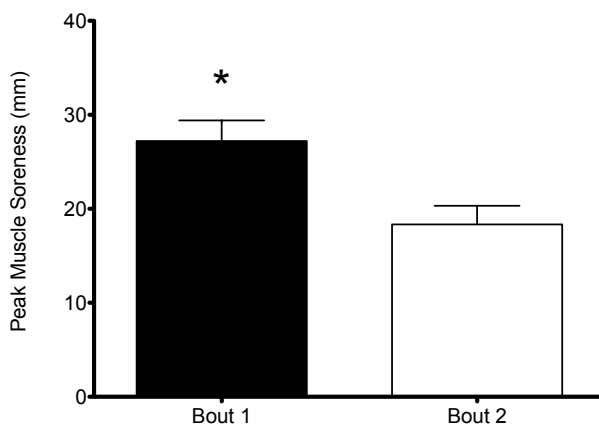


Figure 35: Comparison between the first (Bout 1) and second (Bout 2) bouts for peak muscle soreness upon palpation of the upper arm (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).

#### 4.2.8.7 PPT

Muscle tenderness developed ( $p<0.05$ ) at 1 day post-exercise for both conditions and there was a significant difference ( $F_{1,15}=11.023$   $p<0.000$ ) between bouts. Additionally, there was a significant difference ( $F_{1,15}=16.891$ ,  $p<0.000$ ) in upper arm PPT (average of 3 bicep sites) between bouts (Figure 36), with the second bout recovering to baseline values by day 5 compared to sham treatment that was still 13% below baseline values and still had not recovered by day 7. Post hoc tests revealed significant differences at 60 minutes, 1 – 5 and 7 days post-exercise between bouts. Similarly, the magnitude of difference for the recovery of muscle tenderness between the first and second bouts was 3% greater than the magnitude of difference between e-cell™ and sham treatment.

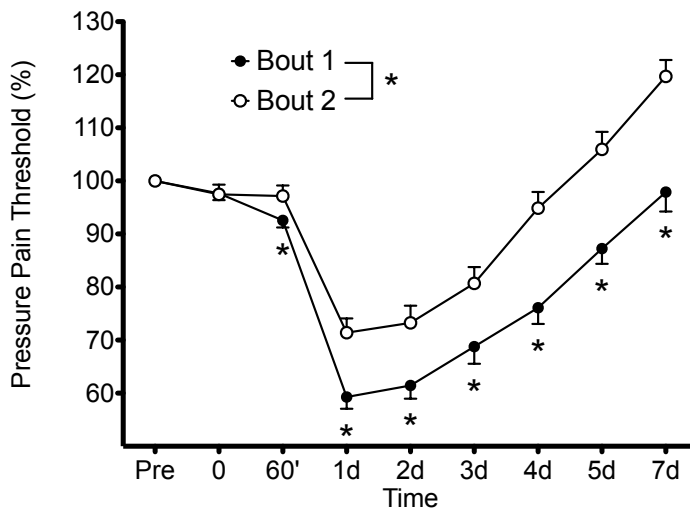


Figure 36: Comparison between the first (Bout 1) and second (Bout 2) bouts for the normalised changes in PPT of the upper arm (average of 3 sites including the mid-belly of the biceps brachii, and 3 cm above and below the mid-belly) at baseline (Pre), immediately post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p<0.05$ ).

#### 4.2.8.8 Plasma CK Activity

Plasma CK activity was significantly higher after day 2 for the first bout and day 3 for the second bout. In addition there was significantly ( $F_{1,15}=8.995$ ,  $p=0.009$ ) lower increases in plasma CK activity for the second bout compared to the first (Figure 37). For example when plasma CK activity peaked on day 5, there was a 56% reduction after the second bout ( $1123.5 \pm 416.2$ mm) compared to the first bout ( $2547.5 \pm 725.8$ mm). Based on post-hoc tests, there were significant differences on days 3 – 5 and 7 days post-exercise between conditions. Comparatively, the

magnitude of difference on day 5 for plasma CK activity between the first and second bouts was 7% greater than the magnitude of difference between e-cell™ and sham treatment.

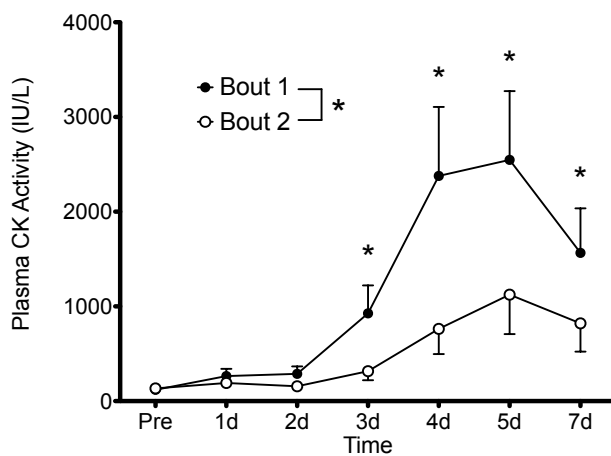


Figure 37: Comparison between the first (Bout 1) and second (Bout 2) bouts for the changes in plasma CK activity at baseline (Pre), immediately Post (0), 60 minutes post (60') and 1 – 5 and 7 days after eccentric exercise. \* Indicates a significant difference between bouts ( $p < 0.05$ ).

#### 4.2.8.9 Peak Plasma CK Activity

Peak plasma CK activity (Figure 38) post exercise occurred between days 4 and 5 and was 50% lower ( $t=6.405$ ,  $df=15$ ,  $p=0.010$ ) after the second bout ( $1386.2 \pm 470.3$  IU/L) compared to the first bout ( $2748.3 \pm 777.1$  IU/L). Additionally, the magnitude of difference for peak plasma CK activity between the first and second bouts was 7% greater than the magnitude of difference between e-cell and sham treatment.

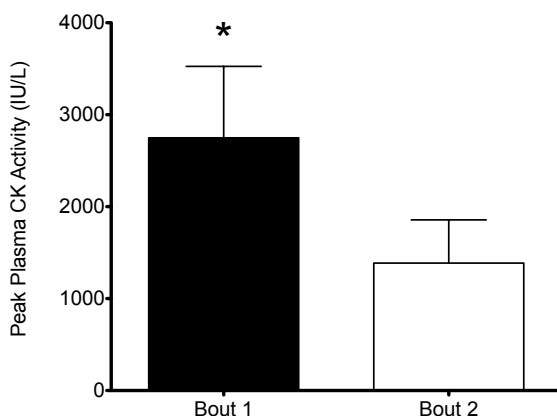


Figure 38: Comparison between the first (Bout 1) and second (Bout 2) bouts for peak plasma CK activity after eccentric exercise between bouts. \* Indicates a significant difference between bouts ( $p < 0.05$ ).

#### 4.2.8 Comparison between the Effect of Treatment and Repeated Bout Effect

Our previous analysis showed that both e-cell™ treatment and the contralateral repeated bout effect enhanced the rate of recovery from muscle damage compared to sham treatment and the first bout of eccentric exercise respectively. Therefore, a comparison was made to examine whether e-cell™ treatment or the contralateral repeated bout effect was more effective at enhancing recovery from EIMD. To examine the magnitude of effect between e-cell™ treatment and the contralateral repeated bout effect, normalised changes in MVC torque, ROM and PPT from baseline (pre: 100%) and absolute changes in CIR, SOR and plasma CK activity were used. In Figure 39, peak SOR and plasma CK activity as well as day 5 measures for MVC torque, ROM, CIR and PPT were used to calculate the magnitude of difference between conditions and exercise bouts for the dependent variables. Compared with the magnitude of change after the treatment, the second bout of exercise resulted in significantly faster recovery of MVC torque ( $p=0.030$ ) and ROM ( $p=0.041$ ), and smaller increases in SOR ( $p<0.000$ ) and PPT ( $p=0.047$ ). However, no significant difference was seen for CIR ( $p=0.107$ ) and plasma CK activity ( $p=0.083$ ).

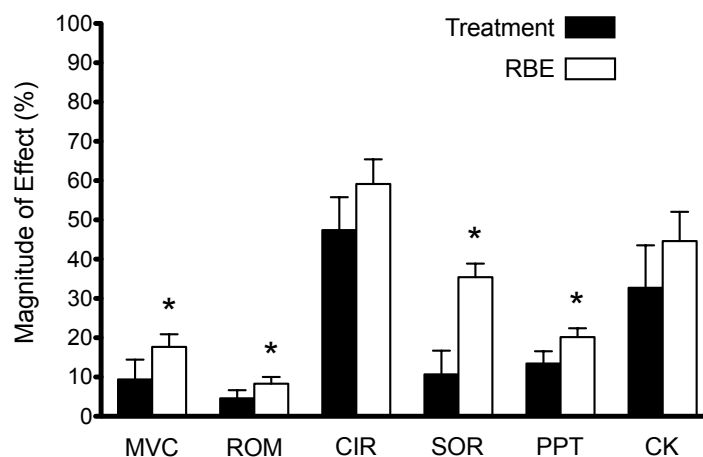


Figure 39: Comparison of the magnitude of recovery between the first and second eccentric exercise bouts and e-cell™ and sham treatment conditions for MVC torque, range of motion, upper arm circumference and pressure pain threshold on day 5 after eccentric exercise, peak soreness and CK activity after eccentric exercise. RBE = contralateral repeated bout effect. \* Indicates a significant difference between treatment and exercise ( $p<0.05$ ).

#### 4.2.9 Comparison between the First and Second Bouts of Eccentric Exercise for the e-cell™ Treatment Effect

To examine the magnitude of effect between e-cell™ and sham treatments after the first and second bouts of exercise, normalised changes in MVC torque, ROM and PPT from baseline (pre: 100%) and absolute changes in CIR, SOR and plasma CK activity were used. In Figure 40, peak SOR and plasma CK activity as well as day 5 measures for MVC torque, ROM, CIR and PPT were used to calculate the magnitude of effect between conditions for the dependent variables. Comparatively, the e-cell™ treatment was less effective after the second bout of exercise for the recovery of MVC torque (12%), ROM (5%), CIR (25%), SOR (14%), PPT (6%) and plasma CK activity (29%) compared to the first bout because of the contralateral repeated bout effect.

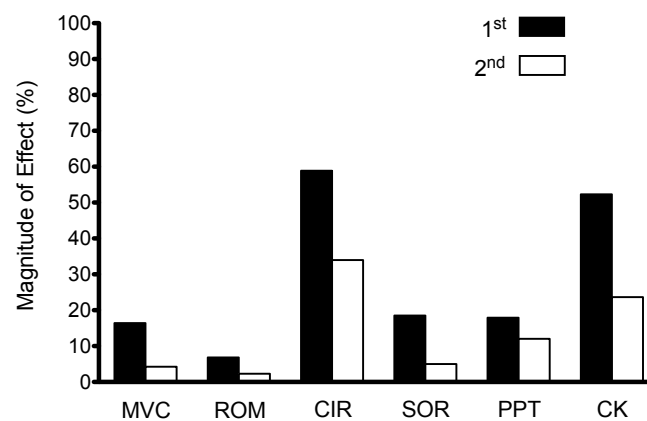


Figure 40: Comparison of the mean magnitude of recovery between e-cell™ and sham treatment in the first and second eccentric exercise bouts for peak SOR and CK activity; and MVC torque, ROM, CIR and PPT on day 5 after eccentric exercise.



## **CHAPTER FIVE**

### **DISCUSSION**

The purposes of this thesis were to investigate: the influence of 30 minutes e-cell™ treatment on muscle temperature, blood flow and oxygenation when it was applied to the elbow flexors compared to sham treatment (Study 1); the acute, overall, and gender effects of 30 minutes e-cell™ treatment, applied over 5 consecutive days after eccentric exercise of the elbow flexors, on the associated symptoms and markers of eccentric exercise-induced muscle damage in comparison to sham treatment (Study 2).

In relation to the research questions, the Study 1 results showed that: 1) e-cell™ treatment increased muscle temperature by  $\sim 0.5^{\circ}\text{C}$  compared to sham treatment; 2) however, no significant differences in muscle blood flow and oxygenation were evident between conditions. In addition, Study 2 results included: 3) no significant acute changes in the dependent variables from pre- to post-treatment for either e-cell™ and sham conditions except for an  $\sim 8\%$  decrease in MVC torque after both conditions; 4) no significant differences between genders for any of the dependent variables except for a significantly faster recovery of PPT scores for men than women; and when compared with the sham treatment, the recovery of MVC torque and ROM was significantly faster, with swelling, peak muscle soreness and peak plasma CK activity also significantly smaller for e-cell™ condition. Interestingly, after further analysis, when comparing the first and second bouts regardless of the treatment condition, the changes in all dependent variables were significantly attenuated after the second bout than the first bout, and the difference in the magnitude between bouts was greater than the differences between the treatment conditions. This chapter will discuss

the main results shown above separately, the potential action of the device, and integrate the findings to conclude the project.

## 5.1 Study 1

To the best of my knowledge, no previous studies have investigated the effects of low frequency PEMFT on muscle temperature, muscle blood flow or oxygenation of the elbow flexors. Any heat produced in the target muscle after low frequency (5 – 100Hz) PEMFT was thought to dissipate through the circulating blood (Adey, 1993). However, the present study found that e-cell™ treatment increased muscle temperature by  $\sim 0.5^{\circ}\text{C}$  ( $\sim 1.5\%$  increase), but sham treatment did not. Given that the devices were applied at the same time and under the same conditions, it is reasonable to assume that the temperature increase was caused by the e-cell™ treatment. Despite this, the magnitude of muscle temperature increase observed in the present study was much less than that reported in studies using higher frequency (27.12 - 2450MHz) devices such as diathermy (shortwave and microwave) treatment. For example, microwave diathermy studies have reported a  $\sim 3^{\circ}\text{C}$  muscle temperature increase of the biceps brachii after 10 minutes of treatment (Nosaka, et al., 2004) and a  $\sim 7^{\circ}\text{C}$  increase following 20 minutes of treatment (Nosaka, et al., 2007). It is unclear how the PEMFT treatment increased muscle temperature but some speculation is possible. Higher frequency electromagnetic devices ( $>1\text{MHz}$ ) are known to generate electromagnetic fields that stimulate a flow of current in tissues, accelerating the charged ions, which collide with adjacent molecules producing energy and increasing collisions which leads to heating (Robertson et al., 2006). Thus, it is possible that the lower frequency device used in the present study was able to replicate similar heating effects but to a lesser extent.

The physiological importance of the temperature increase in the present study is questionable given thermal therapies, believed to promote healing, require much greater increases in muscle temperature to enhance blood flow (Giombini, Di Cesare, Safran, Ciatti, & Maffulli, 2006).

Therefore, despite the temperature increase after 30-minutes of e-cell™ treatment, there is no evidence to suggest that such a small passively induced muscle temperature increase is physiologically meaningful.

Advocates of PEMFT treatment suggest that it can effectively treat soft tissue injuries by increasing muscle blood flow (Markov, 2007), believing that increased blood flow can promote the healing of damaged tissues like those affected by muscle damage. However, there are no documented reports of increased muscle blood flow to passive muscle when low frequency PEMFT treatment is applied. The mechanism by which PEMFT is believed to influence blood flow is relatively unknown but it is speculated that nitric oxide maybe the molecule responsible for vasodilation following PEMFT exposure (Kavaliers, Choleris, Prato & Ossenkopp, 1998). In the present study near infrared spectroscopy (NIRS) was employed to determine changes in muscle oxygenation and blood flow. It was found that 30-minutes of e-cell™ treatment had no effect on muscle blood flow or oxygenation compared to sham treatment. However, it should be noted that e-cell™ treatment was applied to healthy individuals with the target tissue (biceps brachii) undamaged. Proponents of low frequency PEMFT would argue that enhanced muscle blood flow could only occur if the PEMFT device was applied to injured tissue. However, pilot data using two men who were of similar characteristics to those used in the present study measured changes in muscle blood flow and oxygenation of the elbow flexors in the non-dominant arm using NIRS during the 30 minutes of e-cell™ treatment applied at 30 minutes, and 1 – 4 days after the same eccentric exercise used in the present study, also showed no increase in muscle blood flow and oxygenation.

Therefore, it was concluded that e-cell™ treatment induced a small increase in muscle temperature but had no effect on muscle blood flow or oxygenation. Despite the lack of changes in muscle blood flow and oxygenation, it does not necessarily mean that e-cell™ treatment can not

enhance the healing of injured tissue, because there are other potential physiological mechanisms of PEMFT, suggested in Figure 1, that were not been tested for in the present study.

## **5.2 Study 2**

### **5.2.1 Exercise**

To investigate the efficacy of interventions, arm-to-arm comparison models are often used (Nosaka, et al., 2007; Nosaka, et al., 2004; Zainuddin, et al., 2006). The present study used an arm-to-arm comparison design in preference to a between-subjects design. The arm-to-arm comparison model was thought to be advantageous, because only one group of participants were required thus the total number of participants was reduced, and the within-subjects design allows for reduced variability in response to exercise created by heterogeneous participants (Newton, Sacco, Chapman, & Nosaka, 2013). Indeed, there were no significant differences in the dependent variables at pre- and immediately post-exercise when arm dominance, treatment and bout order were counterbalanced.

The eccentric exercise protocol used in this study was effective for inducing significant losses in strength and ROM, increases in swelling, tenderness and plasma CK activity as well as moderate increases in muscle soreness. The changes in the dependent variables after maximal eccentric exercise of the elbow flexors such as the immediate losses in MVC torque (~55% of pre-exercise measures) were equivalent to those of the previous studies in which a similar exercise protocol was used (Newton, et al., 2008; Nosaka, et al., 2007; Zainuddin, et al., 2006). Thus, the exercise protocol induced sufficient muscle damage to validate the efficacy of e-cell™ treatment.

### **5.2.2 Reliability of Measurements**

For the test-retest reliability of the dependent variables (Table 1), the ICC measures were in the 0.81 – 1.0 range indicating good reliability (Landis & Koch, 1977). In addition, the CV values

were less than 10% for all variables indicating good reliability that allows for the detection of a possible treatment effect. No significant differences in pre-exercise measures were evident for any dependent variables, and the exercise protocols were performed similarly between the e-cell™ and sham treatment groups as indicated by the similar average peak torque (Figure 16) production and overall work performed during exercise (Figure 17). Similarly, there were no significant differences in any dependent variables immediately after exercise between e-cell™ and sham conditions. Thus, the eccentric exercise appeared to induce similar magnitude of muscle damage to both arms. Therefore, it is reasonable to assume that if there are any differences in the dependent variables between e-cell™ and sham conditions occurring after 60 minutes post-exercise, the changes can be attributed to the effects of the treatment, given the primary treatment was applied 30 minutes post-exercise. Lastly, when comparing between the first and second bouts of exercise, there were no significant differences in pre- and immediately post-exercise measures for any of the dependent variables.

### **5.2.3 Gender Effect**

In the present study, no gender differences were found for the changes in muscle damage markers following maximal eccentric exercise of the elbow flexors except for PPT (Table 2), where a significantly faster recovery was seen for men than women, but the magnitude of difference was small. Similar findings have been reported in a previous study where females expressed significantly higher sensitivity and lower thresholds to PPT compared to males (Chesterton, Barlas, Foster, Baxter, & Wright, 2003). As suggested previously in the methods section of this thesis, females with high levels of oestrogen can experience attenuated symptoms from muscle damaging exercise (Kendall & Eston, 2002). The mechanism of this protective effect is not fully understood but it is believed that elevated levels of oestrogen have antioxidant properties facilitating cell membrane stability attenuating the magnitude of muscle damage (Carter, Dobridge, and Hackney,

2001). In the present study, when comparing the effect of e-cell™ and sham treatments for each gender group separately, essentially the results were the same as those based on both groups combined. Consequently, the comparisons between the e-cell™ and sham treatments shown below were made for all participants.

The lack of gender differences found in the present study is in accordance with previous gender studies (Rinard, et al., 2000; Sayers & Clarkson, 2001), but these studies did not measure PPT. Despite the lack of gender differences seen in the present study, there is conflicting evidence in the literature with some studies reporting that gender differences exist for the changes in muscle damage markers particularly with regards to losses in MVC torque and smaller increases in plasma CK activity (Stupka et al., 2000). For example, Seawright et al. (2008) compared the muscle damage markers between 58 women and 42 men after 50 maximal eccentric contractions of the elbow flexors and reported that women showed greater relative MVC torque losses than men immediately after exercise, but men had significantly higher peak CK activity than women. This was contrary to our findings where we found no significant MVC torque losses between genders immediately post-exercise and additionally, no gender differences in plasma CK activity. Furthermore, despite the previous findings from Seawright et al. (2008), our results revealed that females exhibited greater increases in plasma CK activity than men, although this was not significantly different. A study by Carter, Dobridge, and Hackney (2001), found that females with high levels of oestrogen had significantly smaller increases in plasma CK activity 72 hours following a 30 minute downhill running eccentric exercise protocol compared to low estrogen level females. In the present study, females were deliberately tested during the mid-follicular phase of their menstrual cycle (when oestrogen levels were low) to minimise any protective effect caused by high levels of oestrogen. Thus, controlling of the menstrual cycle at the beginning of the exercise bouts may have blunted any gender differences that may have otherwise been seen. Despite the conflicting previous research, the results of the present study suggest that when the menstrual cycle

is controlled for, gender had little effect on changes in the indirect markers of muscle damage after the maximal eccentric exercise of the elbow flexors.

#### **5.2.4 Acute Effect**

The acute effect was based on the measures taken before and immediately after e-cell™ and sham treatments. No significant changes in the dependent variables except MVC torque were found before and immediately after either treatment performed 1-4 days after eccentric exercise (Figures 18 - 22). MVC torque decreased significantly around 8% immediately after both treatments (Figure 18). In the present study, the decreases seen in MVC torque were most likely related to factors associated with a relaxation effect because the subjects were required to remain still and seated for the entire 30 minute treatment duration, which may have led to a reduced efficiency of excitation-contraction coupling, decreased central motor drive and motor neuron excitability, or a combination of all three (Gandevia, 2001).

It is unclear why no acute effect of e-cell™ treatment was seen, particularly as an overall effect was evident. Given that PEMFT is reported to reduce pain and inflammation in musculoskeletal injuries (Hedan & Pilla, 2008; Trock, et al., 1993), acute changes in muscle soreness, tenderness and swelling after e-cell™ treatment may have been expected. It has been previously suggested that PEMFT can enhance muscle blood flow (Markov, 2007), which can increase venous drainage and reduce swelling. However, the present study was unable to detect any significant change in blood flow from Study 1, and subsequently no acute effect on upper arm circumference or other markers of muscle damage. Nevertheless, it might be that the beneficial effects of the treatment could take effect sometime within the 24-hour period between treatment applications. Therefore, it is possible that the effect of e-cell™ treatment could have been observed in the hours after the 30 minutes of application in a similar manner to cold-water immersion where the benefits of the cooling effect occur in the hours after the treatment has ceased (Pournot,

Bieuzen, Duffield, Lepretre, Cozzolino & Hausswirth, 2011). However, the exact mechanism is unknown and any future studies investigating the effects of e-cell™ treatment would be advised to monitor the subsequent hours after the treatment application.

#### **5.2.5 Effect of PEMFT on recovery from muscle damage**

There were no acute effects of e-cell™ treatment on the changes in most of the dependent variables but interestingly, there was a significantly faster rate of recovery after e-cell™ treatment for all of the dependent variables except for extension soreness after maximal eccentric exercise compared to sham treatment (Figures 23 - 30). The recovery of MVC torque is perhaps the most important marker of muscle damage, since it affects exercise performance and activities of daily living. To the best of my knowledge, no previous studies have found any enhanced recovery of MVC torque after the use of a therapeutic electrotherapy treatment, although some of them reported significant effects on other variables such as muscle soreness and plasma CK activity (Bakhtiary, et al., 2007; Lau & Nosaka, 2011; Zainuddin, et al., 2005). The present study showed a significantly faster rate of recovery ( $10.3 \pm 5.0\%$ ) for MVC torque after e-cell™ compared to sham treatment at 7 days post-exercise, but MVC torque did not fully recover to baseline measures (Figure 23). Post-hoc tests revealed significant differences were present on 2, 5 and 7 days post-exercise. Thus, it appears the physiologically beneficial effects of e-cell™ treatment for MVC torque recovery were not immediate and took time to develop. This is in accordance with the lack of acute response seen for e-cell™ treatment reported previously in the present study for days 1 – 4 post-exercise (Figure 18). The present study was the first to show a more rapid recovery of MVC torque of the elbow flexors after eccentric exercise following the application of low frequency PEMFT. It is difficult to compare the results of the present study with other electrotherapy studies treating muscle damage, because there are differences in the type and magnitude of muscle damaged, and the mode, duration and the applied time of the electrotherapies. It is unclear from the present study whether longer



treatment duration would generate a similar or greater magnitude of MVC torque recovery. Further studies are necessary to investigate whether modifications to treatment duration and parameters would generate a more rapid MVC torque recovery.

In terms of muscle function, it should be noted that not only MVC torque but also the recovery of ROM of the elbow joint was enhanced by e-cell™ treatment. There were significantly smaller decreases in elbow joint ROM for e-cell™ treatment compared to sham treatment (Figure 24). Similarly, Spodaryk (2002) observed significantly smaller decreases in ROM on 2 days after applying a low frequency PEMFT device for 20 minutes over 5 days after exhaustive eccentric dumbbell exercise of the elbow flexors compared to sham and control groups. Even though e-cell™ treatment enhanced the rate of recovery of the elbow joint ROM, the magnitude of difference between e-cell™ and sham treatment in the present study appears less significant than other electrotherapies. Previous studies using microwave (Nosaka, et al., 2007) and vibration (Lau & Nosaka, 2011) therapy also reported improved recovery in elbow joint ROM, but the magnitude of effect in these studies appears to be greater than that observed in the present study. For example, Nosaka et al. (2007) and Lau et al. (2011) found significant differences between their respective electrotherapies and control condition after EIMD on days 1 - 4 and 3 - 7 respectively compared to only day 1 seen in the present study. Thus, it appears that low frequency PEMFT may not greatly enhance elbow joint ROM compared to other thermal and mechanical electrotherapies. It is unlikely e-cell™ treatment had any influence on joint stiffness (EANG) given the relatively small muscle temperature increase found in Study 1. Spodaryk (2002) proposed that PEMFT treatment retarded the perception of pain allowing for greater extension in elbow joint ROM; although in the present study, this did not appear possible since there was no difference in soreness measures between treatment conditions on day 1 after exercise. All things considered, despite the statistically significant differences found for elbow joint ROM in the present study between conditions, it appears the effect of e-cell™ treatment was not as clinically significant as other electrotherapies.

Swelling transpires within the muscle immediately after maximal eccentric exercise-induced muscle damage of the elbow flexors and typically peaks around five days post-exercise (Nosaka & Clarkson, 1996), which was confirmed in the present study. The amount of swelling induced post-exercise in this study was similar to that of previous studies (Chen et al., 2012; Zainuddin et al., 2006). In the present study there was significantly less swelling 60 minutes and 2 – 5 and 7 days post-exercise after e-cell™ compared to sham treatment; and furthermore, significantly less ( $47.4 \pm 8.4\%$ ) peak swelling was observed on day 5 after e-cell™ treatment compared to sham (Figure 25). Interestingly, after the first 30 minute application of e-cell™ treatment there was significantly less swelling (60 minutes post-exercise) compared to sham treatment, suggesting that low frequency PEMFT may suppress oedema that occurs during the early stages of secondary damage, which has been shown in a previous animal study (Lee, Maffulli, Li, & Chan, 1997). This is further supported by studies that have shown PEMFT can reduce oedema in musculoskeletal injuries (Bentall, 1986; Markov & Pilla, 1995). Therefore, based on the upper arm circumference results from the present study, it appears that PEMFT can effectively reduce swelling of the upper arm.

Regarding DOMS, which is one of the most commonly used indirect markers of eccentric exercise induced muscle damage (Cheung, et al., 2003), e-cell™ treatment induced a significant reduction in palpation soreness (Figure 26) at 2, 4 and 7 days post-exercise and about a 10% reduction in peak soreness (Figure 27) compared to sham treatment. There was also significantly faster recovery of PPT values (Figure 28) after e-cell™ treatment with significantly less tenderness (9 – 15%) seen everyday from 2 days post-exercise returning to baseline measures by day 4 compared to day 7 for sham condition. This was not surprising given that Spodaryk (2002) also reported significantly less tenderness (~20%) for days 3 - 5 post-exercise after applying low frequency PEMFT and may lend credence helps to the potential increased inhibition of group III and IV nerve fibres (Figure 1) which may have assisted to reduce the sensation of pain. In the present study, even though e-cell™ treatment attenuated palpation soreness, the magnitude of effect

may not be as significant as other therapeutic interventions. For example, Zainuddin et al. (2005) employed 10 minutes of massage therapy 3 hours after 60 maximal eccentric contractions of the elbow flexors that resulted in significant decreases (20 – 40%) in the severity of soreness measures compared to control condition. Furthermore, Lau et al. (2011) applied 30 minutes of vibration therapy 30 minutes and 1 - 4 days post-eccentric exercise of the elbow flexors and found significant reductions (25 – 30%) in peak palpation soreness between days 2 – 5. In the present study, it should be noted that while e-cell™ treatment attenuated palpation soreness, VAS measures from extension soreness were not significantly different between conditions. It is unclear why e-cell™ treatment would have an attenuating effect on palpation soreness and not extension soreness; but perhaps there are different mechanisms of pain linked to palpation soreness compared to soreness associated with movement that low frequency PEMFT devices may influence. Nevertheless, e-cell™ treatment had a small but significant attenuation of palpation and peak soreness after EIMD but is perhaps not as significant compared to other therapeutic interventions such as vibration therapy.

Another indirect marker of muscle damage is plasma or serum CK activity that typically peaks 4 – 6 days after maximal eccentric exercise of the elbow flexors, which was confirmed in the present study (Clarkson, Nosaka, & Braun, 1992). Plasma CK activity increased significantly in both treatments after exercise; however, significantly less mean (Figure 29) and peak plasma CK activity (Figure 30) was seen after e-cell™ compared to sham treatment. To the best of my knowledge, this is the first study to show that PEMFT can attenuate increases in plasma CK activity. It is difficult to compare the results from the present study with other electrotherapy studies due to the differing treatment and exercise protocols. However, it appears the magnitude of e-cell™ treatment effect on plasma CK activity is greater than other electrotherapy studies. For example, Lau et al. (2011) and Nosaka et al. (2004) found no significant difference between their respective treatments (vibration and microwave diathermy respectively) and control condition on reducing increases in plasma CK activity. In the present study the reduced plasma CK activity after e-cell™

treatment could possibly be explained by smaller CK efflux from the damaged muscle (Figure 1) but is unlikely to be caused by increased clearance of plasma CK from circulatory factors as no changes in muscle blood flow were found from Study 1. However, there is no evidence to support these speculations in the present study.

The results from the present study support the effectiveness of e-cell™ treatment in the attenuation of symptoms associated with EIMD. Previously, PEMFT has been shown to be effective in the recovery of muscle tenderness and losses in ROM following EIMD, but to the best of my knowledge, this is the first study to demonstrate the effectiveness of PEMFT in the recovery of muscle strength, soreness, swelling and plasma CK activity. Thus, the findings from this study, in regards to the recovery of muscle damage markers following EIMD, are important for athletes to assist in their recovery after training and competition as well as the general population.

It is difficult to determine how e-cell™ treatment enhanced the recovery of muscle damage but some speculation is possible. It is well known that secondary muscle damage (inflammatory processes that follow the primary damage of eccentric exercise) associated with an inflammatory response can contribute to swelling and prolonged strength losses (Clarkson & Hubal, 2002). Additionally, inflammation in skeletal muscle is characterised by the infiltration of neutrophils and macrophages that are associated with muscle injury and repair (Hernandez et al., 1987). Neutrophils are also known to proliferate around the site of injury in the early stages of inflammation. With this in mind, it has been shown that adenosine (thought to be an endogenous anti-inflammatory agent that activates A2a receptors found on neutrophils) can bind to neutrophil receptors and decrease inflammatory processes (Huang, Apasov, Koshiba, & Sitkovsky, 1997). Varani et al. (2002) showed that low frequency PEMFT exposure can significantly enhance the function and expression of adenosine A2a receptor activity in human neutrophils in vitro, which could play an important role in modulating inflammatory processes that could benefit therapeutic healing (Cronstein, Montesinos, & Weissmann, 1999). Therefore, it could be speculated that e-cell™ treatment helped to attenuate the early inflammatory response to EIMD and facilitate the recovery of strength and

swelling. Electromagnetic fields are also believed to affect cell membrane function by influencing the rate of ion binding and transport to receptor sites and influence tissue repair (Bersani et al., 1997; Markov, 2007). The reduced efflux of plasma CK into the blood stream reported in the present study may support this argument (Figure 1). As previously mentioned, PEMFT treatment has been shown to reduce acute/chronic inflammation occurring from musculoskeletal injuries. All things considered, it is believed the primary function of low frequency PEMFT treatment is to suppress the extravascular oedema during the early stages of an inflammatory response.

It is not fully understood how the e-cell™ treatment attenuated palpation soreness and PPT. However, it could be speculated that the electromagnetic fields from low frequency PEMFT devices may influence DOMS and muscle tenderness by impeding the sensory input from the nociceptors to the afferent fibres (type A $\delta$  and C) reducing the perception of pain (Figure 1) (Robertson et al., 2006). As previously reported within this discussion, e-cell™ treatment also reduced swelling around the elbow flexors, which may have also contributed to the smaller increases in the sensitivity of the nociceptors to palpation soreness, as swelling is believed to contribute to hyperalgesia of the nociceptors (Sluka, Jordan, & Westlund, 1994). However, based upon the comparison between the first and second bouts of eccentric exercise for the e-cell™ treatment effect (Figure 39), it appears that PEMFT had the greatest attenuating effect on markers of inflammation since the greatest magnitude of protection conferred by e-cell™ treatment was evident on swelling (Figures 39 & 40). Further studies are necessary examine the underlying mechanisms of PEMFT treatment.

#### **5.2.6 Repeated Bout Effect**

In the present study, when the second bout of exercise was performed 4 weeks after the first bout (ignoring the treatment effect between e-cell™ and sham conditions) there were significantly smaller changes in all of the dependent variables on the contralateral arm compared with the first bout, suggesting an arm-to-arm cross transfer effect (Figure 31 - 38). At least three studies have

reported the existence of the contralateral repeated bout effect for the elbow flexors (Howatson & Van Someren, 2007; Newton, Sacco, Chapman, & Nosaka, 2013; Starbuck & Eston, 2012). However, it should be noted that the first and second bouts were not the same conditions such that one of the bouts was for e-cell™ condition and the other was for sham condition. In contrast, the previous studies (Howatson & Van Someren, 2007; Newton et al., 2013; Starbuck & Eston, 2012) investigated the contralateral repeated bout effect without any additional effect.

For the changes in MVC torque in the present study, a significantly faster rate of recovery for strength was seen after bout 2 compared to bout 1, with significant differences observed on days 2 – 5 and 7 days post-exercise with ~12% greater strength recovery observed on day 2 after the second bout compared to the first, and this trend continued to day 7 (Figure 31). Previous studies have also reported significantly faster recovery of strength on the contralateral arm after the second bout of exercise compared to the first (Howatson & Van Someren, 2007; Newton et al., 2013; Starbuck & Eston, 2012). Our findings were similar to observations reported by Newton et al. (2013), in which two bouts were separated by 4 weeks, the same as that of the present study. However, the magnitude of strength recovery in the present study does not appear to be as significant as that found by Howatson and Van Someren (2007) and Starbuck and Eston (2012) whose subjects performed exercise bouts with only 2 weeks separation. It may be that the contralateral repeated bout effect is attenuated with increasing the interval between bouts as shown in the ipsilateral repeated bout effect (Nosaka, Sakamoto, Newton, & Sacco, 2001).

A significantly faster rate of recovery for ROM was also observed for days 1 – 5 following bout 2 compared to bout 1 (Figure 32). Interestingly, previous studies exhibiting the contralateral repeated bout effect found no significant difference between bouts 1 and 2 for the recovery of ROM following EIMD (Howatson & Van Someren, 2007; Newton et al., 2013; Starbuck & Eston, 2012). It is not clear why significant differences in ROM were evident in the present study and not in the previous contralateral repeated bout studies. It must be noted that Howatson and Van Someren (2007) and Starbuck and Eston (2012) only measured elbow joint ROM for three time points (pre-,

48 and 96 hours and pre-, 24 and 48 hours respectively) instead of nine time points in the Newton et al. (2013) and present study which may have influenced the statistical significance of their findings.

Besides the enhanced muscle function, there were also significantly smaller increases in upper arm circumference after bout 2 compared to bout 1 (Figure 33). Newton et al. (2013) also reported significantly less swelling after bout 2 compared to bout 1, but the magnitude of effect after the second bout in the present study appears to be greater given that significant differences were found for every time point after 60 minutes post-exercise compared to day 7 only in the Newton et al. (2013) study. Interestingly, Howatson and Van Someren (2007) found no significant contralateral repeated bout effect for upper arm circumference; although a direct comparison should not be made since the interval between bouts differed to the present study. Starbuck and Eston (2012) did not measure upper arm circumference.

Compared to bout 1, palpation (Figure 34), peak (Figure 35) and extension soreness were all significantly attenuated in bout 2. Significant differences were seen from days 2 – 5 post-exercise for palpation soreness, while peak soreness was ~35% lower after the second bout compared to the first. Similarly, the recovery of muscle tenderness was significantly faster after bout 2 compared to bout 1, with PPT values returning to baseline after 5 days post-exercise in the second bout compared to day 7 in the first bout (Figure 36). The three previous contralateral repeated bout effect studies did not include PPT measures. However, with regards to DOMS, Howatson and Van Someren (2007) and Starbuck and Eston (2012) also found significantly less muscle soreness develop in the elbow flexors after bout 2 compared to bout 1 although a direct comparison should be treated with caution as the previously mentioned studies assessed extension soreness only. In contrast, Newton et al. (2013) found no significant difference in extension soreness of the elbow flexors between the first and second bouts.

The second bout of exercise also attenuated increases in plasma CK activity compared to the first with significant differences seen from day 3 onwards (Figure 37). In addition, significantly less (~45%) peak plasma CK activity was evident following bout 2 compared to bout 1 (Figure 38). The

blunted plasma CK activity following the second bout in the present study is in accordance with previous studies (Howatson & Van Someren, 2007; Newton et al., 2013; Starbuck & Eston, 2012).

These findings from the present study provide further evidence for the existence of the contralateral repeated bout effect. These results follow a similar trend to that found in previous research and suggest the adaptations to a contralateral repeated bout of exercise are primarily determined by centrally mediated neural mechanisms as there is no direct stimulus for cellular or mechanical adaptations to develop in the unexercised limb (Howatson & Van Someren, 2007; Newton et al., 2013; Starbuck & Eston, 2012). It should be noted that the contralateral repeated effect found in the present study could be a combination of the contralateral repeated bout effect and the treatment effect.

The crossover design was chosen in this study, as it requires a smaller number of subjects and allows for reduced variability in molecular responses to exercise created by heterogeneous subjects (Chen, Hubal, Hoffman, Thompson, & Clarkson, 2003). The present study showed that the magnitude of the e-cell™ treatment effect was greater for the first bout (the subjects who had either the e-cell™ or sham treatment for the first bout only were compared) than the second bout (the subjects who had either the e-cell™ or sham treatment for the second bout only were compared) using a smaller number (n=8) of subjects (Figure 40). Interestingly, the magnitude of the e-cell™ treatment effect was smaller for the second bout than the first bout. This suggests that the contralateral repeated bout effect could have affected the results such that the smaller effect found in the second bout was the combination of the treatment effect and the contralateral repeated bout effect. Importantly, the magnitude of the treatment effect found for the first bout was more similar to the results of the overall magnitude of treatment effect (Figure 39 & 40). Therefore, it appears that the crossover design is acceptable for validating the intervention. However, it should be cognisant that the contralateral repeated bout effect could affect the results when the arm-to-arm comparison model is used. Future studies assessing the effects of prophylactic or therapeutic interventions on muscle damage may look to extend the washout period between exercise bouts if



an arm-to-arm comparison model is used, or separate subjects into either control or intervention group so that a prior bout of exercise does not influence the outcome measures.

### **5.2.7 Comparison between the Treatment Effect and the Repeated Bout Effect**

As discussed above, it appears that the magnitude of the contralateral repeated bout effect was greater than the effect of e-cell™ treatment (Figure 39). For example, on day 5 e-cell™ treatment only improved the rate of recovery for MVC torque, ROM, peak soreness and PPT by approximately 9%, 4%, 11% and 13%, respectively (Figure 40). On the other hand, the contralateral repeated bout effect improved the rate of recovery for the same muscle damage markers on day 5 by almost 18%, 8%, 35% and 20% respectively (Figure 39). It is not realistic that one arm is damaged to protect the other arm from muscle damage, but several studies have shown that non-damaging exercise consisting of either low-intensity eccentric contractions (Chen et al., 2011) or maximal contractions at a long muscle length (Chen, Nosaka, Pearce, & Chen, 2012) confers a protective effect against muscle damage induced by maximal eccentric contraction. These studies have shown that the magnitude of muscle damage is greatly reduced when non-damaging exercise was performed previously (Chen et al., 2011, Chen et al., 2012). Furthermore, it appears that the protective effect induced by non-damaging or pre-conditioning exercise may be greater than was shown by the e-cell™ treatment found in the present study. Therefore, pre-conditioning the muscle with a prior bout of exercise could be more effective at attenuating symptoms associated with EIMD compared to e-cell™ treatment. Since there are no costs for the pre-conditioning exercise, it might be that e-cell™ treatment may not be the best choice for the attenuation of muscle damage induced by eccentric exercise.

### 5.3 Conclusion

In summary, the present study showed recovery of muscle damage markers were faster with e-cell™ treatment compared with sham treatment. However, it is evident that the contralateral repeated bout effect may have been a confounding factor that provided a protective effect in the second bout of exercise for both conditions. It has been reported that pre-conditioning the muscle using maximal isometric contractions or sub-maximal eccentric exercise, which are non-damaging, can have a strong protective effect against muscle damage. However, it is not known whether the magnitude of the protective effect conferred by pre-conditioning exercise is stronger than the magnitude of the e-cell™ treatment effect. Therefore, if the e-cell™ treatment effect is weaker than the effect of pre-conditioning exercise, then pre-conditioning exercise should be recommended in preference to e-cell™ treatment because it can be administered with minimal cost and the equipment can be easier to access. However, if no pre-conditioning exercise was performed, and muscle damage was induced, e-cell™ treatment seems to be a good option to enhance recovery from eccentric exercise-induced muscle damage. There are many causes of muscle damage, and eccentric exercise-induced muscle damage is only one of them. Further studies are necessary to investigate the effect of e-cell™ treatment on other soft tissue injuries, since it is anecdotally believed to enhance recovery from more severe injuries such as a skeletal muscle tears.

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# APPENDICES

## APPENDIX A: ETHICS APPROVAL

### 6044 BANYARD ethics application

#### Research Ethics

**Sent:** Tuesday, 1 March 2011 5:01 PM  
**To:** Henry BANYARD  
**Cc:** Ken NOSAKA; Research Assessments  
**Attachments:**  [Conditions of approval.pdf \(50 KB\)](#) [Open as Web Page]

Dear Henry

**Project Number:** 6044 BANYARD

**Project Name:** Effects of pulsed electromagnetic field therapy on symptoms associated with eccentric exercise induced muscle damage

**Student Number:** 6042260

The ECU Human Research Ethics Committee (HREC) has reviewed your application and has granted ethics approval for your research project. In granting approval, the HREC has determined that the research project meets the requirements of the *National Statement on Ethical Conduct in Human Research*.

The approval period is from 1 March 2011 to 30 March 2012.

The Research Assessments Team has been informed and they will issue formal notification of approval. Please note that the submission and approval of your research proposal is a separate process to obtaining ethics approval and that no recruitment of participants and/or data collection can commence until formal notification of both ethics approval and approval of your research proposal has been received.

All research projects are approved subject to general conditions of approval. Please see the attached document for details of these conditions, which include monitoring requirements, changes to the project and extension of ethics approval.

Please feel free to contact me if you require any further information.

Regards  
Kim

**Kim Gifkins**, Research Ethics Officer, Office of Research & Innovation, Edith Cowan University, 270 Joondalup Drive, Joondalup, WA 6027 [research.ethics@ecu.edu.au](mailto:research.ethics@ecu.edu.au) Tel: +61 08 6304 2170 | Mobile: 0428 035 397 | Fax: +61 08 6304 5044 | CRICOS IPC 00279B

## **APPENDIX B: STUDY 1 - INFORMATION LETTER**



### **Information Letter to Participants**

#### **Title of the Project: Effects of Pulsed Electromagnetic Field Therapy on Symptoms Associated with Eccentric Exercise-Induced Muscle Damage.**

##### **Study 1**

Investigator: Harry Banyard (MSc. Candidate)

Principle Supervisor: Professor Ken Nosaka

Co-Supervisor: Associate Professor Michael Newton

School of Exercise, Biomedical and Health Sciences

Edith Cowan University

270 Joondalup Drive, Joondalup WA 6027

Thank you for expressing an interest in the study. The purpose of this information letter is to provide you with an overview of the study in which you may participate in as a subject.

#### **Purpose of the study**

The purpose of this study is to investigate whether 30 minutes of e-cell™ treatment increases muscle temperature, blood flow and oxygenation when it is applied to the elbow flexor muscles (in particular the biceps brachii).

#### **Background**

Pulsed electromagnetic field therapy (PEMFT) is a therapeutic treatment that produces magnetic waves to penetrate deeply through tissues without contact, where the magnetic pulses are believed to enhance cellular repair. Previous research has shown PEMFT to reduce pain, swelling and inflammation relating to musculoskeletal injuries, and enhance the tissue regeneration process. For this to occur it seems likely that PEMFT can increase muscle oxygenation and blood flow, but no previous study has investigated the effects of PEMFT on muscle temperature or these other factors. A portable PEMFT device called e-cell™ produces low frequency, low power electromagnetic

fields, and has been anecdotally claimed to enhance the healing processes of soft tissue injuries. Therefore this will be the first study to investigate whether PEMFT can enhance muscle temperature, muscle oxygenation and blood flow simultaneously.

## **Methods**

As a participant in this study you are required to attend 2 testing sessions (24 hours apart) for a duration of approximately 45 mins/session at Edith Cowan University, Joondalup Campus, commencing in the exercise physiology lab, building 19, room 19.150. A company (Global Energy Medicine) has provided two e-cell devices that generate electromagnetic pulses at different frequencies. You and the investigator are blinded to the devices (only informed as Device A and Device B). The testing session will involve a series of assessments designed to test the effectiveness of the e-cell™ device to increase muscle temperature, muscle oxygenation and blood flow.

## **Subjects**

As a volunteer, you must be aged between 18 to 45 years for this study. You must complete an informed written consent form and a medical questionnaire before participating in the study.

## **Procedure**

During the testing session one arm will receive e-cell™ treatment at a low frequency and for the other testing session the other arm will receive treatment at a different frequency. You will be asked to lay supine on a massage table and required to keep your treatment arm as still as possible until the treatment period concludes to minimise changes in blood flow due to movements. The device (similar in shape and size to a computer mouse and weighing approximately 100g) will be placed longitudinally along the lateral aspect of your biceps brachii (outer upper arm) and held in place by a Velcro strap. The treatment will be applied for 30 min. The device will be switched on, where green and red lights will flash to indicate it is operating and then turned off after 30 min of treatment indicated by the sound of a double beep.

## **Muscle Temperature**

A thermometer will measure your biceps brachii muscle temperature with a needle thermistor probe that will be inserted to a depth of 20 mm at a 45 angle into the belly of your biceps brachii. Three measurements will be taken 5 min before, immediately after, and 10 min after treatment.

### **Muscle Oxygenation and Blood flow**

Near infrared spectroscopy (NIRS) is a non-invasive technique that will be employed to monitor muscle oxygenation and blood flow in the biceps brachii muscles. The probe unit of the NIRS system will be firmly attached to the skin at the mid-belly of your biceps brachii with double-sided adhesive tape to ensure no sliding of the probe on the skin. The NIRS probe in relation to the treatment device will be aligned adjacently. The NIRS system will record your muscle oxygenation and blood flow levels commencing 5 min prior (resting value) to “e-cell” treatment and continue until 10 min after the “e-cell” treatment concludes.

### **Potential Risks**

In very rare instances, the muscle temperature procedure can lead to bleeding or bruising that might cause pain and make using the muscle difficult for a few days. To avoid the chances of infection, the investigator will wear gloves and use a sterilized needle. The insertion site will also be cleaned and prepared with alcohol wipes.

### **Potential Benefits**

You will have the chance to observe how current research techniques are performed and you may also gain an insight and understanding about the test involved.

### **Privacy and Confidentiality**

All information collected during this research remains confidential and will not be used for any other purpose other than this study. All data collected will be stored securely on ECU premises and kept for 5 years after the completion of the project and then destroyed.

### **Participation in the Study**

Participation in this research is entirely voluntary and you may refuse to participate or withdraw at anytime without adverse consequences.

If you have any questions about the research project or require further information you may contact the following:

***Student Researcher:*** Henry Banyard

***Telephone:*** (08) 6 304 5156

***Email:*** h.banyard@ecu.edu.au

***Principal Supervisor:*** Prof. Ken Nosaka

***Telephone:*** (08) 6 304 5655

***Email:*** [k.nosaka@ecu.edu.au](mailto:k.nosaka@ecu.edu.au)

***Co-Supervisor:*** Associate Prof. Michael Newton

***Telephone:*** (08) 6 304 4132

***Email:*** m.newton@ecu.edu.au

If you have any ethical concerns with regards to your participation in this study you may contact:

***Research Ethics Officer:*** Kim Gifkins

***Phone:*** (08) 9304 2170

***Address:*** Human Research Ethics Committee, Edith Cowan University, 100 Joondalup Drive,  
Joondalup WA, 6027

***Email:*** research.ethics@ecu.edu.au

Thank you for your time,

Yours sincerely,

Harry Banyard

## APPENDIX C: STUDY 1 - INFORMED CONSENT FORM



### Subject Informed Consent Form

#### Study 1

I \_\_\_\_\_, consent to participating in the research project entitled: **“Effects of Pulsed Electromagnetic Field Therapy on Symptoms Associated with Eccentric Exercise-Induced Muscle Damage”**.

#### **Statement indicating consent to participate**

I confirm the following:

- I have been provided with the “Information Letter” explaining the research study
- I have read and understood the information provided and the procedures of the study
- I have been given an opportunity to ask questions and I have had any questions answered to my satisfaction
- I am aware that if I have any additional questions, I can contact the research team
- I understand that participation in the research project will involve:
  - Two testing sessions where one arm will receive e-cell™ treatment and the other arm will receive sham treatment
  - Measurements of muscle temperature, muscle oxygenation and muscle blood flow
  - Possible muscle soreness after muscle temperature measurements
- I understand that my information provided will be kept confidential, and that my identity will not be disclosed without consent
- I understand that the information provided will only be used for the purposes of this research project, and I understand how the information is to be used
- I understand that I am free to withdraw from further participation at any time, without

explanation or penalty

- I freely agree to participate in the project

---

**Participant Name** \_\_\_\_\_ **Date (DD/MM/YYYY)** \_\_\_\_\_

**Researchers Name** \_\_\_\_\_ **Date (DD/MM/YYYY)** \_\_\_\_\_



## APPENDIX D: STUDY 1 - MEDICAL QUESTIONNAIRE



### Medical Questionnaire

**Project Title:** Effects of pulsed electromagnetic field therapy on symptoms associated with eccentric exercise induced muscle damage.

The following questionnaire is designed to establish a background of your medical history, and identify any injury and/or illness that may influence your testing and performance. Please answer all questions as accurately as possible, and if you are unsure about any aspect of this form, please ask for clarification. All information provided is strictly confidential.

#### **Personal Details**

Name: \_\_\_\_\_  
Date of Birth (DD/MM/YYYY): \_\_\_\_\_ Gender: Male / Female

#### **PART A YES / NO DETAILS**

1. Are you a male over 45 years, or female over 55 years, who has had a hysterectomy or are postmenopausal? Y / N \_\_\_\_\_
2. Are you a regular smoker, or have you quit in the last 6 months? Y / N \_\_\_\_\_
3. Did a close family member have heart disease or surgery, or stroke before the age of 60 years? Y / N \_\_\_\_\_
4. Do you have, or have you ever been told you have blood pressure above 140/90 mmHg, or do you currently take blood pressure medication? Y / N \_\_\_\_\_
5. Do you have, or have you ever been told you have a total cholesterol level above 5.2 mmol/L (200 mg/dL)? Y / N \_\_\_\_\_
6. Is your BMI (weight/height) greater than 30? Y / N \_\_\_\_\_

#### **PART B YES / NO DETAILS**

1. Have you ever had a serious asthma attack during exercise? Y / N \_\_\_\_\_
2. Do you have asthma that requires medication? Y / N \_\_\_\_\_
3. Have you had an epileptic seizure in the last 5 years? Y / N \_\_\_\_\_

4. Do you have any moderate or severe allergies? Y / N \_\_\_\_\_

5. Do you, or could you reasonably have an infectious disease? Y / N \_\_\_\_\_

6. Do you, or could you reasonably have an infection or disease that might be aggravated by exercise? Y / N \_\_\_\_\_

7. Are you, or could you reasonably be pregnant? Y / N \_\_\_\_\_

### **PART C YES / NO DETAILS**

1. Are you currently taking any prescribed or non-prescribed medication?

Y / N \_\_\_\_\_

2. Have you had, or do you currently have any of the following:-

- Rheumatic Fever Y / N \_\_\_\_\_
- Heart Abnormalities Y / N \_\_\_\_\_
- Diabetes Y / N \_\_\_\_\_
- Epilepsy Y / N \_\_\_\_\_
- Recurring back pain that will make exercise problematic, or where exercise may aggravate pain? Y / N \_\_\_\_\_
- Recurring neck pain that will make exercise problematic, or where exercise may aggravate pain? Y / N \_\_\_\_\_
- Neurological disorders that would make exercise problematic, or where exercise may aggravate the condition? Y / N \_\_\_\_\_
- Neuromuscular disorders that would make exercise problematic, or where exercise may aggravate the condition? Y / N \_\_\_\_\_
- Recurring muscle/joint injuries that would make exercise problematic, or where exercise may aggravate the condition? Y / N \_\_\_\_\_
- A burning or cramping sensation in your legs when walking short distances?  
Y / N \_\_\_\_\_
- Chest discomfort, unreasonable breathlessness, dizziness or fainting, or blackouts during exercise? Y / N \_\_\_\_\_

## PART D YES / NO DETAILS

1. Have you had any influenza in the last week? Y / N \_\_\_\_\_

2. Do you currently have an injury that might affect, or be affected by exercise?

Y / N \_\_\_\_\_

3. Have you had any minor or major injuries in the past 3 months? Y / N \_\_\_\_\_ If so, please list. Has this injury stopped you training or competing in one or more sessions? If so, how many? \_\_\_\_\_

4. Is there any other condition not previously mentioned that may affected your ability to participate in this study? Y / N \_\_\_\_\_

Declaration – (to be signed in the presence of the researcher)

I acknowledge that the information provided in this form, is to the best of my knowledge, a true and accurate indication of my current state of health.

### Participant

Name: \_\_\_\_\_ Date (DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_

### Researcher

Name: \_\_\_\_\_ Date (DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_

### Practitioner (*only if applicable*)

I, Dr \_\_\_\_\_ have read the medical questionnaire and the information / consent form provided to my patient, Mr / Miss / Ms / Mrs \_\_\_\_\_, and clear him / her medically for involvement in exercise testing.

Name: \_\_\_\_\_ Date(DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_

## **APPENDIX E: STUDY 2 - INFORMATION LETTER**



### **Information Letter to Participants**

**Title of the Project: Effects of Pulsed Electro Magnetic Field Therapy on Symptoms  
Associated with Eccentric Exercise-Induced Muscle Damage.**

Study 2

Investigator: Henry Banyard (MSc. Candidate)

Supervisor: Professor Ken Nosaka

School of Exercise, Biomedical and Health Sciences  
Edith Cowan University  
270 Joondalup Drive, Joondalup WA 6027

Thank you for expressing an interest in the study. The purpose of this information letter is to provide you with an overview of the study in which you may participate in as a subject.

#### **Purpose of the study**

We are interested in investigating the potential effect of e-cell™ treatment in reducing changes of muscle damage markers such as maximal voluntary contraction (MVC) strength, upper arm circumference, range of motion (ROM), muscle soreness, and plasma creatine kinase (CK) activity following eccentric exercise of the elbow flexors.

#### **Background**

Pulsed electro magnetic field therapy (PEMFT) is a therapeutic treatment that produces magnetic waves to penetrate deeply through tissues without contact, where the magnetic pulses are believed to enhance cellular repair. Previous research has shown PEMFT to reduce pain, swelling and inflammation relating to musculoskeletal injuries, and enhance the tissue regeneration process. A portable PEMFT device called e-cell™ produces low frequency, low power electromagnetic fields, and has been anecdotally claimed to enhance the healing processes of muscle injuries. However, no

experimental studies have yet examined the effects of e-cell™ treatment on markers of muscle damage induced by maximal elbow extension (eccentric) exercise. Therefore this will be the first study to investigate whether 30 minutes of e-cell™ treatment performed 30 minutes, 1, 2, 3 and 4 days after eccentric exercise of the elbow flexors will reduce the associated symptoms and markers of eccentric exercise-induced muscle damage.

## **Subjects**

As a volunteer, you must be aged between 18 to 45 years for this study. You must complete an informed written consent form and a medical questionnaire before participating in the study. Female subjects will also be asked to complete a menstrual history questionnaire. You are also requested not to perform unaccustomed exercise during the experimental period.

Participants are required to attend 16 sessions consisting of a familiarisation session (45 mins), a reliability testing session (30 mins), 2 exercise sessions (180 mins/session) and 12 testing sessions (90 mins/session) at Edith Cowan University, Joondalup Campus, commencing in the exercise physiology lab, building 19, room 19.150.

## **Familiarisation session:**

You will attend a familiarisation session at least one week before you participate in the study. Your height and weight measurements will be recorded and you will complete a medical questionnaire to ensure you do not present contraindications to participate in the study. You will perform 2 maximal static (isometric) contractions at 90° and 2 maximal elbow flexion (concentric) contractions at a velocity of 30°·s<sup>-1</sup> and 210°·s<sup>-1</sup> during this session. No elbow extension (eccentric) contractions will be performed to minimise any muscle damage to the elbow flexors. However you will be shown and briefed on the eccentric exercise protocol. Measurements such as range of motion, arm circumference, muscle soreness and pressure pain threshold and plasma CK activity will also be recorded.

## **Exercise Day**

A company will provide two identical e-cell™ devices; one being the actual e-cell™ and the other will not generate electromagnetic pulses (sham). Subjects will perform a bout of maximal eccentric exercise of the elbow flexors of each arm 4 weeks apart. Female subjects will perform the exercise after the luteal phase (lowest oestrogen levels) of their menstrual cycle, since oestrogen may have an apparent protective effect on skeletal muscle and may therefore reduce the markers of eccentric

exercise-induced muscle damage (Kendall & Eston, 2002). One arm will receive e-cell™ treatment and the other arm will receive sham treatments on five occasions such as 30 minutes after the exercise, and 1, 2, 3 and 4 days following the exercise. The treatment duration for each time point will be 30 minutes, which is normally used in the e-cell™ treatment. To establish intra-rater reliability for all dependant variables, two baseline measures will be taken at 3 days prior to and immediately before the first eccentric exercise bout. Therefore the experiment period will include one block of 8 days of testing (3 days before exercise, before and after exercise, 1, 2, 3, 4, 5, and 7 days post exercise) and one block of 7 days of testing (before and after exercise, 1, 2, 3, 4, 5, and 7 days post exercise). In the testing, isokinetic and isometric strength, range of motion, arm circumference, muscle soreness and pressure pain threshold, and blood samples to assess plasma CK activity will be taken.

The exercise session consists of 10 sets of 6 maximum voluntary eccentric contractions of the elbow flexors against the lever arm of the isokinetic dynamometer moving at a constant velocity of  $30^{\circ}\cdot\text{s}^{-1}$ . You will be positioned on a seated preacher arm curl bench with a supinated forearm position. The elbow joint will be forcibly extended from a flexed position ( $90^{\circ}$ ) to a fully extended position ( $180^{\circ}$ ) in 3 seconds. Subjects will be verbally encouraged to generate a maximal isometric force at the starting position and to maximally resist against the elbow extending action throughout the full range of motion. After each eccentric action, the isokinetic dynamometer will return the arm to the flexed position while you are asked to relax the arm at a constant velocity of  $9^{\circ}\cdot\text{s}^{-1}$ , creating a 10 second passive recovery between contractions. The rest period between sets will be 90 seconds. A company (Global Energy Medicine) has provided two e-cell devices that generate electromagnetic pulses at different frequencies. You and the investigator are blinded to the devices (you are only informed of Device A and Device B).

### **Recovery Day**

The recovery session days will involve a series of assessments that will be performed before and immediately after e-cell™ treatment. During the testing session one arm will receive e-cell™ treatment at a particular frequency and for the other testing session the opposite arm will receive e-cell™ treatment at a different frequency. You will be asked to lay supine on a massage table and required to keep your treatment arm as still as possible until the treatment period concludes to minimise changes in blood flow due to movements. The device (similar in shape and size to a computer mouse and weighing approximately 100g) will be placed on the outside of your biceps brachii muscle (longitudinally along the lateral aspect of your biceps brachii) and held in place by a

Velcro strap. The treatment will be applied for 30 min. The device will be switched on, where green and red lights will flash to indicate it is operating and then turned off.

## Measurements

The following measurements will be taken from the exercise arm.

- 1. Maximal Static (Isometric) Strength:** You will be asked to perform two 3-s maximal isometric contractions at an elbow joint angle of 90°, 120° and 150° (where 180° represents a fully extended elbow joint angle) on the dynamometer in this order with 30 seconds rest between contractions at the same joint angle and 60 seconds rest between contractions at different joint angles.
- 2. Range of Motion:** A plastic goniometer will be used to examine the range of motion (ROM) of the elbow joint. Three types of joint angles will be measured; relaxed elbow joint angle (arm relaxed by side), extended elbow joint angle (maximal arm extension without moving the elbow) and flexed elbow joint angle (maximal arm flexion without moving elbow). ROM measurement is calculated by subtracting flexed elbow joint angle from extended elbow joint angle.
- 3. Upper Arm Circumference:** A constant tension tape will be used to measure circumference of the exercise limb while the arm is hanging relaxed by your side (palms facing the thigh). The measurements will be taken from 3 upper arm sites and 1 forearm site marked by a semi-permanent ink marker.
- 4. Muscle Soreness:** The level of muscle soreness will be assessed using a 100 mm visual analogue scale (VAS). On the scale, 0 mm indicates no pain and 100 mm represents extreme pain. You will be asked to mark your level of perceived soreness on the VAS while the corresponding joint is flexed and extended by the investigator. Palpation will also be applied using the index and middle fingers slowly in a circular motion 5 times on four sites of the upper arm including the mid-belly of the biceps brachii, 3 cm above and below the mid-belly and the brachialis.
- 5. Pressure Pain Threshold (PPT):** A device (electronic algometer) will be used to measure pain in the exercised arm. Force will be gradually applied until you report the first feeling of noticeable pain.
- 6. Plasma CK activity:** A small amount of blood (30 µl) will be collected from your finger and the blood will be analysed for plasma CK levels.

### **Potential Risks**

You may experience some degree of muscle soreness and decreases in muscle strength and ROM for some days after exercise which may affect daily activities, therefore care must be taken. You may also experience swelling of the upper arm and forearm. These are typical symptoms of unaccustomed eccentric exercise induced muscle damage and will disappear in a week or so. If symptoms exist for longer than a week you should inform the investigator who will provide you with a letter explaining the study you participated in which can be presented to a doctor.

### **Potential Benefits**

The potential benefits include the chance to observe how research is performed and gaining an insight and understanding about the test involved.

### **Privacy and Confidentiality**

All information collected during this research remains confidential and will not be used for any other purpose other than this study. All data collected will be stored securely on ECU premises and kept for 5 years after the completion of the project and then destroyed.

### **Participation in the Study**

Participation in this research is entirely voluntary and you may refuse to participate or withdraw at anytime without adverse consequences.

If you have any questions about the research project or require further information you may contact the following:

***Student Researcher:*** Harry Banyard

***Telephone:*** (08) 6 304 5156

***Email:*** [h.banyard@ecu.edu.au](mailto:h.banyard@ecu.edu.au)

***Principal Supervisor:*** Prof. Ken Nosaka

***Telephone:*** (08) 6 304 5655

***Email:*** [k.nosaka@ecu.edu.au](mailto:k.nosaka@ecu.edu.au)

***Co-Supervisor:*** Associate Prof. Michael Newton

***Telephone:*** (08) 6 304 4132

***Email:*** [m.newton@ecu.edu.au](mailto:m.newton@ecu.edu.au)



If you have any ethical concerns with regards to your participation in this study you may contact:

***Research Ethics Officer:*** Kim Gifkins

***Phone:*** (08) 9304 2170

***Address:*** Human Research Ethics Committee, Edith Cowan University, 100 Joondalup Drive,  
Joondalup WA, 6027

***Email:*** [research.ethics@ecu.edu.au](mailto:research.ethics@ecu.edu.au)

Thank you for your time,

Yours sincerely,

Harry Banyard

## APPENDIX F: STUDY 2 - INFORMED CONSENT FORM



### **Subject Informed Consent Form**

#### **Study 2**

I \_\_\_\_\_, consent to participating in the research project entitled: **“Effects of Pulsed Electro Magnetic Field Therapy on Symptoms Associated with Eccentric Exercise-Induced Muscle Damage”**.

#### **Statement indicating consent to participate**

I confirm the following:

- I have been provided with the “Information Letter” explaining the research study
- I have read and understood the information provided and the procedures of the study
- I have been given an opportunity to ask questions and I have had any questions answered to my satisfaction
- I am aware that if I have any additional questions, I can contact the research team
- I understand that I may experience severe muscle pain in the days after exercise
- I am aware that my muscles will be weak for a week or two, or more than a month in rare instances, which may affect the performance of daily activities
- I am aware that my muscles may be swollen for several days after exercise
- I understand that my information provided will be kept confidential, and that my identity will not be disclosed without consent
- I understand that the information provided will only be used for the purposes of this research project, and I understand how the information is to be used
- I understand that I am free to withdraw from further participation at any time, without explanation or penalty

- I freely agree to participate in the project

---

**Participant Name** \_\_\_\_\_ **Date (DD/MM/YYYY)** \_\_\_\_\_

**Researchers Name** \_\_\_\_\_ **Date (DD/MM/YYYY)** \_\_\_\_\_

**Signatures (Participant)** \_\_\_\_\_ **(Researcher)** \_\_\_\_\_

## APPENDIX G: STUDY 2 - MEDICAL QUESTIONNAIRE



### Medical Questionnaire

The following questionnaire is designed to establish a background of your medical history, and identify any injury and/or illness that may influence your testing and performance. Please answer all questions as accurately as possible, and if you are unsure about any aspect of this form, please ask for clarification. All information provided is strictly confidential.

#### Personal Details

Name: \_\_\_\_\_

Date of Birth (DD/MM/YYYY): \_\_\_\_\_

Gender: Female/ Male

#### PART A

Yes / No

#### DETAILS

- |   |   |   |       |
|---|---|---|-------|
| 1. Are you a male or female over the age of 45 years?   | Y | N | _____ |
| 2. Are you a regular smoker or have you quit in the last 6 months?                                | Y | N | _____ |
| 3. Did a close family member have heart disease or surgery, or stroke before the age of 60 years? | Y | N | _____ |

4. Do you have, or have you ever been told you have blood pressure above 140/90 mmHg, or do you current take blood pressure medication?      Y      N      \_\_\_\_\_
5. Do you have, or have you ever been told you have, a total cholesterol level above 5.2 mmol/L (200 mg/dL)?      Y      N      \_\_\_\_\_
6. Is your BMI (weight/height<sup>2</sup>) greater than 30 kg/m<sup>2</sup>?      Y      N      \_\_\_\_\_

## **PART B**

1. Have you ever had a serious asthma attack during exercise?      Y      N      \_\_\_\_\_
2. Do you have asthma that requires medication?      Y      N      \_\_\_\_\_
3. Have you had an epileptic seizure in the last 5 years?      Y      N      \_\_\_\_\_
4. Do you have any moderate or severe \_\_\_\_\_ allergies?      Y      N      \_\_\_\_\_
5. Do you, or could you reasonably, have an infectious disease?      Y      N      \_\_\_\_\_

6. Do you, or could you reasonably, have an infection or disease that might be aggravated by exercise?      Y      N      \_\_\_\_\_
7. Are you currently taking contraceptive tablets?      Y      N      \_\_\_\_\_
8. Are you, or could you reasonably be pregnant?      Y      N      \_\_\_\_\_

## PART C

1. Are you currently taking any prescribed or non-prescribed medications?

Y      N      \_\_\_\_\_

2. Have you had, or do you currently have, any of the following?

### DETAILS

- Rheumatic fever      Y      N      \_\_\_\_\_
- Heart abnormalities      Y      N      \_\_\_\_\_
- Diabetes      Y      N      \_\_\_\_\_
- Epilepsy      Y      N      \_\_\_\_\_

- Recurring back pain that would make      Y      N      \_\_\_\_\_  
exercise problematic, or where exercise  
may aggravate the pain
- Recurring neck pain that would make      Y      N      \_\_\_\_\_  
exercise problematic, or where exercise  
may aggravate the pain
- Any neurological disorders that would Y N      \_\_\_\_\_  
make exercise problematic, or where  
exercise may aggravate the condition
- Any neuromuscular disorders that would Y      N      \_\_\_\_\_  
make exercise problematic, or where  
exercise may aggravate the condition
- Recurring muscle or joint injuries that      Y      N      \_\_\_\_\_  
would make exercise problematic, or  
where exercise may aggravate the  
condition
- A burning or cramping sensation in your Y      N      \_\_\_\_\_  
legs when walking short distances
- Chest discomfort, unreasonable      Y      N      \_\_\_\_\_

breathlessness, dizziness or fainting,  
or blackouts during exercise

## PART D

Have you had flu in the last week?                      Y        N        \_\_\_\_\_

Do you currently have an injury that might    Y        N        \_\_\_\_\_  
affect, or be affected by, exercise?

\*Is there any other condition not previously mentioned that may affect your ability to participate in  
this study?

Y        N        \_\_\_\_\_

## PART E (Female Subject)

Oestrogen may have a protective effect on muscle damage and could potentially reduce the markers of eccentric exercise-induced muscle damage. Therefore the purpose of the following questions is to determine the most suitable testing period for female subjects.

- Are you currently taking birth control pills / estrogen pills?    Y        N \_\_\_\_\_
- If yes, what type? \_\_\_\_\_
- Date of your last two menstrual cycles? \_\_\_\_\_  
\_\_\_\_\_

### **Declaration** – (to be signed in the presence of the researcher)

I acknowledge that the information provided in this form, is to the best of my knowledge, a true and accurate indication of my current state of health.

### **Participant**

Name: \_\_\_\_\_ Date (DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_



**Researcher**

Name: \_\_\_\_\_ Date (DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_

**Practitioner** (*only if applicable*)

I, Dr \_\_\_\_\_ have read the medical questionnaire and the  
information / consent form provided to my patient, Mr / Miss / Ms / Mrs \_\_\_\_\_  
\_\_\_\_\_, and clear him / her medically for involvement in exercise testing.

Name: \_\_\_\_\_ Date(DD/MM/YYYY): \_\_\_\_\_

Signature: \_\_\_\_\_