Evaluation of the Effectiveness of Laser Acupuncture on Osteo-arthritic Knee Pain: A Randomised, Double-blind, Placebo-controlled Clinical Research Trial

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Certificate of Original Authorship

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as part of the collaborative doctoral degree and/or fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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March 2017

Dedication & Acknowledgements

Dedication

This study is dedicated to the memory of:

- My proud parents, Lee Wing-wah and Yuen Sin-ching, and sister, Lee Chi-kin, each of whom encouraged the virtue of passion, dedication, determination and persistence – the very qualities that made completion of this study possible. Dad, Mum, Sister, you are forever in my thoughts; and

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Outcome Measures

Professor Nicholas Bellamy – Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Grant J. Devilly – Credibility/Expectancy Questionnaire (C/E)

Ronald Melzack – Short form McGill Pain Questionnaire (SF-MPQ)

Adam O. Horvath – Working Alliance Inventory Short Form – WAI (C)

Kenneth Wallston – Multi-dimensional Health Locus of Control Form C (MHLC-C)

Abstract

Background and Objectives

Worldwide, osteoarthritis (OA) is the major cause of musculoskeletal pain and mobility disability in elderly people. The objective of this randomised, double-blind, placebo-controlled clinical trial was to evaluate the effectiveness of laser acupuncture on osteoarthritis knee (OAK) pain. Traditional acupuncture philosophy, treatment principles and techniques were integrated with modern laser technology. The study tested the null hypothesis that laser acupuncture does not reduce pain and stiffness and improve physical function in OAK.

Study Design and Methods

Forty participants screened against Kellgren-Lawrence OA scale 2-3 and other inclusion/exclusion criteria were randomised equally into two groups – active and sham laser acupuncture – using computer-generated sequential numbers. Both the operator and participants were blinded to allocation.

An 810 nm 100mW Class 3B infra-red laser fitted with two identical probes – one active and one deactivated by the manufacturer – was used in the study. This type of laser provided a credible placebo arrangement because its invisible beam produces neither heat nor sensation when applied to the skin, thus eliminating potential bias.

At each treatment, the laser delivered 18J for two minutes to two sets of OAK-specific acupuncture points targeting Phlegm Retention and Blood Stasis and the underlying causes and symptoms according to the TCM paradigm. The 13 acupuncture points were aimed at reducing dampness and swelling, tonifying the Kidney, clearing blockages and stagnation of Qi and Blood, and soothing the Liver. In terms of Western science, laser is known to regenerate osteoblasts and cartilage, and produce analgesic effects through the release of serotonin and endorphins.

Treatments were administered three times a week over four weeks (i.e. a total of 12 treatments). Assessments occurred at four-week intervals with four time points over three months using a General Linear Model with repeated measures. Data were

analysed on an intention-to-treat basis. All data were carried forward, limiting bias for the six participants who dropped out. Participants experienced no adverse effects.

WOMAC (the gold standard for assessing OAK), VAS, McGill Pain Questionnaire, Credibility/Expectancy Questionnaire, Working Alliance Inventory and Multi-dimensional Health Locus of Control measured treatment outcomes, plus the psychometric and placebo effects of the practitioner-patient relationship and the power of others respectively.

Results

Study results rejected the null hypothesis, accepting the alternative hypothesis that the novel integration of laser with TCM methods safely reduces OAK pain and stiffness and improves physical function. All primary outcome measures scored $p < 0.05$. The vascular density of acupuncture points appears to amplify two energy-transporting systems – one based on TCM channel theory; the other cellular and peripheral nerve transduction signaling believed to occur in photo-biomodulation – thus magnifying and accelerating healing and metabolic processes. The study identified, for the first time, the importance of selecting optimum laser parameters, precise TCM diagnosis for OAK disease differentiation with specific acupuncture point formulae targeting the underlying causes and symptoms of OAK. Additionally, placebo assessment measured the importance of the patient-practitioner relationship, bonding, faith and task compliance in working towards mutual treatment goals.

Conclusion: The study indicates that irradiating specific acupuncture points according to the TCM paradigm offers a safe and effective treatment for OAK. Further studies are needed to confirm these findings.

List of Conference Presentations and Posters Arising from the Research

- Rees, L.M.K..; Meier, P.; late Rogers, C.; late Smith, N. Preliminary results of randomised, placebo-controlled clinical trial evaluating the effectiveness of laser acupuncture on osteoarthritic knee pain. Presented at Laser Helsinki 2012 World Congress Helsinki, Finland, August 2012.

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- Rees, L.M.K.; Meier, P.; late Rogers, C.; late Smith, N. Preliminary results of randomised, placebo-controlled clinical trial evaluating the effectiveness of laser acupuncture on osteoarthritic knee pain. Poster presentation Society of Acupuncture Research International Conference, Beijing, China, 30 May - 1 June 2014.

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acupuncture on osteoarthritic knee pain. Presented at Society for Acupuncture Research 2017: Advancing the Precision Medicine Initiative Through Acupuncture Research, San Francisco, California, USA, 27-29 April 2017.

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Chapter 1 Introduction

1.1 Introduction

Osteoarthritis (OA) is a chronic muscular-skeletal disorder characterised by the deterioration of cartilage in joints. The disease creates pain and stiffness and impairs movement. OA most commonly affects joints in the knees, hands, feet, spine, shoulder and hip.

OA is the single most common cause of disability in older adults, according to the *2010 Global Burden of Disease Study* (Cross et al. 2014). The burden of musculoskeletal disorders like OA and other forms of rheumatism account for 6.8% of Disability Adjusted Life Years (DALYs), a measure of disease burden expressed as the number of years lost due to ill-health, disability or early death (Murray et al. 2016).

The prevalence of OA worldwide is increasing through population ageing and an increase in obesity. An estimated 10% to 15% of adults aged over 60 years have some degree of OA (Haq I 2003). It affects 9.6% of men and 18% of women aged over 65 years (Tanna 2013b). Furthermore, as the global population ages, WHO expects the burden of OA will increase dramatically. The United Nations estimates that, by 2050, people aged over 60 years will account for more than 20% of the world's population (*World Population to 2300* 2004). Of that 20%, an estimated 15% will have symptomatic OA and one third will be severely disabled. By 2050, it is estimated that some 130 million people will suffer from OA worldwide and 40 million of them will be severely disabled.

In Australia, the United States of America and the United Kingdom, OA is the most common joint disorder. OA affects about 1.4 million Australians or about 7.3% of the population ('A Picture of Osteoarthritis in Australia' 2007; Dr Prescott 2007). In the U.S., about 27 million Americans are living with OA and the life-time risk of developing

the condition is about 46% (Arthritis Foundation 2016). The ageing population and obesity epidemic are expected to increase the number of people affected with symptomatic OA. In the U.K, a total of 7.3 million people, or about a third of people aged 45 years and over, have sought treatment for OA. Of these, 4.11 million people or around 18% of the population aged 45 and older are estimated to have OAK (Arhtritis Research UK 2016).

In Australia alone, $1.6 billion or 2.5% of selected disease-allocated health-care expenditure was attributed to OA in 2008-9 (Australian Institute of Health and Welfare 2016). Of this expenditure on OA, 76.7% or $1.256 million was for hospital-admitted patient services; 17.2% or $282 million for out-of-hospital medical costs and 6.0% or $99 million) for prescription pharmaceuticals. These estimates exclude a range of other costs incurred by people with OA, such as privately purchased and privately insured health services like physiotherapy and over-the-counter medicines (e.g. paracetamol and glucosamine). Also excluded were costs of other drugs prescribed to counter the adverse effects associated with some OA treatments or for surgical costs related to GI bleeding triggered by OA medications.

In biomedicine, the current approaches to managing OA rely mostly on expensive pharmaceutical treatments. Some of these treatments produce adverse side effects that can lead to other complicating health issues and even death. To help counter such issues, this study investigated laser acupuncture as an effective low-cost alternative treatment for OA.

1.2 Why the Knee is Susceptible to Osteoarthritis

The knee is the largest and one of the most complex joints in the body**.** The stress and impact of weight and twisting and turning actions, makes the knee one of the most common sites for OA. It can make walking, standing and sitting extremely painful. OAK can impact on sports careers and people with physically demanding work. It also can limit climbing stairs, bathing and personal care, or driving a car. In severe cases, OAK is a substantial barrier to mobility and independence, and it significantly compromises

wellbeing and quality of life. Obesity is a strong risk factor for OAK and overweight people are 14 times more likely to develop the condition than those of a healthy weight (Sowers & Karvonen-Gutierrez 2010).

OA mostly affects cartilage, hard, slippery connective tissue that covers the ends of bones where they meet to form a joint. Healthy cartilage allows bones to glide over each other, absorbing energy from the shock of physical movement. In OAK, the surface layer of cartilage breaks and wears away. This causes bones under the cartilage to rub together, causing pain, swelling and restricting movement of the joint. Over time, the joint may lose its normal shape and small deposits of bone — called osteophytes or bone spurs — may grow on the edges of the joint. Pieces of bone or cartilage can break off and float inside the joint space, causing more pain and damage (National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) 2016).

1.3 Managing Knee Osteoarthritis

Currently, osteoarthritis cannot be cured and will likely worsen over time (Woolf & Pfleger 2003). OAK is generally managed through a combination of non-pharmacological and pharmacological measures. These include lifestyle modifications, maintaining a healthy weight, appropriate exercise, knee strengthening exercises, and taping and bracing the knee. Painkillers, anti-inflammatory gels or injections of corticosteroids into the joint are sometimes used to help relieve pain. The use of non-steroidal anti-inflammatory drugs (NSAIDs), however, is not always successful and can lead to gastro-intestinal bleeding. For severe stages of knee OA, joint replacement is an option.

1.3.1 Osteoarthritis Treatment Guidelines

A number of physician-based organisations around the world have established guidelines that recommend a pragmatic, individualised, patient-centred approach to

treating OA. This involves minimising toxicity, controlling pain, maintaining and improving the range of movement and stability of affected joints, and limiting functional impairment. The general aim is to manage OA without surgery but, as the following guidelines show, not all physician groups appear to agree on what constitutes a uniform multi-disciplinary approach.

Osteoarthritis Research Society International

The Osteoarthritis Research Society International (OARSI) has developed evidence-based guidelines for the non-surgical treatment of knee OA in four patient groups: (1) patients with knee-only OA and no co-morbidities; (2) patients with knee-only OA with co-morbidities; (3) patients with multi-joint OA and no co-morbidities; and (4) patients with multi-joint OA with co-morbidities.

Co-morbidities include diabetes, hypertension, cardiovascular disease, renal failure, gastro-intestinal bleeding, depression or a physical impairment limiting activity, including obesity (McAlindon et al. 2014)

The OARSI guidelines, developed by 13 experts from medical disciplines covering primary care, rheumatology, orthopaedics, physical therapy, physical medicine and rehabilitation and evidence-based medicine in 10 countries and a patient representative, inform patients, physicians and allied healthcare professionals worldwide.

The guidelines recommend a set of non-pharmacological core treatments for OAK sufferers listed in order from highest to lowest as a benefit-to-risk score.

Treatment modalities considered appropriate for knee OA include biomechanical interventions, intra-articular corticosteroids, land-based and water-based exercise, self-management and education, strength training and weight management. Treatments appropriate for specific clinical sub-phenotypes include acetaminophen (paracetamol); balneotherapy; capsaicin; use of a walking stick, duloxetine, oral NSAIDs, COX-2 selective and non-selective; and topical NSAIDs. For weight

management, the OARSI guidelines specifically recommend OAK patients achieve a 5% weight loss within a 20-week period for treatment to be effective.

Medical Journal of Australia

The Medical Journal of Australia (MJA) recommends managing OA patients without surgery, although joint arthroplasty is indicated for joint failure with intractable pain (Grainger & Cicuttini 2004).

Pharmacological measures the MJA lists for use as an adjunct include paracetamol, NSAIDs and cyclo-oxygenase-2-specific inhibitors (COX-2), glucosamine and chondroitin, opioids, intra-articular visco-supplementation and topical analgesia. Major side effects of some pharmacological treatments are heart attacks and gastro-intestinal bleeding (GIB). The risk of upper GIB increases about four fold among users of non-aspirin NSAIDs when compared to non-users (Mellemkjaer et al. 2002).

The MJA recommends educating the patient about the disease process, its prognosis and the role self-management can play in reducing OA pain and improving quality of life. Patient inactivity due to pain leads to reduced muscle bulk around OA-affected joints and joint instability. Exercise reduces pain and disability by strengthening muscle, improving joint stability, increasing the range of movement and improving aerobic fitness. Other benefits include improved self-esteem, better general health and weight loss. Studies of overweight patients with knee OA have shown that even modest weight loss (less than 5kg) has significant short-term and long-term reductions in OA symptoms (Christensen R. et al. 2007).

American College of Rheumatology

Like OARSI, the American College of Rheumatology (ACR) recommendations for the management of knee OA are based on the consensus judgement of a Technical Expert Panel (TEP) from a wide range of disciplines. They are informed by available evidence

and cover the use of pharmacological and non-pharmacological treatments (American College of Rheumatology 2013).

The ACR TEP strongly recommends that patients with symptomatic OAK participate in cardiovascular (aerobic) and/or resistance land-based exercise or aquatic exercise and lose weight if required. Conditional recommendation is given to participation in self-management programs; manual therapy combined with supervised exercise; psychosocial interventions; medially directed patellar taping; medially wedged insoles if lateral compartment OA is present; laterally wedged subtalar strapped insoles if medial compartment OA is present; instruction in the use of thermal agents; walking aids as needed; traditional Chinese acupuncture; and instruction in the use of transcutaneous electrical stimulation (TENS).

The ACR TEP notes the conditional recommendation for acupuncture and TENS applies only when the patient with knee OA has chronic moderate to severe pain and is a candidate for total knee arthroplasty, but either is unwilling to undergo the procedure, has comorbid medical conditions or is taking concomitant medications that lead to a relative or absolute contraindication to surgery or a decision by the surgeon not to recommend the procedure.

The ACR TEP makes no recommendation for participation in balance exercise, either alone or in combination with strengthening exercises; wearing laterally wedged shoes; receiving manual therapy along with wearing knee braces; and using laterally-directed patellar taping. No reason is given for not making a recommendation on these options.

Pharmacological modalities conditionally recommend for the initial management of patients with OAK include acetaminophen, oral and topical NSAIDs, tramadol or intra-articular corticosteroid injections. The ACR TEP conditionally recommends that nutritional supplements (e.g. chondroitin sulphate, glucosamine) or topical capsaicin not be used. Again, no reason is given for this decision.

If the health care provider chooses to initiate acetaminophen to the full dosage of up to 4,000mg/day, the patient should be counselled to avoid all other products that

contain acetaminophen, including over the counter (OTC) cold remedies as well as combination products with opioid analgesics.

If there is no satisfactory clinical response to full-dose acetaminophen, then the ACR TEP strongly recommends using oral or topical NSAIDs or intra-articular corticosteroid injections (Hochberg et al. 2012).

For patients aged 75 years and over, topical rather than oral NSAIDs are recommended.

The ACR TEP strongly recommends the use of opioid analgesics and conditionally recommends the use of duloxetine for patients with symptomatic OAK who have not had an adequate response to both non-pharmacological and pharmacological modalities and are either unwilling to undergo or are not candidates for total joint arthroplasty (Chou et al. 2009).

American Academy of Orthopaedic Surgeons

The 2013 American Academy of Orthopaedic Surgeons' (AAOS) guidelines for treating OAK say a lack of evidence makes it unable to recommend, for or against, the use of a range of treatments (AAOS 2013), including physical agents (such as electro-therapeutic modalities); manual therapies (e.g. joint manipulation, chiropractic therapy, massage therapy or myofascial release); valgus-producing knee braces; and lateral wedge insoles.

AAOS recommends the use of NSAIDS for knee OA, but it does not recommend opioids or pain patches, intra-articular corticosteroids, hyaluronic acid, growth factor injections or platelet-rich plasma, arthroscopy or partial meniscectomy. AAOS does not recommend taking glucosamine and chondroitin, despite their wide use as an over-the-counter remedy. AAOS also strongly recommends acupuncture not be used because of a lack of "statistically significant" evidence about its effectiveness.

Although many of the medico groups listed above continue to recommend the use of oral NSAIDS for pain relief and more powerful opiates, the health risks associated with these drugs are widely known.

The use of opioids has been cited as a growing problem in Australia and the United States. The University of New South Wales National Drug and Alcohol Research Centre found there were 551 accidental opioid overdoses in 2008, with 20 per cent resulting from pharmaceutical opioids (Roxburgh & Burns 2012). In the same year, 73.8 per cent of 20,044 prescription drug overdoses in the U.S. involved opioid analgesics, exceeding the number of deaths from heroin and cocaine combined (Centers for Disease Control 2011).

1.4 Study Aims

The primary recommendation of the organisations noted above is to treat OA using some form of pharmacological intervention with the use of ancillary therapies. There appears to be little regard for the potential complications of drug-based therapies. Therefore, the rationale for this study was to investigate the potential of a viable alternative to pharmacological therapy. The primary aim was to assess the effectiveness of laser acupuncture compared to sham laser in reducing pain and stiffness and improving physical function in individuals suffering from osteoarthritis of the OAK. This was measured by two primary outcome measures – the disease-specific Western Ontario and McMasters Universities Index (WOMAC), which assesses three dimensions of pain, disability and joint stiffness in knee and hip OA; and a visual analogue scale (VAS) for pain. A secondary measure, the Short-Form McGill Pain Questionnaire (SF-MPQ) was also used to validate outcomes from the two primary measures. A unique feature of this study was the use of three additional outcome measures – the Credibility/Expectancy Questionnaire (C/E), Working Alliance Inventory Short Form C (WAI-C) and Multi-dimensional Health Locus of Control Form C (MHLC-C) – to investigate the placebo effect and the effect of patient/practitioner interaction on treatment outcomes.

1.4.1 Hypothesis

The null hypothesis stated that:

H_o: Laser acupuncture does not reduce pain, stiffness and improve physical function in individuals with OAK.

In the event that the null hypothesis is rejected, the alternative hypothesis would be accepted, i.e.

H_a: Laser acupuncture reduces pain, stiffness and improves physical function in individuals with OAK.

In addition, four specific research questions were postulated to investigate the influence of laser acupuncture on treatment outcomes:

a) Can the study establish a valid and effective trial design for replication in future laser acupuncture studies on OAK?

b) Can strict adherence to the TCM paradigm (i.e. using the diagnostic pattern-differentiation, treatment rationale/principle and formulae-specific acupuncture points that treat the underlying causes and symptoms of OAK) influence laser acupuncture treatment outcomes?

c) Will the study lead to more appropriate laser parameters for the treatment of OAK?

d) Assess whether the therapeutic alliance between the practitioner and participant impacts on treatment outcomes?

1.5 Format of Thesis

Chapter 1: Introduction

This chapter explores why the knee is susceptible to chronic osteoarthritic pain and current approaches to the management of degenerative OAK. It outlines the aim of this study to test the effectiveness of laser acupuncture as a safe drug-free treatment. The following format of the thesis is described to help guide the reader.

Chapter 2: Background to the Study

This section backgrounds the study and looks at three acupuncture-related treatments for osteoarthritis knee pain – needle acupuncture, low-intensity laser therapy and laser acupuncture – and their individual mechanisms. Issues confronting laser studies in terms of method and placebo are examined. A rationale for the design of this laser acupuncture study is presented. The credible placebo and methods employed to measure active and sham laser treatments are also detailed along with the unique features of this study.

Chapter 3: Literature Review

This chapter defines the search strategy for the literature review and critiques specific aspects of the four types of studies reviewed – laser acupuncture for OAK, low-intensity laser therapy (LILT) for OAK, laser acupuncture for other pain conditions and LILT for other pain conditions. Specific aspects examined are sample sizes and randomisation; blinding and placebo; diagnosis for inclusion and exclusion; inclusion and exclusion criteria; laser wavelengths, power density, output power, fluence and

total energy dosages; treatment programs; treatment sites/acupuncture points; outcome measures and assessment periods. This section concludes with a summary of findings and an explanation of how those findings were applied to this study.

A secondary review of the literature undertaken after the completion of the trial reported in this study is presented to update any developments in the field since the original literature review.

Chapter 4: Method

The rationale for this RCT and the way it provides a replicable treatment regimen not found in previous osteoarthritis (OA) studies are discussed in this chapter. Ethics approval processes are defined along with recruitment of participants, and inclusion and exclusion criteria. Other key design elements of the trial are detailed along with randomisation and double blinding, TCM assessment, laser equipment, laser contraindications, interventions, treatment setting and the assessment of treatment and placebo outcomes with the two primary measures (WOMAC and VAS) and four secondary measures (Short-Form McGill Pain Questionnaire, Credibility/Expectancy Questionnaire, Working Alliance Inventory - Short Form (C) and Multi-dimensional Health Locus of Control Form C respectively. The section ends with an explanation of the statistical methods employed in the study. The findings of a literature search and manualisation process undertaken to establish the Western biomedical and TCM view of osteoarthritis knee pain are described. The TCM disease pattern associated with OAK is explained along with processes that led to the selection of specific acupuncture points and laser parameters.

Chapter 5: Results

This chapter presents descriptive statistics on participant demographics and the results observed from the two primary outcome measures – WOMAC and VAS. These data

are provided in the form of commentary, tables and figures. The overall effects from all outcome measurements are also presented. Within group and between group comparisons at different time points are provided along with between group mean comparisons for WOMAC and VAS. Within group comparisons and between group comparisons at different time points are also given for Short-Form McGill Pain Questionnaire (SF-MPQ), Credibility/Expectancy Questionnaire (C/E), Working Alliance Inventory Short Form C (WAI-C) and Multi-dimensional Health Locus of Control Short Form C (MHLC-C).

Chapter 6: Discussion

This chapter opens with a summary of the hypothesis tested in this RCT and findings relating to the effects of laser acupuncture on OAK pain, stiffness and physical function and placebo factors relating to treatments. The results are further explored as they relate to the specific research questions postulated about the influence of laser acupuncture on treatment outcomes. Development of the trial method is discussed together with key aspects relating to the conduct of robust and reliable trials, including the need to follow recommendations made by Consolidated Standards of Reporting of Trials (CONSORT), STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) and World Association for Laser Therapy (WALT) (see Appendices 1, 2 & 3 respectively). Findings are compared against results of previous studies with a focus on key research elements, such as randomisation, double blinding and credible placebo methods. Reasons are postulated for the positive outcomes achieved in this study in terms of reduced OAK pain and stiffness and improved physical function. A point of focus is the need for accurate TCM disease pattern differentiation. The importance of irradiating specific acupuncture points is outlined together with difficulties in establishing the correct laser dosage and addressing other treatment variables. Features of the study are noted, including outcome measures used to assess pain and factors relating to placebo aspects of laser acupuncture treatments and their link with Traditional Chinese Medicine (TCM). Overall results achieved with the principal outcome measures, WOMAC and VAS, are outlined and comparisons made with other studies. Attention is drawn to the need for a clear

definition of what constitutes laser acupuncture and difficulties posed by differences in the way acupuncture points and trigger points respond to laser light. The chapter concludes with comments about the study's limitations and possible inferences and their implications for future research.

Chapter 7: Conclusion

This final chapter provides an overview of what this unique study has achieved – confirming the effectiveness of laser acupuncture for reducing OAK pain and stiffness and improving physical function by scoring a statistically significant difference between active laser and sham laser groups. Also explained are how the study assessed, for the first time, the way factors relating to the placebo effect influence treatment outcomes. Suggestions are made for further research into the role psychological influences play in the treatment process and for a more open-minded approach to laser acupuncture studies based on TCM principles. An expansion of laser treatment recommendations provided by the current single source – the World Association of Laser Therapy – is advocated. Recommendations are made for replicating the study to confirm its validity and strengthen its design to help define how this painless and side-effect free dual modality might help the many thousands of people who currently rely on expensive medications that often have undesirable side effects to maintain their quality of life and wellbeing.

Chapter 2 Background to the Study

This chapter reviews some of the background issues to the current study, including acupuncture use in OAK; acupuncture-related treatments; TCM-based acupuncture concepts of health and how they differ from Western medical acupuncture and their impact on research studies; how acupuncture, LILT and laser acupuncture mechanisms relieve pain; design and methodology issues confronting laser research; rationale for an authentic laser acupuncture RCT; and the importance of the placebo arrangement.

2.1 Acupuncture Use in OA

Most medical guidelines for managing OAK pain appear to have little faith in acupuncture as a treatment. However, organisations other than those reviewed earlier take a more positive view.

The World Health Organisation (WHO), for example, has long recognised the benefits of acupuncture for a range of disorders. A 2003 WHO report on more than 100 clinical trials investigating the effectiveness of acupuncture lists knee pain as a proven treatment (World Health Organisation 2009). The same report notes that acupuncture has also been shown to have a therapeutic effect on osteoarthritis, but more proof is required.

A WHO background update on osteoarthritis (Tanna 2013a) further advises that complementary or alternative therapies are gaining popularity as an OA therapy among consumer groups. Given the role it plays in improving health services in Third World countries with limited financial resources, WHO advocates more research to evaluate the efficacy and cost-effectiveness of alternative treatments for all types of OA.

2.2 Acupuncture-related Treatments

The British Acupuncture Council (BAC), the United Kingdom's main regulatory body for the practice of traditional acupuncture, recommends the modality as an OA treatment option (British Acupuncture Council 2016). The BAC's position is supported by several systematic reviews. These reviews have found that real acupuncture is statistically superior to sham acupuncture and usual medical care for OA of peripheral joints/knee and hip/knee alone, offering similar benefit to active interventions such as exercise (Kwon, Pittler & Ernst 2006); (White et al. 2007a; White et al. 2007b); (Manheimer et al. 2007). Other OA studies acknowledge acupuncture is safe and has a clinically relevant cost-benefit (Kwon, Pittler & Ernst 2006); (White et al. 2007a); (Manheimer et al. 2010; Manheimer et al. 2007).

A Cochrane Review of acupuncture trials completed in 2009 found small, but statistically significant short-term effects on pain with a standardised mean difference on multiple scales -0.28, [95% CI, -0.45 to -0.11]. However, many of the trials suffered from incomplete blinding (Manheimer et al. 2010).

Transcutaneous electrical nerve stimulation, electro-acupuncture and low-intensity laser therapy all demonstrated clinically relevant pain relief in a 2007 systematic review (Visual Analogue Scale 0-100, 18.8 mm [95% CI 9.6 to 28.1], 21.9 mm [95% CI 17.3 to 26.5] and 17.7 mm ([95% CI: 8.1 to 27.3] (Bjordal et al. 2007).

Another form of acupuncture integrated with laser was reportedly pioneered by Zhou Yo-cheng in 1971 (Tuner & Hode 2002). Stimulating acupuncture points with laser appeared to be beneficial. However, this form of integrative modality has not been widely used, and the paucity of authentic laser acupuncture studies sparked the need for this research.

2.3 TCM-based Acupuncture Concepts of Health

Traditional Chinese Medicine (TCM) is based on philosophies and diagnostic treatment principles dating back thousands of years. An integral part of TCM, acupuncture involves inserting fine needles into the skin to stimulate specific acupuncture points. This stimulation is said to balance *Qi* or energy forces within the human body to treat a variety of conditions, including inflammation, oedema, chronic joint disorders and pain, and to maintain good health.

The purported flow of *Qi* in our bodies is regulated through a system of meridians and collaterals that includes 12 regular meridians, eight extra meridians, 15 collaterals, 12 divergent meridians and 12 cutaneous regions (Deng et al. 1987) that connect to other organs, such as the skin, bones and brain.

Each of these channels, regions, collaterals and organs is connected to specific acupuncture points that can unblock and balance the flow and rhythm of *Qi* in the body. This flow of energy has been likened to the flow of water in a river or spring. Each acupuncture point is distinguished by different energy flows and rhythms, and is claimed to have specific and differentiated effects that maintain balance or homeostasis in the human body.

TCM is derived from practical experience in dealing with illness over millennia. Yin and Yang and the Five Elements are the mainstays of physiology, pathology, pattern identification and treatment in the development of Chinese medical theory.

In simple terms, Yin-Yang theory sprang from the observation of nature through the ages. Yin-Yang describes the way phenomena naturally group together in pairs of complementary opposites, i.e. heaven and earth, sun and moon, night and day, winter and summer, male and female, movement and stasis. The TCM classic, *Su Wen*, also known as the *Essential or Simple Questions* in the *Huang Di Neijing* (circa 240 B.C.), sums up Yin and Yang as “the way of heaven and earth”.

Chinese medicine theory believes all phenomena in the universe can be attributed to Yin and Yang. Each aspect of Yin and Yang depends upon each other and are convertible because individual phenomenon possesses both a Yin and a Yang. Yin and Yang are natural complements, counter-balancing each other and are mutually convertible because either may change into its complement.

The concept of Yin and Yang interdependence is widely used in physiology, pathology and treatment in TCM. Two fundamental elements of the human body, Blood and *Qi*, are an example: Blood is Yin and *Qi* is Yang. According to TCM concepts, '*Qi* moves the Blood', meaning Blood circulation relies on the warming and driving power of *Qi*.

Moreover, '*Qi* contains the Blood', i.e. it keeps the Blood within the vessels. The functions of engendering, moving and containing the Blood are summed up in the phrase, 'Qi is the commander of the Blood'.

According to TCM theory, acupuncture clears blockages in meridians and channels and it maintains and balances the flow of Qi or energy, Blood and Fluid through our bodies, helping our physiological system to return to normal and a state of what Western medicine calls homeostasis.

In summary, TCM and acupuncture are rooted in a unique, comprehensive and systematic theoretical structure that employs Yin-Yang theory, Five Elements and meridian systems to balance body, mind, spirit, emotions as a whole and the way they interact with our natural environment.

2.4 How Western Medical Acupuncture Differs from TCM-based Acupuncture

In contrast, Western medical acupuncture has been adapted to "current knowledge of anatomy, physiology and pathology, and the principles of evidence-based medicine" (White 2009). Despite evolving from TCM-based acupuncture, practitioners of

Western medical acupuncture view the modality as a part of conventional medicine rather than a complete 'alternative medical system'.

The scientific evidence-based view is that medical acupuncture acts mainly by stimulating the nervous system. Its known modes of action include local antedromic axon reflexes, segmental and extra segmental neuromodulation and other central nervous system effects (White 2009).

Consequently, Western medical acupuncture is most commonly used in primary care for treating musculoskeletal pain and its practitioners tend to pay less attention to choosing one acupuncture point over another than their TCM-based acupuncture counterparts. Therefore, Western medical acupuncture does not reflect the essence of TCM, which treats the underlying cause of disease as well as the symptoms in an wholistic way.

2.5 Western Medical Acupuncture Impacts on Laser Research

Unfortunately, the disconnect that exists between differing views on what constitutes TCM-based acupuncture and Western medical acupuncture has carried over to the modern-day extensions of these needle-based therapies – TCM-based laser acupuncture and Western medical laser acupuncture.

Consequently, Western medical acupuncture and Western medical laser acupuncture are not based on TCM philosophy and treatment principles targeting the cause and symptoms of disease. Instead Western medical treatments concentrate on providing symptomatic relief. This often leads to variable and inconsistent research findings.

In exploring these disconnects, it is necessary to compare current evidence-based understanding of the mechanisms produced by needle acupuncture and its light-based counterparts, low-intensity laser therapy and TCM-based laser acupuncture.

2.6 How Acupuncture, Low-intensity Laser Therapy & Laser Acupuncture Relieve Pain

Needle Acupuncture Mechanisms

In general terms, acupuncture is believed to stimulate the nervous system, causing the release of neuro-chemical messenger molecules. Subsequent biochemical changes stimulate the body's homeostatic mechanisms, promoting physical and emotional well-being. Stimulation of certain acupuncture points has been shown to affect areas of the brain that are known to reduce sensitivity to pain and stress (Hui et al. 2009).

Acupuncture appears to relieve pain by releasing endorphins and other neuro-humeral factors, modulating pain sensation with endogenous opioids (Uryu et al. 2007), (Ahsin et al. 2009); regulating the metabolism of pathways and genes (Tan et al. 2010); reducing inflammation, increasing blood circulation and reducing swelling and inhibiting the activity of cytokines (mediators of inflammation), including interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF)-alpha (Su et al. 2012).

Other anticipated effects are thought to involve spinal mechanisms, including the Gate Control Theory (Melzack & Wall 1965). That theory provided a framework for explaining observed pain relief resulting from stimulation of somatic afferent nerves.

In summary, all of these mechanisms are thought to help relieve OA pain through needle acupuncture, which appears to correlate with the findings of a number of studies (Ahsin et al. 2009; Han 2004; Pomeranz & Cheng 1979; Zhao 2008). Therefore, it is reasonable to postulate that integrating laser with acupuncture may be of similar benefit for OAK.

Low-intensity Laser Therapy Mechanisms

Low-intensity laser therapy (LILT), also known as photo-biomodulation, is a therapeutic light-based procedure that has been used in Europe, notably Russia, since the 1960s

(Chung et al. 2012). LILT involves irradiating tissue or cells with low levels of red and near infrared (NIR) wavelengths of light in the 600nm to 1000nm range.

The therapy is called ‘‘low intensity’’ because it uses energy densities that are low compared to high-powered lasers used for ablating, cutting and thermally coagulating tissue. Lasers used in LILT are also known as ‘‘cold lasers’’ because they do not heat tissue. Originally, it was thought that LILT required coherent laser light but, more recently, light emitting diodes (LEDs) have come into use. Debate about the differing clinical effects of these two light sources is continuing. Nevertheless, LEDs are often grouped with laser diodes in cluster probes.

Cellular Response

LILT causes photo-chemical and photo-biological responses in cells and tissue at primary and secondary levels. At the optimum dosage, the primary response of laser light increases cellular function, particularly the stimulation of adenosine triphosphate (ATP) in mitochondria, which constitutes the fuel and energy store of cells (Passarella et al. 1984). This is particularly evident if the function of the cell is impaired.

Secondary responses to LILT include, but are not limited to increased cell metabolism and collagen synthesis in fibroblasts (Abergel et al. 1984); increased action potential of nerve cells (Rochkind et al. 1986); and stimulation of the formation of DNA and RNA in the cell nucleus (Karu 1982).

Despite its 50-year history, the clinical effects of LILT are not well understood. However, it has been found to decrease inflammation by reducing the levels of biochemical markers (prostaglandin E2, messenger ribonucleic acid cyclooxygenase-2, IL-1β, TNF-α), neutrophil influx, oxidative stress, oedema and haemorrhaging (Bjordal et al. 2006). LILT-induced analgesia also appears to mediate peripheral opioid receptors in chronic joint disorders (Bjordal et al. 2003).

Other studies show LILT promotes healing of wounds, deeper tissues and nerves; and treats neurological disorders and pain (Chow et al. 2009); stimulates the production of

endorphins and relieves neuropathic pain (Laakso et al. 1994) and provides an analgesic effect (Mrowiec et al. 1997)

While LILT is used to treat a wide variety of ailments, it remains controversial as a therapy. Its underlying biochemical mechanisms remain poorly understood and its use is largely empirical. A large number of parameters – wavelength, fluence, power density, pulse structure and timing of the applied light – must be chosen for each treatment. Choosing incorrect parameters can reduce the effectiveness of a treatment or produce a negative therapeutic outcomes (Huang et al. 2009). For example, the choice of light source is crucial because LILT is characterised by a biphasic dose response and doses higher or lower than the optimal value may have no therapeutic effect. In fact, lower doses of light are often more beneficial than high doses (Huang et al. 2011).

It can thus be presumed that the inappropriate choice of light source and dosage has led to negative results in some published LILT studies. However, it remains possible that LILT can relieve pain by stimulating the production of endorphins and reduce inflammation, oedema and the symptoms associated with chronic joint disorders, such as OAK pain. Consequently, there may be some benefit to combining the principles behind laser acupuncture mechanisms.

Laser Acupuncture Mechanisms

Like LILT, laser acupuncture is a non-invasive technique involving the stimulation of traditional acupuncture points or *ah shi* points with the same wavelengths (600nm to 1,000nm) used in LILT (Hu, Hung & Hung 2013).

Laser acupuncture produces local and distant analgesic effects that may be mediated by different mechanisms (Hu, Hung & Hung 2013). Studies have shown laser acupuncture elicits activity in parts of the brain. The cerebral effects of laser acupuncture at both GB43 acupuncture points were investigated with functional magnetic resonance imaging (fMRI) (Siedentopf et al. 2005). The results showed laser acupuncture produced significant, predominantly ipsilateral brain activation within the

thalamus, nucleus subthalamicus, nucleus ruber, brain stem and Brodmann areas 40 and 22. No significant brain activations were seen within the placebo group. The fact that the observed effects were primarily ipsilateral supports the assumption that laser acupuncture is mediated by meridians since they do not cross to the other side of the body (Siedentopf et al. 2005).

Other evidence for laser acupuncture-mediated effects stems from studies involving fMRI that demonstrate visual cortex activation in response to laser irradiation of BL67 (Whittaker, 2004). This acupuncture point, located lateral to the corner of the small toe nail, is sometimes used to treat eye pain. Intriguingly, the fMRI recorded no visual cortex activation when an inactive laser probe was applied to BL67.

Furthermore, the role of endogenous opiate-like peptides and serotonin in laser acupuncture anaesthesia has been demonstrated (Choi, Srikantha & Wu 1986). It is therefore reasonable to assume laser acupuncture may have increased clinical benefit, given the similarities between the possible pain control mechanisms in acupuncture and low-intensity laser therapy and the photo-biological and photo-chemical effects of laser.

Laser Advantages

Hence, there appears to be some evidence to suggest that the use of laser on specific acupuncture points can mediate specific biomechanisms and subsequently be used to mediate specific health conditions. Laser acupuncture also offers a number of advantages over needle acupuncture. It is aseptic, non-invasive, painless, generates little or no heat, and no side effects or complications have been reported in studies. Another plus for people with needle phobia or a low pain tolerance is that, unlike needle acupuncture, laser acupuncture does not elicit *de qi* when acupuncture points are stimulated. *De qi* is a composite of unique – and, to some, unpleasant – sensations that many TCM practitioners believe is essential to clinical efficacy (Hui et al. 2007). Some studies claim laser acupuncture to be more effective than needle acupuncture

for some medical conditions and it requires less time to administer (Hu, Chang & Hung 2010).

Moreover, laser and acupuncture both appear to work in similar ways in terms of analgesic/anti-inflammatory effects and improved micro-circulation/metabolic healing effects. How this occurs is not completely understood. However, the vascular density of acupuncture points (Liu et al 2014) appears to amplify two energy transport systems – one based on TCM channel theory; the other cellular and peripheral nerve transduction signaling believed to occur in photo-biomodulation. It is therefore reasonable to postulate that the dual energy systems may accelerate and magnify healing and metabolic processes for degenerative OAK.

But as with needle acupuncture, there appears to be two schools of thought when it comes to the application of medical laser acupuncture and low-intensity laser therapy – and both tend to follow the Western medicine model.

Medical laser acupuncture and low-intensity laser therapy are generally applied to trigger points, acupuncture points and tender points either with a single laser probe or with a cluster probe with little or no consideration of TCM principles.

Disconnect Between Modalities

In summary, scientific analyses of the mechanisms of acupuncture, Western medical laser acupuncture and TCM-based laser acupuncture indicates that the disconnect between these three modalities relates to the theoretical differences between the TCM-based and Western Medical models. While the TCM-based model relates more to ancient philosophy, channel theory, the diagnostic view of disease, treatment principle and formulae specifically targeting disease patterns that treat the cause and symptoms, the Western medical model focuses on localised effects on tissues, cells and bones and scientific metabolic analysis. Consequently, these fundamental differences lead to different treatment approaches that are difficult to compare from a research point of view. Hence, it was important to design a laser acupuncture clinical

research study that was consistently based on the essence of fundamental TCM concepts.

2.7 Design & Methodology Issues Confronting Laser Research

In designing a robust and reliable laser acupuncture research study, a number of issues needed to be addressed. Firstly, the differences in fundamental concepts outlined above are a key issue because they have given rise to what might be considered *faux* laser acupuncture, i.e. irradiating a mix of trigger points, tender points and acupuncture points, either with a single laser probe or a cluster probe to provide symptomatic relief with little or no consideration of TCM principles. In contrast, *real* TCM-based laser acupuncture has generally focused on acupuncture points and *ah shi* points, treating the cause and symptoms of identified disease patterns in an wholistic way.

Furthermore, most laser acupuncture researchers appear not to fully understand both laser science and the TCM paradigm. This lack of knowledge may account for the variable results achieved in many laser studies. Laser science is a particularly daunting area that seems to confuse a number of researchers. For example, the selection of laser parameters is based on laser-tissue/cellular interaction and the syndrome targeted for treatment. Parameters include choice of wavelength, class of laser, power density, spot size, dosage, mode of application and frequency of treatment.

Another cause of confusion is the Arndt-Schulz Law, which needs to be addressed to counter the bi-phasic dose response in photo-biomodulation. In simple terms, the laser dose needs to be at an optimum level to achieve a positive result. A dosage that is too high or too low can be ineffective and in some cases may produce an inhibitory rather than a stimulatory effect.

Knowledge about TCM treatment principles and the need to develop disease-specific acupuncture point formulae to address the presenting condition are equally important. Standardising acupuncture point formulae is a feature of TCM since a

number of acupuncture points rather than a single acupuncture point need to be stimulated or irradiated to address both the underlying causes and symptoms of a particular condition. Therefore laser acupuncture researchers are required to have a thorough knowledge of both laser science *and* TCM philosophy and principles to be able to conduct reliable TCM-based laser acupuncture clinical research.

Regardless of the type of intervention – be it LILT, medical laser acupuncture or TCM-based laser acupuncture – many of the reviewed studies had design flaws. Those flaws indicated a lack of knowledge about design methods, particularly randomisation, sampling, blinding, placebo control, confounding issues, acupuncture concepts and principles, laser science and the use of inappropriate laser parameters for specific syndromes.

These issues, which are examined further in the literature review chapter that follows, led to the proposition explored for the first time in this study: does laser acupuncture applied in strict accordance with the TCM paradigm and measured against the robust methodology of a double-blind, randomised, placebo-controlled clinical trial improve OAK treatment outcomes?

2.8 Rationale for an Authentic Laser Acupuncture RCT

Driving this and other laser studies is an overwhelming need for a drug-free alternative treatment for OAK. Indeed, the devastating effects of this incurable degenerative disease are so severe that the World Health Organisation (WHO) ranks OA 12th in a list of 24 severe health conditions and health-impacting issues confronting public health (Kaplan et al. 2013).

This study in particular was encouraged by evidence-based RCTs and fMRI analyses (outlined earlier) showing that needle acupuncture and LILT share many similarities in the treatment of OAK. Furthermore, the literature indicates that needle acupuncture stimulates the central nervous system through the release of endorphins, endogenous opioid-like substances and through other neuro-humoral factors, i.e. changing the way

the brain and spine process pain. Acupuncture has also been found to reduce inflammation and disperse swelling – symptoms common to the joint tenderness, swollen joints and morning stiffness found in OAK.

Similarly, LILT is known to reduce inflammation and oedema in chronic joint disorder (Bjordal et al. 2013); promote healing of wounds, deep tissues and nerves; and treat neurological disorders and pain (Chow et al. 2009). As with acupuncture, LILT also relieves neuropathic pain by stimulating the analgesic effects of endorphins and opioid-like substances. Additionally, both appear to manipulate the flow of energy or stimulate changes in the human body, albeit in slightly different ways.

It was therefore hypothesised that integrating LILT and the real essence of TCM-based acupuncture concepts – and strictly applying traditional treatment principles used over thousands of years – might benefit OAK pain.

To test this theory, *real* TCM-based laser acupuncture, applied according to CONSORT/STRICTA/WALT recommendations, was used to treat two OAK disease patterns identified in TCM – Blood Stasis and Phlegm Retention.

2.9 Importance of Placebo Arrangement

The placebo effect has been known to have a powerful influence on pain perceptions for more than half a century (Scharf et al. 2006). For research outcomes to be accurate, active treatment groups and control groups must have equal faith that they are being treated with an active intervention. A 1955 study by Henry K. Beecher found the placebo effect to be, on average, equivalent to a 35% improvement in symptoms, with numbers ranging between 21% and 58%, depending on the ailment (Beecher 1955).

The design and interpretation of many acupuncture clinical studies appears to be hampered by a lack of knowledge about the appropriate application of the modality coupled with other confounding issues. At the centre of this argument is the long-standing issue for traditional acupuncture research – finding a convincing placebo.

Acupuncture involves the sensation of puncturing the skin with needles. As such, any subtle sham needling or sham stimulation of acupuncture points or *ah shi* points may produce some physiological changes in the body. Moreover, such changes may in fact result in an active treatment instead of the desired placebo treatment. One study concluded that "summarising all the different sham interventions as 'placebo' controls seems misleading and scientifically unacceptable" (Dincer & Linde 2003).

Unfortunately, placebo issues – and Beecher's work – appears to have been lost on researchers involved in many of the acupuncture-related studies reviewed for this RCT. Inappropriate use of sham lasers was common, indicating a lack of knowledge about placebo effects resulting from the use of unsuitable light sources. In some cases, researchers overlooked the importance of using an instrument to measure differences between active and sham laser acupuncture treatments.

In particular, the sham laser method established for this RCT – an inactive probe and an active infrared probe attached to a Therapeutic Goods Administration-listed base unit supplied by the distributor – provided a credible sham comparator for laser acupuncture. This method offered obvious advantages: 1) Differences between the invisible infrared sham laser probe and the active probe were undetectable to both study participants and the laser operator; 2) The absence of *de qi* in laser acupuncture further masked differences between the sham and active laser probes; 3) The use of a sham laser allowed something not attempted before – an ability to measure the placebo effects of laser acupuncture; and 4) The sham laser assisted double-blinding of participants and the laser operator.

2.10 Unique Features of This Study

A number of unique design features were incorporated into this RCT. In particular, laser acupuncture was applied in the context of an OAK disease diagnoses based on both Western medicine science and technology, and the strict application of the TCM paradigm to identify OAK disease patterns, treatment principles and specific formulae for treating OAK pain.

Other unique elements of this laser acupuncture study included the use of a manualisation process to establish the appropriateness of acupuncture points used to target OAK; laser parameters based on WALT recommendations; and adapting the CONSORT Group's STRICTA Extension for the conduct of evidence-based acupuncture clinical trials.

To confirm the consistency and reliability of this study, three outcome measures – the OAK-specific Western Ontario McMasters University Arthritis Index (WOMAC), Visual Analogue Scale (VAS) and the Short Form McGill Pain Questionnaire (SF-MPQ) – were used to assess the multi-dimensional effects of laser acupuncture on OAK pain. Other unique features included the use of a further three measures to assess placebo effects on the practitioner-patient relationship, patient expectancy and beliefs in the credibility of the practitioner and treatment modality, the importance of bonding, goals and task compliance, and the influencing power of others.

In summary, the lack of OAK research in the laser field appears to be hampered by four inter-linked factors: (1) The differences in concepts that exist between the TCM and Western medical laser acupuncture models; (2) Lack of a comprehensive knowledge of laser science mechanisms and parameters, TCM concepts and how acupuncture and laser therapy work (and the similarities they share); and (3) Lack of knowledge about design methodology for robust and reliable evidence-based research.

In order to develop a sound and robust RCT, it was necessary to examine the strengths and weaknesses of previous clinical studies relating to laser acupuncture and low-intensity laser therapy for OAK as well as the parameters used to address other pain conditions.

Chapter 3 Literature review

This chapter examines clinical trial literature on laser acupuncture and low-intensity laser therapy (LILT) for osteoarthritis knee (OAK) pain. It appraises 27 studies in four critical areas – laser acupuncture and LILT for OAK, and laser acupuncture and LILT for other pain conditions. Key aspects of the research studies are examined, including sample sizes and randomisation; blinding and placebo; diagnosis for inclusion and exclusion; inclusion and exclusion criteria; laser wavelengths, power density, output power, fluence and total energy dosages; treatment programs; treatment sites/acupuncture points; outcome measures and assessment periods. A summary of findings is provided along with details about how those findings were applied to the RCT in this study.

Following development of this RCT, an updated review of the literature found in the period from 2011 to mid-2016 was implemented to gauge any changes or improvements in more recent studies.

3.1 Introduction

Laser acupuncture and low-intensity laser therapy (LILT) utilise photo-biomodulation, a light-based therapy that reduces pain, improves tissue repair and inflammation when a beam of light is applied to the human body. More than 200 randomised clinical trials have been published on photo-biomodulation – half of them dealing with pain from arthritic joints, neuropathic pain syndromes, back and neck pain, and sports injuries (Thorlaser 2016).

However, only two laser acupuncture studies on OAK were found in the period between 1995 and 2010 — an insufficient number for a systematic review. Consequently, the literature review was expanded to cover the strengths and weaknesses of laser acupuncture and low-intensity laser therapy for OAK and other pain conditions.

3.2 Search Strategy

An initial literature review, covering the period between 1995 and 2010, appraised a total of 27 studies, covering four types of clinical research studies identified as relevant to this study: (i) laser acupuncture for OAK; (ii) low-intensity laser therapy for OAK; (iii) laser acupuncture for other pain conditions; and (iv) low-intensity laser therapy for other pain conditions. Reviewing other pain conditions helped provide an insight into the formulation of laser parameters for various pain syndromes and their effectiveness.

The second literature review, covering the 2011 to mid-2016 period and limited to OAK treatments with laser acupuncture and low-intensity laser therapy, kept pace with further developments in OAK research studies.

For the initial literature review, searches were made of online databases (Medline, Pubmed, AMED, EMBASE) and other UTS Library sources. Search terms used were: laser acupuncture + osteoarthritis knee pain, laser acupuncture + knee pain, laser acupuncture + osteoarthritis, laser acupuncture + pain, laser therapy + knee osteoarthritis, acupuncture + knee osteoarthritis, laser therapy + pain, knee pain, acupuncture + osteoarthritis, acupuncture + knee pain.

The same databases were used for the second literature review but, to maintain relevancy, search terms were limited to laser acupuncture and low-intensity laser therapy studies on OAK.

3.3 Search Results

The original search found a total of 45 studies that investigated the use of laser acupuncture and low-intensity laser therapy treatments for OAK and other pain conditions. Laser acupuncture and low-intensity laser therapy (LILT) treatments for other pain conditions were reviewed because both modalities use photo-biomodulation.

Of the 45 reviewed studies, 18 studies were excluded for the following reasons: two were not in English; three were systematic reviews that did not provide details as complete as those contained in the original research papers; 12 were not relevant or specific to the research topic; and full text was not available for the remaining one study (see Figure 1, below).

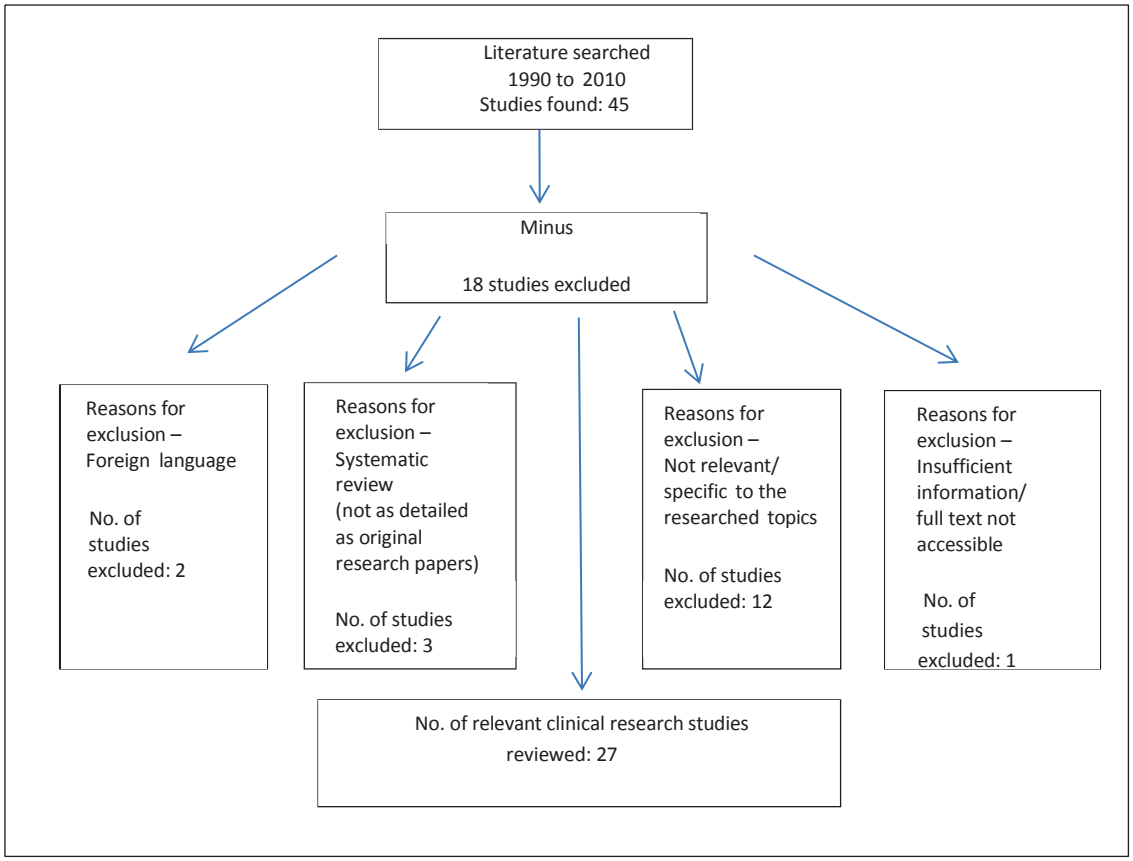

Figure 1 – Results of First Literature Search Covering the Years 1990 to 2010

The 27 laser studies found to be relevant to this review are shown in Table 1 (see below).

Table 1 – 27 Laser Acupuncture & Low-Intensity Laser Therapy Studies Identified in First Literature Search

RESEARCH STUDY	AUTHOR	YEAR OF PUBLICATION
Laser Acupuncture for OAK		
Laser Acupuncture in Knee Osteoarthritis: A Double-Blind, Randomised Controlled Study	(Yurtkuran et al. 2007)	2007
Effect of Combined Laser Acupuncture on Knee Osteoarthritis: A Pilot Study	(Shen et al. 2009)	2009
Total studies	**2**	
Low-intensity Laser Therapy for OAK		
Laser-needle therapy for Spontaneous Osteonecrosis of the Knee	(Banzer, Hubscher & Schikora 2008)	2008
Short-term Efficacy of Low-level Laser Therapy in Patients with Knee Osteoarthritis: A Randomised Placebo-controlled, Double-blind Clinical Trial	(Fukuda et al. 2010)	2010
Efficacy of Different Therapy Regimes of Low-power Laser in Painful Osteoarthritis of the Knee: A Double-blind and Randomised-controlled Trial	(Gur et al. 2003)	2003
The Effect of Low-Level Laser in Knee Osteoarthritis: A Double Blind, Randomised, Placebo-Controlled Trial	(Hegedus et al. 2009)	2009
Efficacy of Interferential Low-Level Laser Therapy Using Two Independent Sources in the Treatment of Knee Pain	(Montes-Molina et al. 2009)	2009
Low-power Laser Treatment in Patients with Knee Osteoarthritis	(Tascioglu et al. 2004)	2004
Infrared Diode Laser in Low Reactive-level Laser Therapy (LLLT) for Knee Osteoarthrosis	(Trelles et al. 1991)	1991
Sub-total	**7 studies**	
Laser Acupuncture for Other Pain Conditions		
Adjuvant Laser Acupuncture in the Treatment of Whiplash Injuries: A Prospective, Randomised Placebo-controlled Trial	(Aigner et al. 2006)	2006
Clinical Equivalence of Laser Needle to Metal Acupuncture Needle in Treating Musculoskeletal Pain: A Pilot Study	(Dorsher 2010)	2010
The Effects of Laser Acupuncture on Chronic Tension Headache – A Randomised Controlled Trial	(Ebneshahidi et al. 2005)	2005
Laser Acupuncture for Chronic Non-specific Low Back Pain: A Controlled Clinical Trial	(Glazov et al. 2009)	2009
Laser Acupuncture in Children with Headache: A Double-blind, Randomised, Bicentre Placebo-controlled Trial	(Gottschling et al. 2008)	2008
Laser Treatment Applied to Acupuncture Points in Lateral Humeral Epicondylalgia – A Double-blind Study	(Haker & Lundeberg 1990)	1990
Emg Analysis After Laser Acupuncture in Patients with Temporomandibular Dysfunction (TMD) – Implications for Practice	(Hotta et al. 2010)	2010
Carpal Tunnel Syndrome Pain Treated with Low-level Laser and Microamperes Transcutaneous Electric Nerve Stimulation: A Controlled Study	(Naeser et al. 2002)	2002
Results of a 1-Year Clinical Study of the Application of Laser Stimulation of the Acupuncture Points Used for Arthritis, Neuropathy, Intractable Pain and Pain From Acute Strain and Sprain	(Stump & Roberts-Retzlaff 2006)	2006
Sub-total	**9 studies**	

RESEARCH STUDY	AUTHOR	YEAR OF PUBLICATION
Low-intensity Laser Therapy for Other Pain Conditions		
Investigation of the Effect of GaAs Laser Therapy on Cervical Myofascial Pain Syndrome	(Altan et al. 2005)	2005
Low-energy Helium Neon Laser Treatment of Thumb Osteoarthritis	(Basford 1987)	1987
Low-Power Laser Treatment for Shoulder Pain	(Bingöl, Altan & Yurtkuran 2005)	2005
Randomised Controlled Trial on Low-level Laser Therapy (LLLT) in the Treatment of Osteoarthritis (OA) of the Hand	(Brosseau et al. 2005)	2005
The Effect of 300mW, 830nm Laser on Chronic Neck Pain: A Double-blind, Randomised, Placebo-controlled Study	(Chow, Heller & Barnsley 2006)	2006
The Effect of Gallium Arsenide Aluminium Laser Therapy in the Management of Cervical Myofascial Pain Syndrome: A Double blind, Placebo-controlled Study	(Dundar et al. 2007)	2007
Comparison of Laser, Dry Needling and Placebo Laser Treatments in Myofascial Pain Syndrome	(Ilbuldu et al. 2004)	2004
Double-blind Randomised Controlled Trial of Low-level Laser Therapy in Carpal Tunnel Syndrome	(Irvine et al. 2004)	2004
Low-power Laser Treatment in Patients with Frozen Shoulder: Preliminary Results	(Stergioulas 2008)	2008
Sub-total	**9 studies**	
Total	**27 studies**	

3.4 Critique on Specific Aspects of the 27 Studies

The 27 laser acupuncture and low-intensity laser therapy studies were critiqued on the following key research features: a) Sample size and randomisation; b) Blinding and Placebo; c) Wavelength; d) Power density; e) Output Power; f) Fluence/Dosage; g) Treatment Program; h) Treatment site; and i) Outcome measures.

To ensure a robust and reliable laser clinical trial, this study employed three standardised conventions, namely laser protocols recommended by the World Association for Laser Therapy (WALT) and clinical research and acupuncture study criteria set by CONSORT and its extension, STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA).

WALT, established in 1994, is the leading international organisation for promoting research, education and clinical applications in the field of phototherapy for the treatment of musculoskeletal pain, health conditions and tissue healing. WALT's multi-national membership includes leading experts in all forms of treatment mediated by

the photo-biomodulating effects of light. WALT has developed a consensus agreement for the design and conduct of clinical studies with low-intensity laser therapy and light-based therapy for musculo-skeletal pain and disorders.

The Consolidated Standards of Reporting Trials (CONSORT) Statement sets a benchmark for clinical studies. First published in 1996, CONSORT is the gold standard for RCTs. Its checklist of 25 items facilitates transparent reporting (CONSORT 2010). This helps avoid biased estimates of treatment effects and thus improves critical appraisal and interpretation of RCTs. Many leading medical journals and major editorial groups have endorsed CONSORT and STRICTA.

In assessing the validity and reliability of the 27 reviewed clinical studies, each was assessed against criteria set by CONSORT and STRICTA, and treatment protocols recommended by WALT. Assessment of the strengths and weaknesses of those studies subsequently informed the development of a methodology that would provide a robust and replicable evidence-based RCT testing the effectiveness of TCM-based laser acupuncture on OAK pain, as will be outlined later in Chapter 3. The following tables and commentaries analyse key elements that informed the design of this study.

3.5 Sample Sizes & Randomisation

3.5.1 Laser Acupuncture for OAK (2 Studies)

Sample Size

In the two laser acupuncture studies for OAK that were reviewed (see Table 2, below), the sample sizes were 40 (Shen et al. 2008) and 52 (Yurtkuran et al. 2007). Both the Shen and Yurtkuran studies did not report how the sample sizes were calculated.

Randomisation

Both researchers used computer-generated numbering systems to randomise participants to active laser and placebo laser treatment groups. The participant split between groups in both studies was uniform.

Table 2 – Sample Sizes & Randomisation Used In Laser Acupuncture OAK Studies (2 Studies)

Study	Sample Size/ Division	Sample Size Rationale	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Groups
Yurtkuran (2007)	N = 52 Treat =27 Placebo = 25	Not reported	Did not comply with CONSORT	✔	Simple randomisation - -Computer generated table of random numbers (Method reported)	Complied with CONSORT	2
Shen (2009)	N = 40 Treat=20 Placebo = 20	Not reported	Did not comply with CONSORT	✔	Excel 2000 software used to generate randomised numbers. (Method reported)	Complied with CONSORT	2
TOTALS	**2 out of 2 provided breakdown**	**2 out of 2 did not report rationale**	**2 out of 2 did not comply with CONSORT**	**2 out of 2 randomised participants**	**2 out of 2 used satisfactory randomisation method**	**2 out of 2 used clear, simple method**	**2 out of 2 used 2 groups**

Summary

Although (Shen et al. 2009) and (Yurtkuran et al. 2007) complied with CONSORT guidelines by describing the randomisation method, both did not follow the CONSORT recommendation that the calculation of sample sizes be explained.

3.5.2 Low-intensity Laser Therapy for OAK (7 Studies)

Sample Size

The seven studies investigating the effect of low-intensity laser therapy on OAK used samplings ranging from one to 152 participants (see Table 3, below). Only one study relied on a single case (Banzer, Hubscher & Schikora 2008).

Randomisation

All seven studies reported using randomisation in varying degrees to allocate participants to two or more treatment groups. Of the two studies that did not use

randomisation, one was a single-case study (Banzer, Hubscher & Schikora 2008); the other a one-group study (Trelles et al. 1991). Only one study (Gur et al. 2003) complied with CONSORT by reporting how randomisation was done.

Five studies used a simple randomisation method, such as randomly-generating envelopes containing information about the type of device or probe to be applied. Some studies employed a third party for randomisation.

Table 3 – Sample Sizes & Randomisation Used in Low-intensity Laser Therapy- OAK Studies (7 Studies)

Study	Sample Size/ Division	Sample Size Rationalise	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Groups
(Banzer, Hubscher & Schikora 2008)	N = 1	Single case study	Sample size too small. Did not comply with CONSORT	Not applicable	Not applicable (Method not reported)	Not robust – Did not comply with CONSORT	Not applicable
(Fukuda et al. 2010)	N = 47 Active = 25 (41 knees) Placebo = 22 (38 knees)	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Avoided selection bias Did not comply with CONSORT	2
(Gur et al. 2003)	N = 90 Group I: N = 30 3J for 5 min. + exercise Group 2: N = 30 2J for 3 min. + exercise Group 3: N = 30 placebo for 3 min. + exercise	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 3 treatment groups by non-treating authors drawing 1 of 90 envelopes labelled A, B or C (Method reported)	CONSORT compliant	3
(Hegedus et al. 2009)	N = 27 Group 1: N = 18 treated Group 2: N = 9 placebo	Not reported	Did not comply with CONSORT	✔	Patients randomly chose sealed envelopes from bowl containing equal number of slips numbered 1 or 2, which corresponded to laser probe numbers. Neither patients nor operator knew which probe was active or placebo (Method reported but did not comply with CONSORT)	Participants not evenly distributed Did not comply with CONSORT	2

Study	Sample Size/ Division	Sample Size Rationalise	Comment on Sample size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Groups
(Montes-Molina et al. 2009)	N = 152 Group 1: Interferential current + laser+ quadriceps strength program Group 2: Laser + dummy + quadriceps strength program	Not reported	Did not comply with CONSORT	✔	Randomisation implemented by tossing a coin for first patient, who was allocated to treatment group and followed by alternating allocation into each of 2 groups (treatment or placebo) (Method reported but did not comply with CONSORT)	Tossing coin not recommended by CONSORT Did not comply with CONSORT	2
(Tascioglu et al. 2004)	N = 60 Group 1: N = 20 Group 2: N = 20 Group 3: N = 20	Not reported	Did not comply with CONSORT	✔	Randomly divided into 3 groups using numbered envelopes. (Method not clearly reported)	Not clear if randomisation was monitored by investigator, which might introduce bias Did not comply with CONSORT	**3**
(Trelles et al. 1991)	N = 40 Single group	Not reported	Did not comply with CONSORT		Not used	Not robust Did not comply with CONSORT	1
Total	**7 studies**	**7 out of 7 not reported**	**7 out of 7 did not comply**	**5 out of 7 used randomisation**		**1 out of 7 complied with CONSORT**	

Summary

All seven studies in this group did not meet the CONSORT requirement to explain how sample sizes were determined. Two studies did not use robust methods.

Issues relating to randomisation were found in a number of studies. Hegedus et al. (2009) did not distribute participants evenly to two groups. Instead he used a "lucky dip" method, with participants selecting sealed envelopes from a bowl. Inside each envelope was a numbered slip corresponding to one of three different treatment types to be applied. Montes-Molina (2009) tossed a coin to decide who should receive the first active treatment. From that point on, allocations to placebo and active treatments were alternated. CONSORT discourages coin tossing as a method of randomisation.

3.5.3 Laser Acupuncture for Other Pain Conditions (9 Studies)

Sample Size

Sample sizes in this group of nine studies testing laser acupuncture for other pain conditions ranged from 10 participants (Hotta 2010) to 100 participants (Glazov et al. 2009). Eight out of nine studies did not report how the sample size was determined. Only one study – a single blind investigation (Ebneshahidi et al. 2005) – followed CONSORT's recommendation to report a rationale for the sample size used.

Randomisation

Six of the nine studies used randomisation (see Table 4, below). The remaining three studies (Dorsher 2010; Hotta et al. 2010; Naeser et al. 2002) were not robust because they were single-group studies. Only one study (Gottschling et al. 2008) reported the method of randomisation and complied with CONSORT and STRICTA reporting requirements.

Table 4 – Sample Sizes & Randomisation Laser Acupuncture Studies Used for Other Pain Conditions (9 Studies)

Study	Sample Size/ Division	Sample Size Rationale	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Pain Condition
(Aigner et al. 2006)	N = 45 Group 1: Treat = 23 5mW laser HeNe Group 2: Placebo = 22	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Not reported)	Not fully compliant with CONSORT	Whiplash injuries
(Dorsher 2010)	N = 30 4 treatments over 4 months laser acupuncture & needle acupuncture delivered minimum 20 days apart	Not reported	Did not comply with CONSORT	X	Single group Not randomised	Not compliant with CONSORT & not robust	Musculo-skeletal pain - OAK - Joint OA - Cervical - Lumbar
(Ebneshahidi et al. 2005)	N = 50 Treat = 25 Placebo = 25	Based on previous experience of number of subjects needed to observe 6-point difference on VAS score with a standard deviation (SD)	Complied with CONSORT. Unfortunately only single blind study.	✔	Randomly assigned to 2 groups (Method not reported)	Not fully compliant with CONSORT	Headache
(Glazov et al. 2009)	N = 100 Treat = 50 Placebo = 50	Not reported	Did not comply with CONSORT	✔	Randomised into 2 parallel groups (Method not explicitly reported)	Not fully compliant with CONSORT	Low back pain
(Gottschling et al. 2008)	N = 43 Migraine group = 22 Tension headache group = 21	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups by computer (Method reported)	Well explained and avoided selection bias CONSORT compliant	Child headaches

Study	Sample Size/ Division	Sample Size Rationale	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Pain Condition
(Haker & Lundeberg 1990)	N = 49 Treatment = 23 Placebo = 26	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Not fully compliant with CONSORT	Lateral humeral epicondylalgia
(Hotta et al. 2010)	N = 10	Not reported	Did not comply with CONSORT	X	Single group No randomisation	Not compliant with CONSORT & not robust	TMJ
(Naeser et al. 2002)	N = 11	Not reported	Did not comply with CONSORT	X	Single group No randomisation	Not compliant with CONSORT & not robust	Carpal tunnel syndrome
(Stump & Roberts-Retzlaff 2006)	N = 55 2 groups treating: a) Arthritis b) Strain	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Not fully compliant with CONSORT	Arthritis & strain
TOTALS		**8 out of 9 did not report**	**8 out of 9 did not comply with CONSORT**	**6 out of 9 randomised**	**Only 1 out of 9 reported method used**	**Only 1 out of 9 fully compliant with CONSORT**	

Summary

It appears that the studies investigating laser acupuncture for other pain conditions did not demonstrate scientific vigour. None of the nine studies complied with CONSORT and WALT requirements for reporting sample size determinations and randomisation methods.

3.5.4 Low-intensity Laser Therapy for Other Pain Conditions (9 Studies)

Sample Size

All but one of nine studies in this group used samplings ranging from 40 participants (Bingol et al. 2005) to 90 participants (Chow et al. 2006), while (Irvine et al. 2004) opted for 15 participants – a sample size considered too small to be reliable (see Table 5, below). Two of the nine studies (Brosseau et al. 2005) (Chow, Heller & Barnsley 2006) provided a rationale for the sample size used.

One study (Basford, Shefield & Harmsen 1999) did not report treatment and placebo group numbers and another study (Dundar et al. 2007) did not identify numbers allocated to two treatment groups. Seven out of nine studies did not comply with the CONSORT requirement to report how sample sizes are determined.

Randomisation

All nine studies used randomisation to allocate participants to two or more groups (see Table 5, below). However, five of the studies did not explain the randomisation method clearly and therefore did not comply with CONSORT criteria.

Table 5 – Sample Sizes & Randomisation Used In Low-Intensity Laser Therapy Studies for Other Pain Conditions (9 Studies)

Study	Sample Size/ Division	Sample Size Rationale	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Pain Condition
(Altan et al. 2005)	N = 53 Active laser 26 + exercise Sham laser + exercise 27	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Not fully compliant with CONSORT	Cervical myofascial pain
(Basford, Shefield & Harmsen 1999)	N = 63 2 groups – group numbers not clear	Not reported	Did not comply with CONSORT	✔	Block randomised into 2 groups, but group numbers not stated (Method reported)	Not fully compliant with CONSORT	Back pain
(Bingöl, Altan & Yurtkuran 2005)	N = 40 Active laser 20 Sham laser 20	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups by drawing from a bag of cards numbered 1-40, i.e. a card for each patient (Method reported) Before and after treatment evaluations performed by a third staff physician (Method reported)	Complied with CONSORT	Shoulder pain
(Brosseau et al. 2005)	N = 88 Active laser 42 Placebo laser 46	Sample size based on power analysis and event rate under population	Complied with CONSORT	✔	Randomly assigned to 2 groups by computer-generated numbers with a blocking factor of 4 (Method reported)	Complied with CONSORT	Hand OA
(Chow, Heller & Barnsley 2006)	N = 90 Active laser 45 Sham laser 45	Sample sizes based on response rates and variances in principal outcome measures from previous studies	Complied with CONSORT	✔	Assigned by computer generated numbers into 2 equal groups	Complied with CONSORT	Neck pain

Study	Sample Size/ Division	Sample Size Rationale	Comment on Sample Size Determination	Randomised	Randomisation Method	Comment on Randomisation Method	Pain Condition
(Dundar et al. 2007)	N = 64 Active laser Sham laser 2 groups (Group numbers not clear)	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups by numbered envelopes (Method not clear)	Method not robust. Not compliant with CONSORT	Cervical myofascial pain
(Ilbuldu et al. 2004)	N = 60 Active laser 20 Sham laser 20 Dry needling 20 + stretch exercise at home and paracetamol usage	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 3 groups (Method not reported)	Not compliant with CONSORT	Myofascial (upper trapezius)
(Irvine et al. 2004)	N = 15 Active laser 7 Sham laser 8	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Not compliant with CONSORT	Carpal tunnel syndrome
(Stergioulas 2008)	N = 52 Active laser 26 Sham laser 26 (Actual number unclear)	Not reported	Did not comply with CONSORT	✔	Randomly assigned to 2 groups (Method not reported)	Not compliant with CONSORT	Frozen shoulder
TOTALS		**2 out of 9 reported**	**7 out of 9 did not comply with CONSORT on sampling**	**9 out of 9**	**3 out of 9 complied with CONSORT**	**6 out of 9 not fully compliant with CONSORT**	

Summary

It appears that the overall quality of the studies on low-intensity laser therapy for other pain conditions was of a slightly better standard than the other modalities reviewed above. However, only two laser therapy researchers (Chow et al. 2006; Brousseau et al. 2005) complied with the CONSORT requirements for reporting clearly both the sample size calculation and randomisation method.

3.5.5 Overall Critique on Sample Size & Randomisation Methods

Sample Size

Calculating sample size for scientifically valid results and ethical research in a clinical trial generally hinges on five key factors (Kadam 2010):

1. *Level of Significance:* Most research studies accept a 5% level of significance, meaning that there is a 5% probability that the observed result is due to chance - not to the intervention – and the 5% chance of erroneously reporting a significant effect is acceptable.

2. *Power of the Study:* Most studies usually accept a power of 80%, meaning that a real difference will be missed 1 in 5 times (20%).

3. *Effect Size:* The effect size is the difference between the value of the variables in a control and a test group. If the effect size is large between study groups, the sample size required for the study is smaller. Conversely, if the effect size between the study groups is small, the sample size of the study group is large.

4. *Underlying Event Rate in the Population:* This factor, which is crucial when calculating sample size, is estimated from results of reported studies found in literature reviews rather than convention.

5. *Standard Deviation:* Standard deviation refers to the measure of dispersion or variability in data. When calculating the sample size, a researcher needs to anticipate variations in the measures being studied. If the population is more homogeneous and has a smaller standard deviation or variance, a smaller sample size is acceptable. Conversely, the greater the variance in standard deviation, the sample size will need to be larger (Kadam & Bhalerao 2010).

As Kadam (2010) explains, the smaller the effect size, the larger the sample required. Consequently, any study that does not allow for the probabilities of the effect size could produce an unreliable outcome. Moreover, such a study could waste resources on a large sample size in trying to prove a small effect size that is clinically irrelevant.

Conversely a study with a small sample size and a small effect size may never be able to achieve statistically significant differences between groups. Standard deviation is another important factor that determines whether a sample has a homogenous baseline or too many variables to produce a fair statistical outcome. It is important that the selection criteria for the sample population are explicit to limit variance in the standard deviation. This makes the sample more homogenous and therefore less variable, which increases the probability of achieving statistical significance between groups.

The literature review highlighted the importance of the relationships between the effect size, standard deviation and the underlying event rate in the population of a study when determining an appropriate sample size to produce a robust and scientifically sound outcome. Only three out of 27 studies (Brosseau et al. 2005, Chow et al. 2006, Ebneshahidi et al. 2005) appeared to comply with CONSORT's sample size criteria and the definitions outlined above by Kadam (2010). This represents a

compliance rate of 11.11%, which does not reflect well on the overall quality of the studies reviewed.

Randomisation

Randomisation is an important criterion to prevent selection bias, minimise the variability of evaluation and provide unbiased assessment of an intervention by avoiding confounding from known and unknown factors (Suresh 2011). To ensure reliability and validity, CONSORT requires studies to report how the method used to generate the random allocation sequence that assigns participants to active treatment and placebo treatment groups. Other essential details include type of randomisation; mechanism used to implement random allocation; stating who generated the random allocation sequence and who assigned participants to interventions. The objective is to eliminate bias when selecting participants for any clinical research and to prevent the probability of over-estimating treatment effects by up to 40% (Schulz & Grimes 2002).

In all, 23 out of 27 studies listed in Tables 3, 4 and 5 used variable degrees of randomisation. However, only seven of the 27 studies reported the randomisation method clearly according to CONSORT criteria. This represents a CONSORT compliance rate of 25.93%, indicating that most studies did little to improve trial reporting standards. Consequently, the 20 studies that did not adequately comply with the CONSORT requirement to report the randomisation method may have potentially produced results that were not reliable and valid.

3.6 Blinding & Placebo

The commentary and tables in the next section examine how each of the 27 studies in the laser acupuncture and low-intensity laser therapy categories designed blinding and placebo arrangements for the treatment of OAK and other pain conditions.

Each laser treatment category is analysed and critiqued on compliance with criteria set for the review of the 27 laser studies: (i) Compliance with CONSORT recommendations; (ii) Use of double blinding; (iii) Appropriateness of the placebo laser device/ arrangement; and (iv) Compliance with expert definitions of what constitutes blinding and placebo. To be classed as robust, each study was required to meet these four criteria when determining reliability and validity.

3.6.1 Blinding

Evidence-based research demands consideration of two key elements – blinding and placebo – both of which may impact on treatment outcomes. Blinding is meant to ensure investigators and participants do not know whether those being treated are in an active or placebo treatment group. Blinding eliminates psychological influences and placebo effects on treatment outcomes and puts the active treatment group and the placebo group on an equal footing. Blinding also results in an unbiased outcome, an equal statistical analysis and makes a clinical trial robust and scientifically sound.

3.6.2 Placebo

The so-called placebo or sham effect refers to the psychological influences on treatment outcomes. Issues arising from placebo usually flow from the type of placebo device or arrangement used to make all participants in a study believe they are having the same treatment as each other. To make this happen, it is essential that the placebo device or treatment administered to the sham group looks and feels the same as that given to the active treatment group. The placebo device or treatment should not be identifiable in any way so that participants in the two treatment groups have the same treatment belief. This helps eliminate statistical bias in treatment outcomes.

3.6.3 Blinding & Placebo Interconnected

The inter-relationship between blinding and placebo is inseparable. Blinding and placebo are both aimed at eliminating psychological influences and the probability of bias and ensuring that both experimental groups (i.e. the active treatment group and the sham treatment group) will respond to treatment in similar ways. If blinding is not successful, the placebo arrangement will fail because participants are no longer blinded to which group they have been allocated. Hence, there is no placebo effect. Conversely, if the placebo arrangement is not credible, blinding fails. Basically, both blinding and placebo share the same essential requirement of not alerting each participant about the group to which they have been allocated so that the blinding and placebo arrangements are credible. If unknown factors are not masked, both blinding and placebo will fail as psychological influences on participants come into play with the potential to skew treatment outcomes.

3.6.4 Laser Acupuncture for OAK (2 Studies)

Blinding

Of the two laser acupuncture for OAK trials reviewed (see Table 6, below), Yurtkuran et al. (2007) was the only researcher to report using double blinding. Shen et al. (2009) used single blinding to evaluate a combined 10.6μm and 650nm laser acupuncture moxibustion treatment for OAK. Moxibustion is a TCM heat treatment that involves burning herbs attached to the handles of needles inserted into acupuncture points.

In the Yurtkuran placebo-controlled RCT, 52 participants with Kellgren-Lawrence Grade 2-3 OAK were assigned to two groups – 27 participants to treatment and 25 to placebo. The study reported that the outcome assessment examiner was blinded and that the statistician was unaware of treatment allocations until data analysis was completed. The report did not clarify whether the operator was also blinded or how participants were blinded. This study therefore did not comply with CONSORT.

Shen et al. (2009) recruited 40 subjects randomly allocated into two groups – one group receiving active laser acupuncture moxibustion; the second group sham treatments. The use of an inactivated CO_2 thermal laser as a sham device was not a credible blinding method because the lack of heat would have been obvious to any participants expecting to receive an alternative form of moxibustion treatment, which involves the application of heat to acupuncture and *ah shi* points.

Placebo

The Yurtkuran and Shen studies employed different types of placebo. Yurtkuran et al. (2007) used a laser therapy device fitted with a switch for either active mode or placebo mode. To make both treatments look the same, a red light on the laser glowed for both active and placebo treatments.

Shen et al. (2009) used a combined 650nm 36mW low-intensity laser and high-intensity 10.6μm CO_2 laser for active and placebo treatments on two groups to evaluate the effects and safety of laser acupuncture moxibustion on OAK. For placebo treatments, the CO_2 laser was not activated.

Table 6 – Blinding & Placebo Laser Acupuncture Studies Used for OAK (2 Studies)

Study	Trial Design	Double Blind	Single Blind	Mixed Blind	Comment on Blinding	Placebo Control	Comment on Placebo	Result
Yurtkuran et al. (2007)	Double blind RCT	✔ Only outcome assessment examiner blinded			Blinding of operator unclear Did not comply with CONSORT Not robust	✔ Laser with a red light switched on and off	Red light on placebo device may produce physiological changes Not credible Not CONSORT compliant Not Robust	Positive for reduce swelling
Shen et al. (2009)	RCT pilot study		✔		Single blind not robust	✔ Inactive thermal laser obvious to placebo group	Not credible Not CONSORT compliance Not robust	Positive
TOTALS		**1 out of 2**	**1 out of 2**		**Not CONSORT compliant & not robust**		**Not CONSORT compliant & not robust**	**2 positive out of 2**

Summary

Yurtkuran et al (2007) did not report explicitly on the blinding of the operator. Also, the study did not clarify whether the red light on the inactive laser was on the base unit or the probe delivering placebo. Such detail is important because a red light on a probe could produce physiological effects in the placebo group, as identified in space exploration experiments (NASA 2005). Experiments carried out in space have demonstrated that red LED wavelengths can boost the energy metabolism of cells to advance plant growth and photosynthesis. These space experiments led to the development of LEDs that are being used on earth to reduce pain and in photo dynamic therapy treatments for cancer. Consequently, the use of red or blue light as a placebo device in OAK studies could produce physiological effects that may impact on treatment outcomes.

The Shen et al. (2009) study's use of single blinding on participants did not demonstrate research vigour. The placebo arrangement involving the use of a CO_2 laser was not appropriate because this type of laser produces heat, even at low power settings. At high settings it can burn the skin. The absence of heat when delivering a placebo moxibustion alternative with an inactive CO_2 laser would have been obvious to even the most naïve blinded participants, making the placebo control not credible.

3.6.5 Low-Intensity Laser Therapy for OAK (7 Studies)

Blinding

The four out of seven studies that applied laser therapy for OAK (see Table 7, below) opted for double blinding. Three of the four studies blinded the operator and participants. However, Montes-Molina et al. (2009) did not explain clearly if the operator or assessor was blinded. Tascioglu et al. (2004) used single blinding on a physician who performed clinical assessments. Banzer et al. (2008) and Trelles et al. (1991) did not use blinding in their respective single case and single group studies.

Placebo

Four of the seven studies in Table 7 (see below) reported using a placebo control. Hegedus et al. (2009) used a 0.5mW laser as a placebo. This was an inappropriate choice because even a low output from that device might produce physiological effects in participants.

Table 7 – Blinding & Placebo Low-Intensity Laser Therapy Studies Used for OAK (7 Studies)

Study	Trial Design	Double Blind	Single Blind	Mixed Blind	Comment on Blinding	Placebo Control	Comment on Placebo	Results
Banzer et al. 2008	Single case study	NA	NA	Single case	Reported Not CONSORT compliant Not robust	No placebo	Not robust	Positive
Fukuda et al.2010	Double blind RCT	✔ Operator & participants blinded			Reportedly CONSORT compliant Robust	✔ Placebo probe sealed	Appears credible Reportedly CONSORT compliant Robust	Positive
Gur et al. 2003	Double blind RCT	✔ Physician & patients blinded			Reported CONSORT compliant Robust	✔ No laser beam emitted	Appears credible Reportedly CONSORT compliant Robust	Positive
Hegedus et al. 2009	Double blind RCT	✔ Operator & patients blinded			Reported CONSORT compliant Robust	✔ 0.5mW placebo device	May produce physiological changes. Not credible Not Robust	Positive

Researcher	Trial Design	Double Blind	Single Blind	Mixed Blind	Comment on Blinding	Placebo Control	Comment on Placebo	Results
Montes-Molina et al. 2009	Double blind RCT - Randomized by coin method No Placebo Unclear double blinding	✔ Double blinding method claimed Operator or assessor blinding unknown			Reporting not explicit Not CONSORT compliant Not robust	No placebo	Not CONSORT compliant	Positive
Tascioglu et al. 2004	Single-blind RCT Placebo control 3 groups		✔ A blinded physician performed clinical assessments		Reported Not robust	✔ (laser device inactive)	Credible placebo Reportedly CONSORT compliant Robust	Negative
Trelles et al. 1991	Single group study Not randomised No double blinding No placebo control	NA		No blinding	Reported Not robust	No placebo	Not robust	Positive
TOTALS		**4 out of 7**	**1 out of 7**		**3 out of 7 CONSORT compliant & robust**	**4 out of 7**	**3 out of 7 CONSORT compliant & robust**	**6 positive out of 7**

Summary

Three studies (Fukuda et al. 2010; Hegedus et al. 2009; Gur et al. 2003) out of seven double-blind studies in the low-intensity laser therapy for OAK category masked operators and participants, complying with CONSORT requirements. Montes-Molina et al. (2009) did not report explicitly who was blinded and therefore was not robust.

The single-blind study (Tascioglu et al. 2004) reported blinding a physician who performed clinical assessments at baseline, at three weeks and at six months. However, this type of single-blinding is not robust as assessor blinding does not eliminate psychological influences in a treatment environment.

Table 7 (above) indicates that some researchers have little or no understanding of the workings of laser-based treatments in respect of their use as a placebo. For example, using a 0.5mW laser as a placebo could have skewed the results of the study by Hegedus et al. (2009) because even a low laser dose could bring about physiological effects. Similarly, Montes-Molina et al. (2009) had no placebo control and the use of 470nm light emitting diodes (LEDs) to illuminate the treatment area was questionable because LEDs also produce physiological effects (NASA 2005). Finally, the Trelles et al (1991) study was not robust because of the absence of blinding and placebo controls.

3.6.6 Laser Acupuncture for Other Pain Conditions (9 Studies)

Blinding

Of the nine trials that focused on laser acupuncture for other pain conditions (see Table 8, below), four studies (Glazov et al. 2009, Gottschling et al. 2008, Haker et al. 1990, Naeser et al. 2002) employed double blinding; two researchers (Aigner et al. 2005, Ebneshahidi et al. 2005) used single blinding; and two researchers (Dorsher 2010, Hotta et al. 2010) used no blinding. Stump et al. (2006) did not report any blinding method.

Three trials (Aigner et al. 2005, Ebneshahidi et al.2005, Stump et al. 2006) were not scientifically robust because of the absence of double blinding or not reporting the use of single blinding. Naeser et al. (2002) blinded the assessor and participants by using a black curtain to block the patients' view of treatments with two types of laser (visible and infrared) and a TENS machine.

Placebo

Six of the nine studies on laser acupuncture for other pain conditions (Aigner et al. 2006, Ebneshahidi et al. 2005, Glazov et al. 2009, Gottschling et al. 2008, Haker et al. 1990, Naeser et al. 2002) used placebo controls (see Table 8, below).

Four studies (Aigner et al. 2005, Glazov et al. 2009, Gottschling et al. 2008 and Haker et al. 1990) used red lights or LEDs as a placebo. However, three researchers (Dorsher et al. 2010, Hotta et al. 2010 and Stump & Roberts-Retzlaff 2006) apparently did not see the need to use a placebo. Consequently, none of these studies demonstrated research vigour.

Table 8 – Blinding & Placebo Laser Acupuncture Studies Used for Other Pain Conditions (9 Studies)

Study	Trial Design	Double Blind	Single Blind	No or Mixed Blinding	Comment on Blinding	Placebo Control	Comment on Placebo	Body part(s)	Result
Aigner et al. 2005	RCT Single blind placebo + cervical collar + paracetamol + chlormeza-one		✔ Did not report who was blinded		Single blind Not robust	✔ 5mW red- light lamp used	Reported Light could produce physiological effects Not credible Not robust	Whiplash injuries	Negative
Dorsher 2010	Non-blinded cohort study - crossover protocol alternating between laser & metal needles			✔ Not blinded	Not blinded Not robust	Not applicable	Reported Cross-over design may have confused treatment effects Not robust	Musculo-skeletal pain - OAK - Joint OA - Cervical - Lumbar	Positive. Laser equal to or more effective than metal needles
Ebneshahidi 2005	Single blind placebo-controlled RCT		✔ Participants blinded		Single bind Not robust	✔ Laser power set to zero	Reported May not eliminate psychological effects Not robust	Headache	Positive

Study	Trial Design	Double Blind	Single Blind	No or Mixed Blinding	Comment on Blinding	Placebo Control	Comment on Placebo	Body part(s)	Result
Glazov 2009	Double blind RTC	✔ Participants & assessors /therapists			Reported CONSORT compliant Robust	✔ Translucent Perspex conical tip & red LED decoy light used	Reported LED may produce physiological effects Not credible Not robust	Low back pain	Negative in terms of comparison. All groups improved.
Gottschling et al. 2008	Double blind placebo controlled bi-centre RCT	✔ Practitioner & patients blinded			Reported CONSORT compliant Robust	✔ Red guide light on both placebo & active probe	Red light may produce physiological effects Not credible Not robust	Child head-aches	Positive
Haker et al. 1990	Double blind RCT	✔ Therapist & patients blinded			Reported CONSORT compliant Robust	✔ Red light for placebo	Report unclear Red light might produce physiological effects Not robust	Lateral humeral epicon-dylalgia	Negative

Study	Trial Design	Double Blind	Single Blind	No or Mixed Blinding	Comment on Blinding	Placebo Control	Comment on Placebo	Body part(s)	Result
Hotta et al 2010	Not randomised No blinding No placebo 1 Group			No blinding	No blinding Not robust	X No placebo	Not robust	TMJ	Positive
Naeser et al. 2002	Double blind placebo controlled crossover RCT 2 types of LASER (visible red and infrared) + microamperes TENS machine used for active and sham treatments	✔ Not strictly double blind (Assessor blinded - not therapist) Subject & staff analysed outcome (not therapist)			Not strictly double blind Not robust	✔ No emission from placebo device + Black curtain blinded subjects' view of treatments	Not robust	Carpal tunnel syndrome	Positive
Stump et al. 2006	1-year clinical study			No blinding	Not reported Not CONSORT compliant Not robust	No placebo reported	Not robust	Arthritis & strain	Positive
Total		**4 out of 9**	**2 out of 9**	**3 out of 9**	**2 out of 9 CONSORT compliant**	**6 out of 9of 9**	**Not CONSORT compliant & not robust**		**6 positive out of 9**

Summary

Only three studies (Glazov et al. 2009, Gottschling et al. 2008, Haker et al. 1990) out of nine (33.33%) complied with CONSORT blinding requirements, reflecting poorly on trial design across this group. The method of blinding participants and the assessor chosen by one study (Naeser et al. 2002) did not eliminate the possibility of bias that could result from treatments administered by an unblinded operator who might favour a particular group (Schulz 2002).

In addition to blinding, evidence-based research demands well-designed placebo methods. A review of the studies as a whole suggests that many researchers may not fully account for the effects of light therapy. For example, the use of a 5mW red light for placebo by Aigner et al. (2005); and a red LED or light by Glazov et al. (2009), Gottschling et al. (2008) and Haker et al. (1990) might still bring about physiological changes as part of a treatment, thereby negating the placebo effect. Turning on a milliampere TENS machine for initial stimulation and then off for placebo (Naeser et al. 2002) made for an equally obvious and therefore unconvincing sham treatment.

As noted in the Dorsher (2010) study, cross-over protocols suggest that it might not be possible to isolate the specific effects between different modalities when an alternative intervention is used as a comparator or placebo instead of an inactive laser. This problem may be compounded in laser studies given that the literature (Chow et al. 2006, Gottschling et al. 2007) indicates the efficacy of laser therapy in relieving pain may vary over periods ranging from 3-4 months. In a cross-over study, such results may make it unclear which type of treatment is most effective over time.

3.6.7 Laser Therapy for Other Pain Conditions (9 Studies)

Blinding

Eight out of nine RCTs investigating laser therapy for other pain conditions (see Table 9, below) opted for double blinding, although four studies (Altan et al. 1998, Basford et al. 1999, Brosseau et al. 2005, Irvine et al. 2004) did not describe their blinding

methods explicitly. Two of the eight studies (Chow et al. 2006, Stergioulas 2008) reported explicitly. However, two studies out of eight blinded the assessor instead of the operator.

Placebo

All nine researchers in this category used placebo controls (see Table 9, below). Three of the nine studies used a credible placebo device while the remaining six did not describe the placebo method or device explicitly. Placebo laser devices in six of the trials were either not well described or not reported (Altan et al. 2003, Basford et al. 1999, Bingol et al. 2005, Dundar et al. 2007, Irvine et al. 2004, Stergioulas 2008). Three of the nine studies produced positive outcomes.

Table 9 – Blinding & Placebo Laser Therapy Studies Used for Other Pain Conditions

Study	Clinical Design	Double Blind	Single Blind	Mixed Blind	Comment on Blinding	Placebo	Comment on Placebo	Body Part(s)	Results
Altan et al. (2003)	Double blind placebo-controlled RCT (Patients and assessor)	✔ (Patients and assessor)			Not reported explicitly Not CONSORT compliant Not robust	✔ Placebo device not turned on	Reporting not explicit Not CONSORT compliant Not robust	Cervical Myofascial pain	Negative
Basford et al. (1999)	Double-blind RCT (Therapist & assessor)	✔ Therapist & assessor masked, but not explained explicitly			Not reported explicitly Not CONSORT compliant Not robust	✔ Inactive probe	Reporting not explicit Not CONSORT compliant Not robust	Back pain	Negative
Bingol et al. (2005)	Double-blind (Assessor) placebo-controlled RCT Mixing laser with exercise may cloud treatment outcomes	✔ Not strictly double blind (Assessor blinded, but not Operator)			Assessor blinding Not robust	✔ Placebo probe turned off	Placebo method not well described Not CONSORT compliant Not robust	Shoulder pain	Negative
Brosseau et al. (2005)	Randomised double blind (Assessor) placebo-controlled RCT	✔ Patients, operator & research team blinded but not detailed			Not explicit Not robust	✔ Inactive probe	Reporting explicit Credible placebo CONSORT compliant Robust	Hand OA	Negative

Study	Clinical Design	Double Blind	Single Blind	Mixed Blind	Comment on Blinding	Placebo	Comment on Placebo	Body Part(s)	Results
Chow et al. (2006)	Double-blind RCT	✔ Subjects & operator blinded			Reported CONSORT compliant Robust	✔ Inactive probe	Reporting explicit Credible placebo Robust	Neck pain	Positive
Dundar et al. (2007)	Double-blind (assessor) placebo-controlled RCT	✔ Patients & assessor blinded			Assessor blinded Not robust	✔ Placebo device switched off	Reporting not explicit Not robust	Cervical myofascial pain	Negative
Ilbuldu et al. (2004)	Design method not stated Assessor blinded 3 groups : 1. Active laser 2. Placebo laser 3. Dry needling Plus home exercises & paracetamol for pain when required			Design method not stated	Not reported explicitly Not CONSORT compliant Not robust	✔ Inactive probe	Reporting explicit Credible placebo Robust	Myofascial (upper trapezius)	Positive In short term
Irvine et al. (2004)	Double-blind placebo-controlled RCT Blinding not reported	✔ Not reported			Not reported Not CONSORT compliant Not robust	✔ Inactive probe	Not described Not CONSORT compliant Not robust	Carpal tunnel syndrome	Negative
Stergioulas (2008)	Double-blind placebo-controlled RCT Patients & operator blinded	✔ Reported Patients & operator blinded			Reported CONSORT compliant Robust	✔ Inactive probe	Not well described Not CONSORT compliant Not robust	Frozen shoulder	Positive
TOTALS	**9**	**8 out of 9**	**1 out of 9 unsure**		**2 out of 9 CONSORT compliant and robust**	**9 out of 9**	**3 out of 9 CONSORT compliant & robust**		**3 positive out of 9**

Summary

Most low-intensity laser therapy studies investigating other pain studies used double blinding. At first glance this appears to be a robust trend. However, four researchers (Bingol et al. 2005, Brosseau et al. 2005, Dundar et al. 2007, Ilbuldu et al. 2004) used questionable blinding methods, masking only the participants and assessor rather than the laser operator. Not blinding the operator could impact on how seriously an operator might perform a treatment they know is sham rather than an active treatment. Again, such practices raise the possibility of skewing treatment outcomes and overall trial results. Five of the nine studies in this particular modality (Altan et al. 2003, Basford et al. 1999, Brosseau et al. 2005, Ilbuldu et al. 2004, Irvine et al 2004) did not report blinding explicitly. The poor standard of reporting did not comply with CONSORT criteria.

All nine studies used a placebo method, but six studies (Altan et al. 2003, Basford et al. 1999, Bingol et al. 2005, Dundar et al. 2007, Irvine et al. 2004, Stergioulas 2008) out of nine did not report explicitly, providing another example of poor reporting. Lack of a clear description of the placebo device or arrangement may not be able to establish the reliability and validity of study outcomes. It also does not demonstrate research vigour.

Some of the treatment groupings researchers used would make assessment and replication difficult. For example, Ilbuldu et al. 2004 opted for three treatment groups – active laser, sham laser and dry needling. Participants also were allowed to do stretching exercises at home and to take paracetamol. Altan et al. (1998) mixed low-intensity laser therapy with exercise. Mixing modalities and combining them with home exercises that participants may not do properly without supervision or allowing participants to use pain killers does not appear to isolate the targeted treatment effect. Modality mixing creates contextual confounding factors in determining which treatment or treatment combination works best. Worse, it makes replication impossible.

3.6.8 Overall Critique on Blinding & Placebo Methods

Of the 27 studies, only 26% reported using double blinding explicitly, were robust and complied with CONSORT requirements. This low rate of compliance reflects poorly on the quality of the study designs. Robust and reliable clinical research demands double blinding to minimise bias in trial outcomes. The poor understanding of the benefits of blinding, coupled with inadequate methods of blinding and vague reporting suggests the need for researchers to strictly follow the RCT guidelines set by CONSORT.

The term "blinding" is defined as keeping trial participants, investigators (usually health-care providers) or assessors (those collecting outcome data) unaware of the assigned intervention so that they will not be influenced by that knowledge (Schulz 2002). Furthermore, blinding reduces differential assessment of outcomes, and biased supplemental care or treatment, and improves participant compliance and retention (Schulz 2002).

Benefits of Successful Blinding

In Table 10 (below), Schulz identifies the following differences in potential benefits accruing from successful blinding:

Table 10 – Potential Benefits Accruing From Successful Blinding

Individuals Blinded	Potential Benefits
Participants	Less likely to have biased psychological or physical responses to intervention
	More likely to comply with trial regimens
	Less likely to seek additional adjunct interventions
	Less likely to leave trial without providing outcome data, leading to lost to follow-up
Trial	Less likely to transfer their inclinations or attitudes to participants

Investigators	Less likely to differentially administer co-interventions Less likely to differentially adjust dose Less likely to differentially withdraw participants Less likely to differentially encourage or discourage participants to continue trial
Assessors	Less likely to have biases affect their outcome assessments, especially with subjective outcomes of interest

As noted by Schulz (2000), there are greater potential benefits to blinding investigators than assessors. Studies with blinded investigators produce less biased outcomes. However, questions also need to be raised about the role of an assessor in a clinical trial. For example, is it the assessor's role to evaluate the participant's condition using subjective measures? Or should the assessor be analysing objective measures, such as x-ray analysis or questionnaires completed by participants?

Schulz (2002) lists assessors as "less likely to have biases affect their outcome assessments, especially with subjective outcomes of interest". However, it could be argued that participants are better placed to identify their own subjective measures, leaving the assessor to analyse these data objectively.

If these data are analysed accurately, there should be no biased effects on treatment outcomes. The assessor's role (and the degree of blinding) depends on the type of outcome measures that are used and analysed. It is therefore essential for any research study to identify the role the assessor is to play in completing or analysing outcome measures objectively or subjectively. If the assessor's role is not to complete the subjective measures, it could be argued that blinding the assessor has no beneficial influence on a study because they are only assessing or analysing factual data, blinded or not.

In considering the differences in potential blinding benefits identified by (Schulz 2002), it appears that research studies in which both participants and investigators are blinded potentially provide a more robust research setting than blinding assessors alone.

Terminology Issues

Terminology used in clinical studies is another issue. CONSORT opposes use of the terms, “double blind”, “single blind” or “triple blind”, citing “great variability in clinician interpretations and epidemiological textbook definitions of these terms” (Moher et al. 2012).

A study of 200 RCTs reported as double blind found 18 different combinations of groups actually blinded when the authors of those trials were surveyed and about one in every five of those trials reported as double blind did not blind participants, healthcare providers or data collectors (Haahr 2006). This shows that double blind, single blind and triple blind can be ambiguous terms and should not be used.

CONSORT argues that instead, authors should explicitly report the status of involved healthcare providers for whom blinding may influence the validity of a trial. Healthcare providers include all personnel involved in a trial – physicians, acupuncturists, laser therapists, physiotherapists and nurses who care for participants during a trial.

Need for Explicit Reporting

Given the inter-relationship that exists between blinding and placebo, another crucial factor to be considered is the way in which the blinding arrangement is reported. It must be explicit to comply with CONSORT requirements. And it must be unambiguous so that the reader can assess the reliability of the clinical research.

In a real world situation, the success of the placebo response can have a significant bearing on clinical differences. These differences indicate that, for best effect, double-blinding should be standardised and only occur between patients and the practitioner.

Blinding the patient and the assessor appears not to provide the same level of psycho-physiological uniformity in the treatment setting as that provided through blinding the patient and practitioner. Not using patient-practitioner blinding could result in a variable psycho-physiological effect and create an unequal population sampling. Consequently, any study using single-blinding or assessor-blinding has the potential to compromise the treatment outcome and statistical analyses.

Active & Sham Interventions

Just as evidence of the blinding method is required in a clinical trial where participants or treatment providers are masked, CONSORT recommends that study authors should state the similarity of the characteristics of the interventions, such as appearance, smell and administration method – all of which should apply equally to the description of the placebo.

An understanding of the purpose of a placebo device or arrangement is essential when designing reliable clinical research involving the use of lasers. The classical definition of a placebo is "any therapy or component of therapy used for its non-specific, psychological or psychophysiological effect, or that is used for its presumed specific effect, but is without specific activity for the condition being treated" (Shapiro & Morris 1978).

Consequently, the results of laser studies using a red light or light-emitting diode (LED) as a placebo control are questionable since they may produce physiological changes in the condition being treated and impact on intervention outcomes (NASA 2005). Such fundamental errors show that some researchers do not understand laser science or do not know how light-based therapies interact with tissue and cellular substrates.

Further complicating assessment of the reviewed studies was the tendency for some researchers not to describe the make and features or manufacturer details of the laser device used in a clinical trial. Information paucity does not demonstrate a rigorous approach to RCT reporting. Moreover, the lack of explicit details makes replication difficult.

Consideration of Placebo Arrangements

It is evident that the placebo arrangement needs to be considered carefully. Three components of the clinical encounter progressively produce incremental improvement in symptoms: (i) The therapeutic ritual (placebo treatment) has a modest benefit

beyond the treatment; (ii) Placebo effects produce statistically and clinically significant improvement; and (iii) The patient-physician relationship is the most robust component of the placebo effect (Kaptchuk et al. 2008).

To add credence to the part played by the patient-physician relationship, Kaptchuk et al. (2008) cites an RCT that found significantly greater clinical effects were associated with placebo acupuncture provided in an empathetic manner when compared with a neutral manner. Moreover, the resulting placebo effect creates participant faith and beliefs to such an extent that it results in psycho-physiological and non-specific effects on participant wellbeing (Abhishek & Doherty 2013).

In simple terms, the placebo response is the symptomatic improvement a patient experiences through receiving an intervention regarded as inert and non-therapeutic (i.e. placebo) for a particular health condition compared to those who receive no treatment. Exploring this phenomenon further, Abhishek & Doherty (2013) found the magnitude of the placebo response was determined by the patient-practitioner interaction. Other factors were treatment response expectancy, knowledge of being treated, patient personality traits and placebo specific factors, such as the route and frequency of administration, branding and treatment costs.

Measurement of Placebo-confounding Factors

Despite the significant amount of research on placebo and its known effects on treatment, it was noted that none of the 27 studies reviewed used an outcome measure to assess factors associated with any placebo effect that might have influenced their research outcomes.

Trial designs should therefore include assessing, with reliable and valid outcome measures, differences between the treatment and placebo groups on determinants of the placebo response and address other factors impacting on the placebo effect. Those factors include credibility, expectancy, practitioner-patient relationship, internal beliefs, chance and influences from other people.

All of these elements point to the importance of examining whether the 27 reviewed studies applied the same standards to blinding and placebo methods. For example, if those standards were not strictly followed, assessment of the study outcomes might be invalid or difficult to validate externally, making comparisons difficult. Such assessments are especially problematic when only six of the 27 (22.22%) of the laser studies under review used a credible placebo.

In summary, only three of the 27 studies (11.11%) complied with CONSORT double-blinding requirements in reporting explicitly on the use of a credible placebo device and clinical setting. This suggests that only three studies (Fukuda et al. 2010, Gur et al. 2002, Chow et al. 2006) were robust, reliable and replicable. The observations, examples and definitions outlined above illustrate the importance of designing a double-blind RCT that blinds the operator and participants; selects a credible placebo device and arrangement that is CONSORT compliant and robust; and measures confounding elements in the placebo effect for reliability and validity.

3.7 Diagnosis of Inclusion & Exclusion Criteria

To establish a homogeneous study population, it is important to have strict diagnostic inclusion and exclusion criteria, including objective measures of diagnostic outcomes in place for any OAK intervention. For any comprehensive study, diagnosis of OAK should be considered from two perspectives – Western medicine and Chinese medicine.

For example, a robust and objective diagnostic process from a Western medicine viewpoint would be supported by specific tools, such as x-rays to screen and confirm OAK is within the range of the Kellgren-Lawrence system for classifying OAK. In Chinese medicine terms, OAK is classified as a Bi Syndrome, which is generally diagnosed through the differentiation of disease patterns and leads to the setting of specific treatment principles and formulae. Table 11 and Table 12 (below) detail how the nine studies relating to OAK went about the process of establishing inclusion criteria for participation in those studies. The 19 remaining studies were not reviewed in this diagnostic section because they dealt with syndromes unrelated to OAK.

3.7.1 Laser Acupuncture For OAK Studies (2 studies)

Inclusion Criteria

The two laser acupuncture OAK clinical trials – Yurtkuran et al. (2007) and Shen et al. (2009) – used Kellgren-Lawrence OA diagnostic scale 2-3 as a benchmark for inclusion, thus meeting study population requirements (see Table 11, below). In addition to radiographic evidence, Shen et al. (2009) also relied on patients reporting moderate or greater clinically significant knee pain on most days during the month before treatment. Shen e al. (2009) was the only study to report that OAK is classified as a Bi Syndrome, which is generally caused by Blood Stagnation and Phlegm-Cold Retention in the knee.

Table 11 – Inclusion Criteria Laser Acupuncture Studies Used for OAK

Researcher	TCM Diagnosis with Disease Pattern	Diagnosis with TCM & Kellgren & Lawrence Grade 2-3	American College for Rheumatology (ACR)*	Kellgren & Lawrence Scale	Diagnosis/ Medical Check	VAS Pain Scale	Age	Medication	Issues
Yurtkuran (2007)	Nil	Nil	✔	✔		> 4/10	42-65 yrs		TCM disease patterns not identified for specific treatment. TCM paradigm not followed
Shen (2009)	Partially – only Bi Syndrome with no pattern differentiation	Partially		✔ At least 1 osteophyte over Grade 2		✔ (moderate or greater pain)	44-71years old		TCM disease patterns not identified for specific treatment. TCM paradigm not followed

Summary

The Yurtkuran and Shen studies did not follow the TCM paradigm. Neither study diagnosed the different disease patterns found in OAK; nor did they use specific TCM formulae or strategies to address disease patterns. Shen mentioned that osteoarthritis was classified as a Bi syndrome in TCM. However, he did not arrange participants in Blood Stagnation and Phlegm-Cold Retention groups. Shen also did not follow TCM principles for treating OAK.

Exclusion Criteria

Yurtkuran et al. (2007) and Shen et al. (2009) both excluded prospective participants on the basis of serious medical conditions, use of local-oral analgesics or NSAIDs, drug interventions, steroid injections, knee surgery and other hormonal metabolic or systemic rheumatological conditions or cardiac-cerebrovascular-pulmonary system disorders or malignancy, e.g. cancer (see Table 12, below).

Yurtkuran et al. (2007) excluded people with knee surgery, serious valgus or varus deformity or who had hormonal, metabolic or systemic rheumatologic issues leading to secondary OAK. Other exclusion criteria were physiotherapy in the previous six months, local oral analgesic or NSAID use in the previous four weeks or the presence of a systemic disease (cardiac-cerebrovascular-pulmonary system or malignancy) that contraindicated physiotherapy and exercise.

Shen et al. (2009) excluded prospects who had received corticosteroid or hyaluronate injections and who had used capsaicin cream topically in the previous six months.

Table 12 – Exclusion Criteria Laser Acupuncture Studies Used for OAK

Study	Surgical Intervention(s)	Drug interventions	Serious Medical Condition(s)	Issues
Yurtkuran (2007)	✔ Knee surgery/ Serious Valgus or Varus deformity	✔ Local-oral analgesic or NSAIDS in previous 4 weeks.	✔ Systemic disease (cardiac-cerebrovascular-pulmonary system or malignancy) –contraindicated to physiotherapy & exercise No hormonal, metabolic or systemic rheumat-ological issues leading to secondary OAK Physio in previous 6 months	Solid exclusion criteria not clouded with other medical conditions
Shen (2009)		Intra-articular corticosteroid or hyaluronate injections. Concomitant topical use of capsaicin cream in previous 6 months.		Solid exclusion criteria not clouded with other medical conditions

Summary of Exclusion Criteria Laser Acupuncture Studies Used for OAK

The exclusion criteria used by Yurtkuran et al. (2007) and Shen et al. (2009) were essential because they ensured that study findings would not be clouded by other OAK treatment regimes or potentially complicating medical conditions. However, they did not adequately address TCM diagnostic criteria and treatment principles.

3.7.2 Low-intensity Laser Therapy Studies Used for OAK (7 Studies)

Inclusion Criteria

None of the seven low-intensity laser therapy OAK studies used TCM diagnostic measures as part of their inclusion criteria (see Table 13, below) because they were not based on acupuncture philosophy and techniques.

Only two studies (Gur et al. 2003, Tascioglu et al. 2004) used ACR guidelines and the Kellgren-Lawrence Grade 2-3 OA severity system as inclusion criteria. One other study (Fukuda et al. 2010) limited itself to Kellgren-Lawrence scale 2-3. Montes-Molina et al. (2009) selected subjects with knee pain of musculoskeletal origin using an orthopaedic physician or a rehabilitation consultant to clinically diagnose knee pathology. Banzer et al. (2008) relied on a medical examination, MRI and the presence of pain to confirm the presence of OAK while Trelles et al. (1991) used x-rays and medical examinations.

Table 13 – Inclusion Criteria Low-Intensity Laser Therapy Studies Used for OAK

Study	American College for Rheumatology (ACR)*	Kellgren & Lawrence Scale	Diagnosis/ Medical Check	VAS Pain Scale	Other Scales	Ages	Medication/ Exercise	Issues
Banzer (2008)	X	X	✔ MRI Presence of pain	Knee pain	X	63 years	Analgesics & NSAIDs Physical therapy Limited weight bearing	Single case study.. No K&L or ACR Not robust
Fukuda (2010)	X	✔ Kellgren & Lawrence Grade 2 - 3	X	X	Timed Up & Go Knee flexion Dynamo-metry 11-point VNPS Lequesne Index	50-78 years	X	Solid inclusion criteria Robust
Gur (2003)	✔	✔ Kellgren & Lawrence Grade 3	Clinically & x-ray verified Pain for at least 6 months	✔	WOMAC Pain Flexion Morning stiffness Painless walking distance/ duration	45-81 years	X	Solid inclusion criteria with ACR & K&L Robust
Hegedus (2009)	X	X	Mild to moderate OAK Thermography Doppler Blood Urine	✔ Pain > 4/10	Pain Flexion Pressure sensitivity Circumference	32-65 years	Dual Energy x-ray Absorbtiometry measurements	No ACR or K&L Not robust
Montes Molina (2009)	X	X	Clinically diagnosed by orthopaedic Physician	✔ Knee pain	X	47-49 years	Analgesics & NSAIDS	No K&L and no ACR to establish standardised baseline Not robust

Researcher	American College for Rheumatology (ACR)*	Kellgren & Lawrence Scale	Diagnosis/ Medical Check	VAS Pain Scale	Other Scales	Ages	Medication/ Exercise	Issues
Tascioglu (2004)	✔	✔ Kellgren & Lawrence Grade 2-3	Not reported	✔	WOMAC	49-72 years	Paracetamol	Solid inclusion criteria with ACR, K&L & WOMAC Robust
Trelles (1991)	X	X	X-rays Arthrosis for < 3 years –condition verified by physician & radiologist	✔ Pain in knee joint using 0-10 scale (nil to unbearable pain)	Pain Flexion	35-70 years	✔ No medication for 15 days before laser treatment Restricted to aspirin during treatment	No ACR & no K&L No standardised inclusion criteria Not robust

*** ACR Criteria for OAK:** a) Using history and physical examination: Knee pain and three of the following factors – > 50 years; < 30 minutes of morning stiffness; bony tenderness; bony enlargement; no palpable warmth of synovial; b) Using history, physical examination and radiographic findings: Knee pain and one of the following factors – > 50 years; < 30 minutes of stiffness; crepitus on active motion; and osteophytes; c) Using history, physical examination and laboratory findings: Knee pain and five of the following factors: > 50 years; < 30 minutes of morning stiffness; bony tenderness; bony enlargement; no palpable warmth of synovial; crepitus on active motion; ESR < 40mm/h; rheumatoid factor < 1: 40; synovial fluid sign of osteoarthritis.

Summary

Four of the seven studies in this category (Banzer et al. 2008, Hegedus et al. 2009, Montes-Molina et al. 2009, Trelles et al. 1991) did not appear to apply any strict inclusion criteria and objective measures, which are vital for scientific studies. Without them, the four studies were not robust because treatment outcomes could not be measured accurately. The Hegedus et al. 2009 study was notable for its use of a wide range of diagnostic tools, including thermography, Doppler, blood and urine analysis, and dual-energy x-ray absorbtiometry measurements.

Exclusion Criteria

Most of the seven studies shown in Table 14 (below) had solid exclusion criteria, focusing on precluding prospective participants on the grounds of presenting medical conditions and medication usage. One study (Trelles et al. 1991) mentioned obesity, which can aggravate OAK symptoms.

Table 14 – Exclusion Criteria Low-Intensity Laser Therapy Studies Used for OAK

Study	**Surgical Intervention(s)**	**Drug interventions**	**Serious Medical Condition(s)**	**Issues**
Banzer (2008)	X	X	X	Not stated Not robust
Fukuda (2010)	X	Use of antidepressants, NSAIDs, steroids, tranquillisers 6 months prior to enrolment Hip OA, acute diseases or other rheumatoid or orthopaedic diseases that would interfere with treatment plus physiotherapy in previous six months	History of cancer Dementia Neurological deficits Pacemaker Type 1 diabetes Arterial hypertension Morbid obesity	Solid exclusion criteria Robust
Gur (2003)	✔ Other causes of unrelated knee pain	X	✔ Cancer Any acute disease Uncontrolled diabetes mellitus Untreated hypertension Neurological deficits (motor or sensory) Psychotic disorders Dementia Mental retardation Other organic mental disorders Drugs used > 6 weeks Intra-articular or periarticular injection therapy Physiotherapy in past 6 weeks	Solid exclusion criteria Combination of medical conditions and medication usage
Hegedus (2009)	✔ Deformity of varus or valgus Ankylosis Intense synovitis Gonitis	✔ No steroids, anti-depressants or sedatives	✔ Abnormal lab results (inflammatory & infectious disease, malignant tumor) Arterial circulatory blockage in lower limb Contra-indications for laser therapy Erosive or destructive alterations detected by radiograph (Kellgren-Lawrence Grade 4)	Solid exclusion criteria Combination of medical conditions and medication usage

Study	Surgical Intervention(s)	Drug interventions	Serious Medical Condition(s)	Issues
Montes Molina (2009)	✔ Knee prostheses	✔ Corticosteroid injections	✔ Knee pain of radicular lumbar origin	Combination of medical conditions & medication
Tascioglu (2004)	✔ No knee surgery		✔ Serious concomitant systemic diseases. Intra-articular fluid effusion. Kellgren & Lawrence Grade 1 and 4. Knee joint diseases other than OA. OA of hip joint or foot joints Previous physical therapy & intra-articular corticosteroid or hyaluronic acid injections in past six months	Solid exclusion criteria Combination of medical conditions & medication usage
Trelles (1991)	X	X	✔ Diabetic patients using insulin Any devitalising systemic disease Evident psychopathology	Solid exclusion criteria Focus on medical conditions and obesity. 25% > average weight

Summary

Hegedus et al. (2009) was the only researcher out of seven studies shown in Table 14 (above) to list contraindications to laser therapy as exclusion criteria. Six out of the seven studies generally set solid exclusion criteria.

3.7.3 Overall Critique on Inclusion & Exclusion Criteria Used in Laser Acupuncture & Low-intensity Laser Therapy OAK Studies

Establishing strict inclusion and exclusion criteria for any study, be it for laser acupuncture or low-intensity laser therapy, makes the population sample more homogeneous and aids statistical analyses. Only one study (Hegedus et al. 2009) listed contraindications for laser treatments among its exclusion criteria, indicating that most researchers lacked awareness or knowledge of basic laser safety. Contraindications include cancer; irradiating over known malignant lesions, pregnancy thyroid and tattoos; taking photo-sensitive medication; and participants with very dark skin/hair.

Although only laser acupuncture OAK studies had the potential to use TCM diagnostic criteria for study inclusion, addressing appropriate TCM inclusion and exclusion criteria is nevertheless important to ensure the integrity of TCM-based research.

3.8 Laser Parameters

This section examines laser parameters used in the 27 reviewed studies, including wavelength, power density, output power, dosage/fluence, application mode, treatment sites, treatment duration, treatment frequency, treatment period/program and total number of treatments and their impact on treatment outcomes. The outcome of this examination aided formulation of the most appropriate parameters for the current investigation. For ease of comparison with the OAK syndrome, laser acupuncture and low-intensity laser therapy studies are grouped together.

To establish optimum laser parameters for the treatment of a specific anatomical region or disease patterns found in OAK and other pain conditions, researchers need to understand laser science, tissue interaction, optical properties of tissue and how cellular substrates preferentially absorb laser light. These factors affect key parameters, such as wavelength and power density and laser dosage/fluence.

3.8.1 Wavelength

Light is made up of packets or quanta of energy that have wave-like properties. Wavelength is measured in nanometers (nm) that match specific electromagnetic spectrums of light. Selecting the correct wavelength is the primary factor in establishing laser parameters for therapeutic treatments. Wavelength determines the depth of penetration of light into tissue. Generally, the shorter the wavelength (e.g. under 700nm), the shallower the penetration depth. Consequently, shorter wavelengths are mostly used for superficial tissue. Conversely, the longer the wavelength (e.g. 780nm to 1064nm), the deeper the penetration depth for deep-seated tissue.

However, this theory is complicated by the optical properties of tissue, coloured chromophores and cellular substrates within the skin that preferentially absorb different wavelengths. Consequently, the targeted cellular substrates and treatment sites may not absorb sufficient energy from the selected wavelength if the optical properties of the targeted treatment site do not correlate with the wavelength. This may affect treatment outcomes.

3.8.2 Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK (9 Studies)

Laser wavelengths commonly used for pain conditions generally fall in the 810nm to 904nm range of the electromagnetic spectrum. Eight out of nine OAK studies that tested the effectiveness of laser acupuncture and low-intensity laser therapy used

wavelengths in the 810nm to 904nm range and reportedly produced positive results as a treatment for OAK (see comparisons provided in Table 15, below).

Two studies (Banzer et al. 2008, Shen et al. 2009) employed two wavelengths. Banzer et al. (2008) used so-called laser needles emitting 685nm and 885nm. Shen et al. (2009) used a laser that combined two wavelengths in a single device – low-intensity 650nm laser and a high-intensity 10.6μm CO_2 laser – that irradiated the ST35 acupuncture point. The objective was to test the heat-producing effects of a CO_2 laser as a high-tech alternative to the TCM heat treatment called moxibustion.

Table 15 – Wavelengths Laser Acupuncture & Laser Therapy Studies Used for OAK

Wavelength	Study	Negative Result	Positive Result	Mixed Wavelengths Used	No. Using Specific Wavelength(s) Used
*650nm *10.6μm	Shen (2009) *Combined wavelengths		 ✔	1	1 1
**685nm & **885nm	Banzer (2008) **Dual wavelength laser needles		✔	1	1 1
810nm	Montes-Molina (2009)		✔		1
830nm	Tascioglu (2004) Hegedus (2009) Trelles (1991)	✔	 ✔ ✔		3
904nm	+Yurtkuran (2007) Gur (2003) Fukuda (2010)		✔ ✔ ✔		3
Totals	**9 studies**	**1**	**8**	**2**	**11**

Key: *Combined wavelengths **Dual wavelengths +Laser acupuncture studies

Summary

The most used wavelengths in this category were in the 830nm to 904nm range, which is in line with World Association of Laser Therapy (WALT) recommendations for treating arthritic conditions (World Association for Laser Therapy 2010).

3.8.3 Laser Acupuncture for Other Pain Conditions (9 Studies)

The nine laser acupuncture studies investigating treatments for other pain conditions used wavelengths ranging from the visible red 632.8nm through to invisible infrared 904nm (see Table 16, below). Six of the nine studies reported positive outcomes. However, two of the positive studies (Dorsher et al. 2010, Stump et al. 2006) did not report the wavelengths used.

Table 16 – Wavelengths Laser Acupuncture Studies Used for Other Pain Conditions

Wavelength (nm)	Study	Negative Results	Positive Results	No. of Studies Using Specific Wavelength(s)
632.8nm (red)	Aigner et al. (2005) Naeser et al. (2002)* * Dual wavelengths	✔	✔	2
780nm	Hotta et al. (2010)		✔	1
830nm	Ebneshahidi et al. (2005) Gottschling et al. (2008) Glazov et al. (2009)	✔	✔ ✔	3
904nm	Haker et al. (1990) Naeser et al. (2002)* *Dual wavelengths	✔		2
*Red laser (nm not reported) *Infrared (nm not reported)	Dorsher et al. (2010) *Dual wavelengths		✔	1 not reported
Not specified	Stump et al. (2006)		✔	1 not reported
Totals	**9 Studies**	**3**	**6**	**7**

Summary

The two studies that did not report the wavelengths (Dorsher et al. 2010, Stump et al. 2006) make replication impossible. However, the most used wavelength was 830nm, which is one of the wavelengths WALT recommends for treating musculoskeletal conditions.

3.8.4 Low-Intensity Laser Therapy Studies Used for Other Pain Conditions (9 Studies)

Four of the nine studies that used low-intensity laser therapy for other pain conditions (see Table 17, below) favoured wavelengths in the 830nm to 904nm range of the invisible light spectrum to treat other pain syndromes. Of the four researchers, two chose 830nm (Dundar et al. 2007, Chow et al. 2006) and two 860nm (Brosseau et al. 2005, Irvine et al. 2004).

Of the remaining five studies, two opted for 904 nm (Altan et al. 2003, Bingol et al. 2005) and one for 1064nm (Basford et al. 1999). Two studies (Ilbuldu et al. 2004) and (Stergioulas 2008) used the visible red wavelength of 632.8nm and 810nm respectively.

Three studies (Ilbuldu et al. 2004, Chow et al. 2006, Stergioulas 2008) reported a positive result, indicating that a number of wavelengths provide a therapeutic effect.

Table 17 – Wavelengths Laser Therapy Studies Used for Other Pain Conditions

Wavelength (nm)	Study	Negative Result	Positive Result	No. of Studies Using Specific Wavelength(s)
632.8nm	Ilbuldu et al. (2004)		✔	1
810nm	Stergioulas (2008)		✔	1
830nm	Dundar et al. (2007) Chow et al. (2006)	✔	 ✔	2
860nm	Brosseau et al. (2005) Irvine et al. (2004)	✔ ✔		2
904nm	Altan et al. (2005) Bingol et al. (2005)	✔ ✔		2
1064nm	Basford et al. (1999)	✔		1
Total	**9**	**6**	**3**	

Summary

It appears that two wavelengths (810nm and 830nm) recommended by WALT for the treatment of musculoskeletal painful conditions produced positive outcomes. Although Ilbuldu et al. (2004) achieved a positive outcome with a wavelength of 632.8nm, the study did not provide a rationale for using a wavelength that has a shallower penetration depth than the recommended IR range to target trapezius muscles. Nevertheless, WALT recommends 810nm to 950nm wavelengths for the treatment of musculo-skeletal conditions (World Association for Laser Therapy 2010).

3.8.5 Conclusions Reached on Wavelength

Wavelengths used in the 27 studies were analysed to guide selection of a wavelength that would provide optimum results in the current laser acupuncture knee pain study.

The most used wavelength was the 830nm, which generated a positive outcome in five out of eight or 62.5% of laser studies. The second most used wavelength – 904nm – recorded a positive result in four out of seven studies (57.14%). The third most used wavelength (632.8nm) produced two positive results out of three studies to give a success rate of 66.66%.

Although only two studies used 810nm – the fourth most popular wavelength – both achieved positive results. This success rate was likely connected with that wavelength's ability to penetrate deeper in human tissue. This feature, coupled with the way the 810nm wavelength correlated with the area to be treated, i.e. the knee, and the fact that the invisible beam would aid randomisation and the development of a credible placebo method, led to the selection of an 810nm device for this laser acupuncture study.

3.9 Power Density

Power density is another important part of laser parameters. Power density refers to "light intensity" or "light concentration". It is the light output power per unit area of the target illuminated by laser light. It is usually measured in W/cm^2 (Tuner & Hode 2002).

The higher the intensity or concentration of light delivered to the target area determines the intensity directed at the treatment site. Photo-biomodulation is based on the local effects of the transport of various substances through cell membrane and tissue. As a result, power density should not be too low even if the number of joules is high and low power cannot be completely compensated by increased time (Tuner & Hode 2002).

3.9.1 Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK (9 Studies)

The power densities of lasers used for OAK in the reviewed studies ranged from $10mW/cm^2$ to $17.8W/cm^2$ (see Table 18, below). However, four out of nine studies did not report the power density of the laser used, despite it being a WALT recommendation.

Table 18 – Power Densities Laser Acupuncture & Low-Intensity Laser Therapy Studies Used for OAK (9 Studies)

Power Density ($W/mW/cm^2$)	Study	Negative Result	Positive Result	No. of Studies Using Particular Output Power(s)
LASER ACUPUNCTURE FOR OAK				
$10mW/cm^2$	Yurtkuran et al. 2007)		✔	1
Not reported	Shen et al. (2009) *Combined laser		✔	1
LOW-INTENSITY LASER THERAPY FOR OAK				
Power Density ($W/mW/cm^2$)	**Study**	**Negative Result**	**Positive Result**	**No. of Studies Using Particular Output Power**
$1.09W/cm^2$	Montes-Molina et al. (2009)	✔		**1**
$3W/cm^2$	Trelles et al. (1991)		✔	1
$10W/cm^2$	Hegedus et al. (2009)		✔	1
$17.8W/cm^2$	Banzer et al. (2008) - laser needles		✔	1
Not reported	Tascioglu et al. (2004)	✔		1
Not reported	Gur et al. (2003)		✔	1
Not reported	Fukuda et al. (2010)		✔	1
TOTALS	**9 studies**	**2**	**7**	**9**

Summary

Although power density is a major parameter that identifies the concentration of energy used in a laser treatment, four out of nine studies (44.44%), did not report the power density. This reflects poorly on study quality and the researchers' understanding of laser science and parameter requirements for therapeutic laser treatments.

3.9.2 Laser Acupuncture Studies Used for Other Pain Conditions (9 Studies)

Power densities used in this category ranged from 0.05 W/cm^2 to 5W/cm^2. Six out of nine studies did not report the power density of the laser used (see Table 19, below).

Table 19 – Power Densities Laser Acupuncture Studies Used for Other Pain Conditions

Power Density W/mW/cm^2	Study	Negative Result	Positive Result	No. Using Particular Output Power
0.05W/cm^2	Glazov et al. (2009)	✔		1
3.8W/cm^2	Gottschling et al. (2008)		✔	1
5W/cm^2	Dorsher (2010) **Dual wavelengths		✔	1
Not reported	Aigner et al. (2005)	✔		1
Not reported	Naeser et al. (2002) *Dual laser		✔	1
Not reported	Haker et al. (1990)	✔		1
Not reported	Ebneshahidi et al. (2005)		✔	1
Not reported	Hotta et al. (1990)		✔	1
Not reported	Stump et al. (2006)		✔	1
Total	**9 studies**	**3**	**6**	**6 out of 9 not reported**

Summary

In this category, 66.67% of the studies did not report the power density of the laser used. This omission reflects poorly on the quality of the studies and makes replication difficult.

3.9.3 Low-Intensity Laser Therapy Studies Used for Other Pain Conditions (9 Studies)

Power densities reported in this category ranged from 0.67W/cm^2 to 3W /cm^2. Seven studies out of nine did not report the power density of the laser used (see Table 20, below).

Table 20 – Power Densities Low-Intensity Laser Therapy Studies Used for Other Pain Conditions

Power Density (W/mW/cm^2)	Study	Negative Result	Positive Result	No. of Studies Using Particular Fluence(s)
0.67W/cm^2	Chow et al. (2006)		✔	1
3W/cm^2	Brosseau et al. (2005)	✔		1
Not reported	Dundar et al. (2007)	✔		1
Not reported	Irvine et al. (2004)	✔		1
Not reported	Stergioulas et al. (2008)		✔	1
Not reported	Basford et al. (1999)	✔		1
Not reported	Altan et al. (2003)	✔		1
Not reported	Bingol et al.(2005)	✔		1
Not reported	Ilbuldu et al. (2004)		✔	1
Total	**9**	**6**	**3**	**7 out of 9 not reported**

Summary

The nine studies in this category had the highest rate of not reporting the power densities of the lasers used in all of the 27 studies reviewed. Some 33.33% failed to report explicitly on power density, which is considered to be a vital piece of information in any robust evidence-based laser study.

3.9.4 Overall Critique on Power Densities Used in Laser Acupuncture & Low-intensity Laser Therapy Studies on OAK & Other Pain Conditions (27 Studies)

Of the 27 studies under review, 17 studies reported a positive result. However, only 10 of the 27 studies, or 37.04 per cent, reported the power density of the laser used (see Tables 18, 19 & 20, above).

Reported power densities ranged from 0.05W/cm^2 to 17.8W/cm^2. Of the 10 studies that reported power densities, the most commonly used were 3W/cm^2 and 10W/cm^2. It appears that a power density as low as 10mW/cm^2 produced a positive outcome.

Not including power density details is a serious omission that impacts on any meaningful assessment of the intensity of light used in a study. Omission also makes replication of a study difficult for future researchers. This RCT used a power density of 1.1W/cm^2, which was within the 0.05W/cm^2 to 17.3W/cm^2 range used by studies that produced a positive result.

3.10 Output Power

The radiant power output (i.e. the output power) refers to the number of photons emitted per second from a therapeutic laser device. Output, specified in milliwatts (mW), provides an indication of the power a laser generates (Baxter 1994). In other words, output power is the strength of the energy produced by a laser device. Output power has a strong relationship with power density, dosage/fluence and irradiation time. The higher the output power, the less time required to deliver a given amount of energy.

3.10.1 Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK (9 Studies)

Output power used in the nine laser acupuncture and low-intensity laser therapy for OAK studies ranged from 4mw to 200mW (see Table 21, below). The most commonly used output power was 50mW and 60mW. Seven of the nine studies reported positive outcomes with Class 3B laser outputs ranging from 4mW (Yurkuran et al. 2007) to 60mw (Trelles et al. 1991, Fukuda et al. 2010) through to a Class 4 CO_2 laser delivering 200mW (Shen et al. 2009).

Table 21 – Output Power Laser Acupuncture & Low-Intensity Laser Therapy Studies Used for OAK

Output Power (mW)	Study	Negative Result	Positive Result	No. of Studies Using Particular Output Power
4mW	+Yurtkuran et al. (2007)		✔	1
10mW average for Group 1 11.2mW average for Group 2	Gur et al. (2003)		✔	1
35mW	Banzer et al. (2008) - laser needles		✔	1
*36mW *200mW	+Shen et al. (2009) *Combined laser		✔	1
50mW	Tascioglu et al. (2004) Hegedus et al. (2009)	✔	✔	3
60mW	Trelles et al. (1991) Fukuda et al. (2010)		✔ ✔	2
100mw	Montes-Molina et al. (2009)	✔		
TOTALS	9	**2**	**7**	**9**

+ Laser acupuncture studies

3.10.2 Laser Acupuncture Studies Used for Other Pain Conditions (9 Studies)

Of the nine laser acupuncture studies treating other pain conditions (see Table 22, below), nine fell in the 5mw to 500mW output power range. Six of the studies reported positive results.

These variations in energy output suggest that some researchers are unsure about the optimum output power that is required for the treatment of pain. Moreover, they do not appear to have grasped the fact that all elements in laser parameters are inter-related and add to the difficulty in finding the perfect combination that addresses the biomodulation (Huang et al. 2009).

Output power is a key determinant of the amount of time needed to deliver a given treatment, i.e. the higher the output power, the shorter the treatment time. Consequently, positive results are sometimes possible with even low-powered lasers – provided that irradiation time is sufficient to produce the required fluence to achieve the desired treatment effect.

Table 22 – Output Power Laser Acupuncture Studies Used for Other Pain Conditions

Output Power (mW)	Study	Negative Result	Positive Result	No. Using Particular Output Power
5mW	Aigner et al. (2005)	✔		1
*5mW & 20mW	Naeser et al. (2002) *Dual laser		✔	1
10mW	Glazov et al. (2009)	✔		1
12mW	Haker et al. (1990)	✔		1
**25Mw & 37.5mW	Dorsher (2010) **Dual wavelengths		✔	1
30mW	Gottschling et al. (2008)		✔	1
39mW	Ebneshahidi et al. (2005)		✔	1
70mW	Hotta et al. (1990)		✔	1
500mW	Stump et al. (2006)		✔	1
Total	9 studies	**3**	**6**	**9**

Summary of Output Power Laser Acupuncture Studies Used for Other Pain Conditions

Table 22 (above) indicates that an output power of 12mW or less did not produce a favourable outcome. However, comparisons are difficult because Naeser et al. (2002) achieved a positive result by using dual lasers with power outputs of 5mW and 20mW.

3.10.3 Low-intensity Laser Therapy Studies Used for Other Pain Conditions (9 Studies)

An output power ranging from 38mW to 300mW was used in low-intensity laser therapy studies investigating other pain syndromes (see Table 23, below).

Table 23 – Output Power Low-Intensity Laser Therapy Studies Used for Other Pain Conditions

Output Power (mW)	Study	Negative Result	Positive Result	No. of Studies Using Particular Fluence(s)
30mW	Brosseau et al. (2005)	✔		1
58mW	Dundar et al. (2007)	✔		1
60mW 60mW	Irvine et al. (2004) Stergioulas et al. (2008)	✔	✔	2
300mW –670mW/cm^2	Chow et al. (2006)		✔	1
542mW -not clear	Basford et al. (1999)	✔		1
27W, 50W, or 27W x 4W - not clear	Altan et al. (2003)	✔		1
50W – not clear	Bingol et al. (2005)	✔		1
Not stated	Ilbuldu et al. (2004)		✔	1
Total	**9**	**6**	**3**	**9**

Summary

Only three studies in this category (Ilbuldu et al. 2004, Chow et al. 2006, Stergioulas 2008) were positive. However, one of these studies (Ilbuldu et al. 2004) did not provide clear details about the output power of the laser used, making comparisons or follow-up research difficult.

3.10.4 Overall Critique on Output Power in Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK & Other Pain Conditions (27 Studies)

The 27 studies showed that laser acupuncture and low-intensity laser therapy treatments for OAK and other pain conditions achieved variable results with an output power as low as 4mW and as high as 542mW. Furthermore, the positive result

achieved with an output power of 4mW (Yurtkuran et al. 2009) indicates that other factors require consideration when setting laser parameters.

3.11 Fluence/Dosage

The fluence of a laser pulse is the optical energy delivered per unit area. In low-intensity laser therapy the common unit of measurement is joules per square centimetre (J/cm^2) (R P Photonics 2016). In laser therapy it is generally accepted that the higher the fluence, the greater the amount of energy delivered to the treatment site. The potential for a positive treatment outcome is increased because the absorption of more energy can accelerate the healing process, provided the parameters do not result in an inhibitory effect, as explained by the Arndt-Schultz Law (Huang et al. 2009). Examination of the 27 studies below provides an insight into how fluence impacts on study outcomes.

3.11.1 Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK (9 Studies)

Of the nine laser acupuncture and low-intensity laser therapy studies listed in Table 24 (see below), eight of the studies produced positive results with fluences ranging from 0.48J/point to 18J/point. It appears that 30J/point was the most commonly used fluence. However, replication of the eight studies would be difficult because most did not specify details about the total treatment time per session.

Table 24 – Fluence/Dosage Per Treatment Session Used In Laser Acupuncture & Low-Intensity Laser Therapy Studies for OAK

Fluence (Joules per Point)	Time per Point	Total Energy Used per Session	OAK Treatment Site	Study	Negative Result	Positive Result
LASER ACUPUNCTURE FOR OAK						
0.48J/pt	120sec (20min)	0.48J/session	SP9	Yurtkuran et al. (2007)		✔
Not specified	20min	Not reported	ST35	Shen et al. (2009)		✔
LOW-INTENSITY LASER THERAPY FOR OAK						
Fluence (Joules per Point)	**Time per Point**	**Total Energy Used per Session**	**OAK Treatment Site**	**Study**	**Negative Result**	**Positive Result**
1.5J/pt to 3J/pt	2min/pt	15J/session 7.5J/session	5 tender & painful points	Tascioglu et al. (2004)	✔	
3J/pt	50sec/pt	27J/session	5 points on medial face of knee 4 points on lateral face near joint capsule & synovial membrane	Fukuda et al. (2010)		✔
Group 1 = 3 J Group 2 = 2J Not stated	Group 1= 5min Group2 = 3min	Group 1 = 30J Group 2=20J	Antero-medial portal & antero-lateral portal	Gur et al. (2003)		✔
3 & 6J/point	30-60sec/ pt	30J-60J/session	Points used unclear	Montes-Molina et al. (2009)		✔
6J/point	Not specified	48J/session	Over femoral & tibial condyles	Hegedus et al. (2009)		✔

Fluence (Joules per Point)	Time per Point	Total Energy Used per Session	OAK Treatment Site	Study	Negative Result	Positive Result
18J/point	60sec/pt	72J/session	4 points around knee	Trelles et al. (1991)		✔
Not specified	Not specified	1,008J/session	Medial condyle & joint cavity	Banzer et al.(2008)		✔
Total				**9**	**1**	**8**

Summary

The two laser acupuncture studies in Table 24 (above) produced positive results by irradiating acupuncture points with a fluence as small as 0.48J/point. In contrast, the positive low-intensity laser therapy studies applied a fluence of more than 3J to local points.

This appears to indicate that the fluence for laser acupuncture need not be as high as those required for low-intensity laser therapy because acupuncture points are energy points that appear to accelerate healing and positive outcomes.

3.11.2 Acupuncture Studies Used for Other Pain Conditions (9 Studies)

Three of the nine studies that used fluences of 0.36J/point or less in this category did not produce a positive result while fluences of 0.9J/point or more had better outcomes (see Table 25, below).

Table 25 – Fluence/Dosage per Treatment Laser Acupuncture Studies Used for Other Pain Conditions

Fluence (Joules per Point)	Time per Point	Total Energy Used per Session	Treatment Syndrome/ Site	Study	Negative Result	Positive Result	Study Issues
0.075 J/cm^2	15sec/pt	Not reported	Whiplash	Aigner et al. * (2005)	✔		Energy level too low
0.2J/point	20sec	Not reported	Back pain	Glazov et al. (2009)	✔		Treatment duration not consistent
0.36J/point	30sec/pt	Not reported	Elbow	Haker et al. (1990)	✔		
0.9J/point	30sec/pt	Not reported	Headache	Gottschling et al. (2008)		✔	
1.3J/point	43sec/pt	Not reported	Headache	Ebneshahidi et al. (2005)		✔	
Mixed joules	Mixed treatment	Unclear	Carpal Tunnel Syndrome	Naeser et al. (2002) *Dual laser		✔	
*30J/point *45J/point		Not reported	Arthritis/ musculoskeletal	Dorsher (2010) *Dual laser		✔	
35J/cm^2	20sec/pt	Not reported	TMD	Hotta et al. (2010)		✔	
30J/point	30sec/pt	Not reported	Arthritic pain	Stump et al. (2006)		✔	
Total		**8**		**9**	**3**	**6**	

Summary

Most of the nine studies in Table 25 (above) did not report the total laser energy used per treatment session, making replication difficult.

3.11.3 Low-intensity Laser Therapy Studies Used for Other Pain Conditions (9 Studies)

Seven of the nine low-intensity laser therapy studies treating other pain conditions did not state the total energy used on participants (see Table 26, below). Reported fluences ranged from 1.8J/point to 7J/point.

Table 26 – Fluence/Dosage Per Treatment Session Laser Therapy Studies Used for Other Pain Conditions

Fluence (Joules/Per Point)	Total Energy Used Per Treatment Session	Treatment Time/Per Point	Treatment Site	Study	Negative Result	Positive Result	Issues
1.8J/point	14.4J	Not reported	8 points on glenohumeral joint	Stergioulas et al. (2008)		✔	
2J (not clear)	Not reported	Not reported	Upper trapezius trigger points	Ilbuldu et al. (2004)		✔	
Not reported	Not reported	2min	Cervical myofascial pain syndrome	Bingol et al. (2005)	✔		Laser parameters not reported
3J	Not reported	1sec	15 points	Brosseau et al. (2005)	✔		
6J	Not reported	15sec/pt	20 $1cm^2$ X $1cm^2$ sites over carpal tunnel	Irvine et al. (2004)	✔		Unclear parameter Reporting not explicit

Fluence (Joules/Per Point)	Total Energy Used Per Treatment Session	Treatment Time/Per Point	Treatment Site	Study	Negative Result	Positive Result	Issues
7J	42J	2min/point	Cervical region	Dundar et al. (2007)	✔		
Not reported	Not reported	30sec	Up to 50 points for max. of 30min	Chow et al. (2006)		✔	Joules not reported
Not reported	Not reported	2min	Trapezius 4 points bilaterally	Altan et al. (2005)		✔	
Not reported	Not reported	90sec/8 symmetric points along lumbo-sacral spine	Symmetric points along lumbo-sacral spine	Basford et al. (1999)	✔		Laser parameters not reported
Total	**7 out of 9 not reported**			**9 studies**	**5**	**4**	4 out of 9 did not report explicitly

Summary

Only four of the nine studies in this category reported positive results. Lack of details made it impossible to draw any meaningful conclusions about optimum energy levels.

3.11.4 Overall Critique on Fluence/Dosage Used in 27 Studies of Laser Acupuncture & Low-intensity Laser Therapy for OAK & Other Pain Conditions

Only six out of 27 studies (22.22%) in the OAK and other pain categories reported details about fluence, irradiation time per point and total energy used per intervention session. This low percentage reflects poorly on the robustness of these studies, the majority of which failed to meet CONSORT standards for reporting explicitly on clinical trials.

For the treatment of OAK, fluences as low as 0.48J per point and up to 18J per point produced positive results. For other pain conditions, the fluence range for a positive outcome was 9J to 45J. This wide range indicates that different energy levels are required for different anatomical sites with thicker muscles or tissue or smaller or larger joints. For example, the thigh or back may need higher joules, whereas finger joints may need less because the transmission of light to deeper tissue might result in more scattering and less absorption, hence the need for higher energy. Additionally, different stages of disease patterns will require energy variations.

Ethnicity is another factor for consideration. Darker skin may absorb more energy at the superficial level than lighter skin due to the absorption of coloured chromophores, i.e. skin pigments or cellular substrates. This suggests there may be a wide range of appropriate dosages in using laser acupuncture for OAK. Careful consideration must therefore be given to choosing the most appropriate dose.

In the treatment of medial knee arthritis with a 780-860nm GalAlAs laser, WALT suggests reducing dosage by 30% when inflammation is under control. Therapeutic dose windows typically range from +/- 50% of given values. This indicates that maximum dosage for knee arthritis pain should not exceed 18J, if the 12J is indeed the given value for the therapeutic dose window. WALT's recommended doses are for white/Caucasian skin types and are reportedly based on clinical trial results or extrapolation of study results with similar pathology and ultrasonographic tissue measurements.

It is evident that few studies followed dosage recommendations made by WALT (2010). For wavelengths of 780 to 860nm, WALT recommends a mean output of 5mW-500mW along with irradiation times of 20-300 seconds on 3-6 points and a dose of 12J delivered on 3-6 points at a minimum of 4J/point. For 904nm treatments on knee anteromedial arthritis, a minimum total dose of 4J is recommended on 4-6 points at a minimum of 1J/point.

3.12 Treatment Programs

For any given condition, the number of low-intensity laser therapy treatments required is generally based on the condition being treated. The laser delivers energy that modulates cellular substrates within the body. Due to its low intensity, a regular dosage is required to stimulate the target tissue or cellular substrates and initiate the healing process. It therefore follows that the accumulative effect of a laser will be reduced with fewer and less frequent treatments, and this may affect the treatment outcome. Hence, WALT recommends a course of treatments delivered daily for two weeks or every other day for 3-4 weeks.

The studies in Tables 27, 28 and 29 (below) show wide variations in laser treatment programs for OAK and other pain conditions. Most studies provided 10-12 treatments.

3.12.1 Laser Acupuncture & Low-intensity Laser Therapy Studies Used for OAK (9 Studies)

In the laser acupuncture for OAK studies, treatment frequencies ranged from 3-5 treatments per week delivered over 2-4 weeks (see Table 27, below). In low-intensity laser therapy studies for the same condition, treatments were administered at intervals ranging from each day to five times a week for a minimum of two weeks and a maximum of three months.

Table 27 – Treatment Programs Laser Acupuncture & Low-Intensity Laser Therapy Studies Used for OAK

No. of Treatments Per Week	Total Treatments	Treatment Period	Study	Negative Result	Positive Result	Study Issues
Daily	Not stated	3 months	Banzer et al. (2008)		✔	Total number of treatments not reported
2	8	4 weeks	Hegedus et al. (2009)		✔	
2	16	8 weeks	Trelles et al. (1991)		✔	
3	12	4 weeks	+Shen et al. (2009)		✔	
3	9	3 weeks	Fukuda et al. (2010)		✔	
5	10	2 weeks	+Yurtkuran et al. (2007)		✔	
5	15	3 weeks	Tascioglu et al. (2004)	✔		
Not stated	15	3 weeks	Montes-Molina et al. (2009)		✔	Treatment frequency not reported
Not stated	10	14 weeks	Gur et al. (2003)		✔	Treatment frequency not reported
Daily to 5 times a week	**8 to 15 treatments**	**2 weeks to 3 months**	**9 studies**	**1**	**8**	**3 out of 9 studies did not report total number of treatments or treatment frequency**

+ Laser acupuncture studies

Summary

Eight of the nine studies in this category reported positive results. However, two of the studies (Montes-Molina et al. 2009, Gur et al. 2003) did not report the treatment frequency. Another study (Banzer et al. 2008) did not report the total number of treatments administered. The lack of such details reflects adversely on the robustness of these studies and raises questions about whether bias might have played a part in their results.

3.12.2 Laser Acupuncture Studies Used for Other Pain Conditions (9 Studies)

In laser acupuncture studies treating other pain conditions, one to three treatments a week were applied for periods ranging from three weeks to four months (see Table 28, below).

Table 28 – Treatment Programs Laser Acupuncture Studies Used for Other Pain Conditions

Treatments Per Week	Total Treatments	Treatment Period	Study/Condition	Negative Result	Positive Result	Study Issues
1	5-10	5-10 weeks	Glazov et al. (2009) – low back pain	✔		Treatment not uniform
1	4	4 weeks	Gottschling et al. (2008) – child headaches		✔	
1	10	10 weeks	Hotta et al. (2010) – temperoman-dibular dysfunction		✔	
1-2	Not reported	9 weeks	Stump et al. (2006) – arthritis		✔	Total number of treatments not reported
2-3	10	Not reported	Haker et al. (1990) – lateral epicondylalgia	✔		Treatment period not reported
3	Reporting unclear	Reporting unclear	Naeser (et al 2002) – carpal tunnel		✔	Complicated cross-over design Participant allocation inconsistent Total number of treatments & duration of treatments unclear
3	9	3 weeks	Aigner et al (2005) – neck whiplash	✔		
3	10	About 3 weeks	Ebneshahidi et al. (2005) – headache		✔	Treatment period not clear
Unclear	2	4 months	Dorsher (2010) – musculo-skeletal pain		✔	Cross-over treatment difficult to estimate & isolate laser & acupuncture needle effects Inconsistent treatment frequency
1 to 3 times a week	**2 to 10 treatments**	**3 weeks to 4 months**	**9 studies**	**3 negative**	**6 positive**	**Issues found in 6 out of 9 studies**

Summary

Six of the nine studies using laser acupuncture for other pain conditions reported positive results. However, five of the nine studies lacked attention to detail. Issues were found in four of the positive studies. Stump et al. (2006) did not report the total number of treatments; Naeser et al. (2002) had inconsistent participant allocation, and was unclear about the total number of treatments administered and the duration of treatments; Ebneshahidi et al. (2005) was not clear about the treatment period; and Dorsher et al. (2010) employed cross-over treatments delivered with inconsistent frequency, making it difficult to estimate and isolate laser and acupuncture needle effects.

3.12.3 Low-intensity Laser Therapy Studies for Other Pain Conditions (9 Studies)

The nine studies in this category used treatment programs ranging from daily interventions (the exact definition was not reported, but presumably delivered five days a week) to three times a week for 2-8 weeks (see Table 29, below).

Table 29 – Treatment Programs Low-Intensity Laser Therapy Studies Used for Other Pain Conditions

Treatments Per Week	Total Treatments	Treatment Period	Study/Condition	Negative Result	Positive Result	Study Issues
Daily	10	2 weeks	Altan et al. (2003) – cervical myofascial pain + exercise	✔		
2	14	7 weeks	Chow et al. (2006) – neck pain		✔	
3	12	Not reported	Ilbuldu et al. (2004) – myofascial pain		✔	Treatment period not reported
3	12	4 weeks	Basford et al. (1999) – back pain	✔		
3	18	6 weeks	Brosseau et al. (2005) – OA hand pain	✔		
3	15	5 weeks	Irvine et al. (2005) – carpal tunnel	✔		
Irregular	12	8 weeks	Stergioulas et al. (2008) – Achilles tendinopathy		✔	Irregular treatment frequency
Not clear	15	3 weeks	Dundar et al. (2007) – cervical myofascial pain	✔		Treatment frequency not clear
Not reported	10	2 weeks	Bingol et al. (2005) – cervical myofascial pain	✔		Treatment cycle not reported
Daily to 3 times a week	**10 to 18 treatments**	**2 to 8 weeks**	**9 studies**	**6 negative**	**3 positive**	**Issues found in 4 out of 9 studies**

Summary

Only three of the nine low-intensity laser therapy studies treating other pain conditions were positive. Issues were found with four of the nine studies. Ilbuldu et al. (2004) did not report the treatment period; Stergioulas (2008) provided treatments at irregular frequencies; Dundar et al. (2007) was not clear about treatment frequency; and Bingol et al. (2005) did not report the treatment cycle.

3.12.4 Overall Critique on Parameters Drawn from Review of 27 Studies of Laser Acupuncture & Low-intensity Laser Therapy

As noted in the review of the 27 laser acupuncture and low-intensity laser therapy studies on OAK and other pain conditions, methodology and reporting issues extended to all of the four design variables considered key to a successful research study, i.e. (i) wavelength; (ii) power density; (iii) output power; (iv) fluence/dosage; and (v) treatment program.

The wide variations in output power used in the studies indicate confusion about the most effective parameters for laser acupuncture and low-intensity laser therapy interventions. In simple terms, there is no one-size-fits-all approach to laser treatment. This is due to the bio-stimulatory and bio-inhibitory effects relating to the use of laser acupuncture and low-intensity laser therapy and other visible light and infrared sources. Used correctly, stimulation and inhibition has been clinically shown to reduce pain, improve tissue repair, resolve inflammation and stimulate the immune system (Huang et al. 2009).

Laser treatments are dependent on what is known as the biphasic dose response or the Arndt-Schultz Curve. Consequently, a small amount of stimulus from a light-based device may produce no biological effect, a moderate stimulus a bio-stimulatory effect and a large stimulus a bio-inhibitory or cytotoxic effect (Huang et al. 2009).

In laser therapy, the increasing stimulus may be related to irradiation time or increased beam intensity. Therefore, the key to a successful treatment outcome hinges on finding the correct combination of factors affecting laser dosimetry, such as wavelength, power density, output power, state of targeted cells, pulse regimes, treatment program and treatment intervals. Other potentially confounding factors are a lack of standardisation on beam measurement and unstable laser and LED performance. Taken together, these factors may mean that some published data is not robust and should be viewed cautiously.

3.13 Treatment Sites

Unlike clinical practice, where needle acupuncture treatments are tailored to suit individual presenting conditions, scientific studies require point prescriptions to be standardised to control variables that occur during acupuncture investigations. Consequently, a review of the literature and a manualisation process was undertaken to determine the most frequently used acupuncture points for OAK. This information was later used to inform the point selection protocol used in this study

3.13.1 Laser Acupuncture & Needle Acupuncture Studies Used for OAK (9 Studies)

Table 30 (below) shows the number of times a particular point was used in nine laser acupuncture and needle acupuncture studies for the treatment of OAK. This analysis led to the identification of nine acupuncture points most commonly used for OAK – ST34, ST35, ST36, GB34, Xiyan, SP6, SP9, SP10 and KD3 (see Table 30, below).

Table 30 – Acupuncture Points Laser Acupuncture & Needle Acupuncture Studies Used for OAK

Laser Acupuncture	**ST34**	**ST35**	**ST36**	**Xiyan**	**SP6**	**SP9**	**SP10**	**GB34**	**GB39**	**KD3**	**BL60**	**Heding**	**BL40**	**CO4**	**Other Points**
(Shen et al. 2010)		1													
(Yurtkuran et al. 1999)						1									
Needle Acupuncture	**ST34**	**ST35**	**ST36**	**Xiyan**	**SP6**	**SP9**	**SP10**	**GB34**	**GB39**	**KD3**	**BL60**	**Heding**	**BL40**	**CO4**	**Other Points**
(Scharf et al. 2006)	1		1	1		2	1	1							
(Itoh et al. 2008)	2	2	2			3	2	2							
(Christensen et al. 1992)	3	3	3				3								LIV4 XL2

Needle Acupuncture	ST34	ST35	ST36	Xiyan	SP6	SP9	SP10	GB34	GB39	KD3	BL60	Heding	BL40	CO4	Other Points
(Witt et al. 2005)	4	4	4	2	1	4	4	3		1	1	1	1		KD10 GB 33 LIV 8 SP 4 SP 5 ST 6 BL20 BL 57 BL58 BL62
(Petrou et al. 1988)		5	5										2	1	ST 43 EX31 EX32
(Takeda et al. 2011)		6				5		4							EX31 EX32
(Molsberger & Hille 1994)	5	7	6					5							BlL9 BL10 Extra 31 Extra 32
(Berman et al. 2004)		8	7	3	2	6		6	1	2	2				
(Vas et al. 2004)			8		3	7		7		3				2	EX-LE 5 ST40

Needle Acupuncture	**ST34**	**ST35**	**ST36**	**Xiyan**	**SP6**	**SP9**	**SP10**	**GB34**	**GB39**	**KD3**	**BL60**	**Heding**	**BL40**	**CO4**	**Other Points**
(Yurtkuran & Kocagil 1999)	6	9				8		8							
(Ng, Leung & Poon 2003)		10													EX-LE 4
(Ammer & Petschnig 1988)			9					9							GB30 GB32 BL54 LIV9
(Jia et al. 2005)	7		10	4		9	5	10							Ah Shi points
Berman (2004)		11	11	5	4	10		11	2	4	3				
(Sangdee et al. 2002)		12		6											LIV8 Trigger points
(Tukmachi et al. 2004)			12	7		11	6	12					3	3	LR3 BL57
Acupuncture Points	**ST34**	**ST35**	**ST36**	**Xiyan**	**SP6**	**SP9**	**SP10**	**GB34**	**GB39**	**KD3**	**BL60**	**Heding**	**BL40**	**CO4**	**Other Points**
Number of Times Used	**7**	**12**	**12**	**7**	**4**	**11**	**6**	**12**	**2**	**4**	**3**	**1**	**3**	**3**	**33**

3.13.2 Trigger Points & Target Treatment Sites

Although the laser acupuncture effects on OAK pain were the primary focus of the literature review, an examination of trigger points and target treatment sites used in low-intensity laser therapy studies was undertaken for comparison purposes. It was found that low-intensity laser therapy studies appeared to adopt a symptomatic approach to OAK treatments, focusing on the synovial region, knee joint (both lateral and medial), joint line and local tender points. Detailed information is presented in Table 31 (below).

Table 31 – Trigger Points/Target Sites Low-Intensity Laser Therapy Studies Used for OAK

Study	Points/Target Sites Used	Result
(Banzer, Hubscher & Schikora 2008)	8 laser needles placed along distal part of femur (medial condyle & joint cavity)	Positive
(Fukuda et al. 2010)	5 points on medial face of knee; 4 points on lateral face in region of joint capsule & synovial membrane	Positive in short term
(Bülow, Jensen & Danneskiold-samsøe 1994)	Periarticular tender points	Negative
(Gur et al. 2003)	2 points - a) antero-lateral; b) antero-medial portals of knee	Positive
(Hegedus et al. 2009)	Over femoral & tibial condyles at the synovia & cartilage in joint line	Positive
(Montes-Molina et al. 2009)	470nm LEDs used to illuminate treatment area 5 knee points irradiated transcutaneously at each treatment session	Positive
Tascioglu et al. (2004)	5 painful points found on clinical examination	Negative
Trelles et al. (1991)	Maximum of 4 points on each knee – 2 on anterior aspect; 2 on median aspect	Positive

3.14 Outcome Measures & Assessment Periods

Primary and secondary outcome measures are used in clinical trials to assess treatment outcomes. Tables 32, 33 and 34 (below) provide an overview of outcome measures and assessment periods used in the 27 studies that used laser acupuncture, low-intensity laser therapy or needle acupuncture to treat OAK.

WOMAC, the disease-specific gold standard for measuring the effects of OA treatments, was the most popular primary outcome measure and was used by 18 of the 27 studies listed in Tables 32, 33 and 34 (below). VAS was also used by 18 of the 27 studies, reflecting its universal appeal as a measure of pain.

Assessment periods varied widely between the three categories – as short as before and after treatment or as long as before treatment, at week 2, at week 6, at six months post-treatment and at one year post-treatment.

Table 32 – Outcome Measures & Assessment Periods Laser Acupuncture Studies Used for OAK

Study	VAS	WOMAC	SF36	McGill Pain Questionnaire	Knee Circumference	Nottingham Health Profile (NHP)	50ft Walk Time	Assessment Period	Result
Shen (2009)		✔						Before Week 2 Week 4	Positive
Yurtkuran (2007)	✔	✔			✔	✔	✔	Before Week 2 Week 12	Positive
Totals	**1**	**2**	**0**	**0**	**1**	**1**	**1**		**2 out of 2**

Table 33 – Outcome Measures & Assessment Periods Laser Therapy Studies Used for OAK

Study	VAS/NRS (0-10 Rating Scale)	WOMAC	SF36	McGill Pain Questionnaire	Range of Knee Flexion & Quality of Life	Other Measures	Patient Self-assessment/ Disability Index Questionnaire	Analgesic Intake	Assessment Periods	Result
(Banzer, Hubsche & Schikora 2008)	NA								Before After Wk 5 After 35 wks	Positive
Fukuda et al. 2010)	✔					Goniometry & dynamometric			Before At 9th session	Positive
Gur et al. (2003)	✔ (0-10 pts)	✔			✔				Before After Wk 4 After Wk 8 After Wk 12	Positive
Hegedus et al. (2009)	✔					Thermography Knee circumference			Before After treatment After Wk 2 After Wk 8	Positive
Montes-Molina et al. (2009)	VAS (pain/standing/ fl/extension/ up & downstairs) Laser more effective than others								Before At 7th session At 15 session	
Tascioglu et al. (2004)	✔	✔								Negative
Trelles et al. (1991)	✔									Positive

Table 34 – Outcome Measures & Assessment Periods Needle Acupuncture Studies Used for OAK

Study	RCT	VAS	WOMAC	SF36	McGill Pain Quest.	Global Assessment	Other Measures	Assessment Period	Result
Berman et al. (2004)			✔	✔			Function scores	Before Wk 4 Wk 8 W 14 Wk 26	Positive in function (WOMAC)
(Witt et al. (2005)			✔	✔				Before After 3 mths After 6 mths	Positive
Itoh et al. (2008) - Trigger points		✔	✔					Before Wk 1 Wk 2 Wk 3 Wk 4 Wk 5 Wk 10 Wk 20	Positive
(Vas et al. 2004)		✔	✔				Profile of Quality of Life in Chronically Ill (PQLC)	Before After	Positive
(Barclay & Lie 2004)			✔	✔				Before Wk 4 Wk 8 Wk 14 Wk 26	Positive
(Manheimer et al. 2006)			✔	✔		✔		Before Wk 8 Wk 26	Positive
(Foster et al. 2007)			✔					Before Wk 2 Wk 6 6 mths 1 year	Negative
Scharf et al. (2006)			✔			✔		Before Wk 13 Wk 26	Negative between acup & sham

Study	RCT	VAS	WOMAC	SF36	McGill Pain Quest.	Global Assessment	Other Measures	Assessment Period	Result
(Tukmachi et aL. 2004)		✔	✔					Before Wk 5 1 mth	Positive
(Williamson et al. 2007		✔	✔				Oxford Knee Score (OKS) Hospital Anxiety & Depression Score (HAD)	Before Wk 7 Wk 12 3 mths after	Negative
(Christensen et al. 1992)		✔	✔					Short term study Over Wk 1, 3, 4, 5 & 9 Long term study Over 50 Wks	Positive
(Ng, Leung & Poon 2003)		✔ 0-10 Pain Scale					Passive ROM Timed Up & Go Test (TUGT)	Before After 2 wks after treatment	Positive
Yurtkuran (1999)		✔ 5-pt scale					50ft walking time, quadriceps muscle strength, active knee flexion	Details not available	Positive & negative in different aspects – e.g. stiffness
Jia (2005) Can't find copy		✔ 4-pt scale						Details not available	Recurrence rate result mixed
(Sangdee et al. 2002)		✔	✔				Lequesne's Functional Index 50 ft walk time	Week 0 Week 4	Positive
(Tillu, Tillu & Vowler 2002)		✔					HSS score Time to walk 50m. Time to climb 20 steps	Before 2 mths	Positive
Scharf (2006)			✔	SF12		✔		Before At 26 wks	Negative
(Jubb et al. 2008)		✔	✔				Euro QoL	Before Wk 5 Wk 9	Positive

3.15 Summary of Findings from Literature Review

Each study under review was examined on the key elements of randomisation; sample size; blinding; placebo; diagnosis; inclusion and exclusion criteria; laser parameters (i.e. wavelength, power density, output power, dosage, treatment programs); and outcome measures. Findings from that examination and a review of other scientific literature pinpointed issues that needed to be addressed in any robust study testing the effectiveness of laser acupuncture on OAK pain.

As an example, Suresh (2011) identified that randomisation methods and sample sizes have the potential to over-estimate treatment effects by up to 40%. The sample size of a study could have a statistically significant impact on treatment outcomes if the effect size is not calculated accurately without due consideration being given to the level of significance, power of the study, underlying event rate in the population and standard deviation (Kadam 2010). Consequently, due consideration was given to calculating the power for this RCT and setting the sample size.

Some of the reviewed studies did not adhere to a strict form of double-blinding. Double-blinding was either not well described or assessor blinding was used instead of the more robust practitioner blinding (Schulz & Grimes 2002).

Another issue found in the literature review was the use of inappropriate placebo devices or methods due to a lack of understanding about light-based science. Clearly, the misunderstanding about how virtually all forms of light can affect treatment outcomes points to the need for researchers to have a thorough grounding in laser science and the mechanisms involved in laser treatments.

Additionally, the placebo effect could be influenced greatly through interaction between participants and practitioner (Kaptchuk et al. 2008). Because none of the reviewed studies measured such interactions, it was felt there was a great need for the current study to assess placebo influences flowing from the participant-practitioner relationship.

Diagnostic measures as well as inclusion and exclusion criteria were found to be problematic in the reviewed studies. Some did not use the Kellgren-Lawrence OA diagnostic scale as part of their inclusion criteria while others might have overlooked the need to exclude participants taking Naloxone, an opioid antagonist that blocks the analgesic effects of laser treatments (Serra & Ashmawi 2010). These considerations were taken into account in the design of this study.

Some "laser acupuncture" trials did not follow TCM philosophies relating to the use of diagnostic and treatment principles for specific disease patterns, leaving the reader to wonder whether some modality other than laser acupuncture was being practised or whether the studies were truly following the TCM paradigm. Some studies also did not explain the rationale for using particular laser parameters, indicating a lack of understanding of laser science and its implications for treatment outcomes. Areas treated and treatment programs varied a great deal. Few studies rationalised the choice of treatment areas. This was a serious oversight because standardising the treatment area is as important as selecting the correct laser parameters.

Findings from the literature review, coupled with the researcher's extensive knowledge of laser science and clinical practice over the past two decades, confirmed that a robust evidence-based RCT was needed to address identified study design gaps. Furthermore, a more robust study design was required to test the effectiveness of laser acupuncture for OAK pain treatments that integrate ancient TCM diagnostic and treatment principles with contemporary Western medical laser practice.

3.16 Review of Contemporary Laser Research (2011-mid-2016)

Despite the growing need for a drug-free OAK treatment, the paucity of laser research into this crippling degenerative condition appears to be continuing. Since the 2008-2010 literature search, a further nine laser OAK studies conducted between 2011 and mid-2016 were reviewed for relevance.

The new studies comprised three on laser acupuncture (Wang et al. 2013, Al Rashoud et al. 2013, Hinman et al. 2011); three on low-intensity laser therapy (Alfredo et al. 2011, Alghadir et al. 2014, Soleimanpour et al. 2014); and three using mixed modalities to investigate the effects of low-intensity laser combined with high-intensity laser therapy (HILT) and low-intensity laser therapy (LILT) combined with monochromatic infrared photo energy (MIPE) and exercise, and neuromuscular electrical stimulation (Kheshie et al. 2014, Ammar et al. 2014, Melo et al. 2016) respectively.

Of the three laser acupuncture studies, two (Al Rashoud et al. 2013, Hinman et al. 2014) used low-intensity Class 3B cold lasers. The third study (Wang et al. 2013) employed a high-intensity Class 4 10.6μm CO_2 thermal laser to mimic heated acupuncture needles tipped with lighted moxibustion herbs in a follow-up to the Shen et al. (2009) study reported in the 2008-2010 literature review.

In this section, results of these nine studies are reviewed, discussed and compared against the current laser acupuncture RCT.

Laser Acupuncture for OAK

Wang et al. (2013)

The Wang et al. (2013) RCT stated that TCM differentiates OAK into three patterns: Yang Deficiency and Cold Coagulation, Kidney Deficiency, and Blood Stasis. The study set out to determine whether Yang-deficient cold coagulation patients responded better to a combination of laser acupuncture administered with a high-intensity 10.6μm CO_2 thermal laser (HILT) and a 650nm low intensity cold laser (LILT) than non-Yang deficient patients. Some 52 OAK patients were allocated to Group A (Yang

deficient, N = 26) or Group B (non-Yang deficient, N = 26). All patients received a 20-minute thermal laser acupuncture treatment at a single acupuncture point, Dubi (ST35), three times a week for two weeks and twice a week for a further four weeks.

WOMAC assessments were performed immediately after the first treatment, and at weeks 2, 6 and 10. Group A function scores were significantly better than those of Group B at week 2 ($p = 0.049$), week 6 ($p = 0.046$) and week 10 ($p = 0.042$), but no significant differences were found between the two groups in pain and stiffness scores at any time point. No significant adverse effect was observed. These results were significantly different to the results achieved in the current study, which showed positive results for pain and stiffness. The most likely cause of the disparity was the fact that the Wang study irradiated just one acupuncture point (ST35), which would have had a limited effect on the Yang-deficiency pattern rather than aiming for the wholistic approach of the TCM paradigm that treats the underlying causes and symptoms of disease.

The Wang study concluded that combined 10.6um-650nm laser treatment might be beneficial to Yang-deficient cold coagulation knee OA patients in improving function, but not to non-Yang-deficient patients.

Comment

This study did not strictly follow TCM treatment principles. Only a single acupuncture point, ST35, was irradiated instead of devising a treatment program utilitising a range of acupuncture points known to be suitable for the treatment of OAK (as was done in the current study). Furthermore, HILT and LILT may produce different treatment outcomes because the underlying physiological effects of HILT (Class 4 lasers) are different to that of LILT (Class 3B lasers). HILT works primarily on using the heating properties of CO_2 thermal lasers to treat Yang-deficient cold coagulation in OAK. The penetration depth of the HILT CO_2 wavelength is shallower than the LILT 650nm, which brings about changes in cellular substrates deep within tissue. Moreover, the thermal properties of HILT combined with the potential for cellular inhibitory effects due to higher energy intensities could contradict the way LILT works. It is therefore doubtful

that further application of TCM principles and the use of additional acupuncture points would have led to an improved outcome for the Wang et al. (2013) study due to the confounding variables resulting from the combined use of HILT and LILT.

Although the Wang study claimed to follow the TCM paradigm by differentiating the OAK disease pattern, it did not address the likely presenting symptoms and causes of OAK. Targeting the Yang-deficiency pattern with a single point (ST35) did not follow the essence of the TCM paradigm. As a result, the underlying cause and presenting symptoms were left untreated.

Furthermore, the use of a CO_2 laser was problematic because mixing a "hot" laser with a 650nm "cold" laser might produce additional confounding factors, which were not acknowledged in the Wang study. Another issue was the lack of clearly defined diagnostic criteria for patients suffering non-Yang deficiency.

Al Rashoud et al. (2013)

The Al Rashoud et al. (2013) study shared some of the unique features of this study's laser acupuncture RCT and claimed to be the first OAK investigation to irradiate more than one acupuncture point. The study evaluated the efficacy of low-intensity laser applied to five acupuncture points commonly used to treat the knee joint in combination with exercise and advice.

Some 49 patients were randomly assigned to two groups – active laser (N = 26) and sham laser (N = 23). A gallium aluminium arsenide 830nm laser with a 30mW output power was used to irradiate five acupuncture points for 40sec/point with 1.2J/point over nine treatments with follow-ups at six weeks and six months. The same laser was used for both groups, but the device was deactivated for the placebo group and only emitted a red light. Patients were assessed with VAS and the Saudi Knee Function Scale (SKFS) at baseline, the fifth treatment session, the last treatment session, six weeks post-intervention and six months post-intervention. SKFS has been developed for use in countries with a high Muslim population.

VAS scores showed a statistically significant improvement in the active laser group ($p < 0.001$) at all assessment periods. VAS showed a statistically significant improvement for the sham laser group at all assessment periods. The exception was at six months post-intervention ($p = 0.103$). SKFS scores also showed a significant improvement in the active laser group compared with the sham laser group at the last treatment session and at six months post-intervention using the Mann-Whitney U-test.

The study reported that short-term application of LILT to specific acupuncture points in association with exercise and advice was effective in reducing pain and improving quality of life in OAK patients. The study reportedly encountered many issues and limitations, citing a lack of standardised protocols for inclusion and exclusion criteria (perhaps a veiled reference to WALT), and the absence of standardised treatment programs relating to laser dosage, treatment times, type of laser and laser application.

Comment

Laser acupuncture mixed with exercise makes it difficult to assess a specific response from laser acupuncture. Although five acupuncture points were used, the study did not apply TCM diagnostic disease pattern differentiation and specific acupuncture points to address OAK (unlike the current study which targeted the underlying causes and symptoms). Hence, the Al Rashoud study did not follow the essence of the TCM paradigm. Also, the use of a red light as a placebo device would have likely caused physiological changes and potentially skewed the treatment outcome.

Although the Al Rashoud study did not rationalise the use of a laser dose lower than that recommended by WALT, it nevertheless produced a positive outcome. However, the positive finding is questionable because treatment was combined with exercise, which might have clouded the laser results. The study also did not elaborate on data relating to OAK symptoms or the SKFS sub-scales. Furthermore, the use of the SKFS as an outcome measure is not well recognised internationally.

Hinman et al. (2014)

This Australian Zelen-design study investigated the efficacy and cost-effectiveness of laser and needle acupuncture that medical practitioners administered to people with chronic knee pain. A total of 282 people aged more than 50 years with chronic knee pain were recruited in metropolitan Melbourne and regional Victoria. Participants originally consented to take part in an observational study, but were covertly randomised into one of four treatment groups. Later, one group continued as originally consented (i.e. control group) receiving no acupuncture treatment (N = 71). The remaining three groups were laser acupuncture treatment (N = 71), needle acupuncture treatment (N = 70) and sham laser acupuncture (N = 70). Interventions were provided by general practitioners using a combination of Western and TCM-style acupuncture treatments in 812 visits over 12 weeks. Laser dosage was 0.2J/point.

Participants and acupuncturists were blinded to laser acupuncture and sham laser acupuncture. Control participants remained unaware of the trial. Primary outcome measures were average knee pain (numeric rating scale, 0 no pain to 10 worst pain possible); minimal clinically important difference (MCID, 1.8 units), and physical function (WOMAC, 0 no difficulty to 68 extreme difficulty); MCID, 6 units) at 12 weeks. Secondary outcomes included other pain and function measures, quality of life, global change and one-year follow-up. Analyses were by intention-to-treat using multiple imputation for missing outcome data. At 12 weeks and one year, 26 (9%) and 50 (18%) participants were lost to follow-up respectively. Analyses showed neither needle nor laser acupuncture significantly improved pain compared with sham at 12 weeks.

Compared with control, needle and laser acupuncture resulted in modest improvements in pain at 12 weeks, but not at one year. Needle acupuncture resulted in modest improvement in function compared with control at 12 weeks, but was not maintained at one year. No differences were reported for most secondary outcomes. The study concluded that neither laser nor needle acupuncture conferred benefit over sham for pain or function in patients older than 50 years with moderate or severe chronic knee pain. The findings of the study, commissioned by the National Health and Medical Research Council, did not support acupuncture for chronic knee pain.

Comment

Hinman el al. (2014) did not rationalise the TCM philosophy and treatment principle for the use of acupuncture points and laser parameters. Furthermore, the dosage of 0.2J per point used was significantly below the range recommended by WALT. The energy level appeared to be too low for the treatment of OAK. Low dosages of laser acupuncture administered by eight medical practitioners who were allowed to irradiate any of more than 30 acupuncture points provided a non-standardised treatment regime that appeared to under-treat a known degenerative condition and would therefore would be unlikely to show any positive outcome at one-year follow-up. Blinding also was not well designed and the use of a red light as a placebo control was inappropriate. Collectively, these factors may have contributed to the negative result achieved in the study. There is also some question surrounding ethical aspects of this study if, as reported, subjects were covertly randomised.

Publication of the Hinman et al. (2014) findings (Journal of American Medical Association 2015) resulted in significant criticism of the study's research integrity and credibility, particularly relating to its design, execution and conclusions. Some critics claimed the Zelen design could have led to the high drop-out rate, a dilution of effectiveness in the acupuncture group and mistakes in the sample-size calculation (White & Cummings 2015). Moreover, the needle acupuncture protocol was not standardised and the under-dosing and frequency of treatments were said to be well below those established in the literature (Zhang, Yue & Lu 2015). Furthermore, the low laser dosage/parameters (10mW with 0.2J/points) might have lacked sufficient power to achieve a therapeutic benefit (Baxter & Tumilty 2015).

Hinman et al. (2014) did not rationalise the use of laser parameters and the choice of wavelength was not reported, ignoring crucial RCT details recommended by CONSORT, STRICTA and WALT. Hence, the study did not comply with established scientific and evidence-based guidelines and requirements for a robust and reliable study. Furthermore, the lack of details about a scientific rationale, treatment principle and

optimum parameters suggested that Hinman did not have a thorough understanding of laser science and its integration with laser acupuncture for the treatment of OAK.

Low-intensity Laser Therapy Studies for OAK

Alfredo et al. (2011)

Alfredo et al. (2011) used low-intensity laser therapy and exercises to treat pain and improve range of motion, muscular strength and quality of life in 40 participants suffering OAK. The American College of Rheumatology and Kellgren-Lawrence OA grading scale assessed participants, who were randomised into two groups – active laser and sham laser.

The active group in this double-blind study received a laser dose of 3J/point (based on WALT recommendations) and exercise while the placebo group was given a sham dose plus exercise. Pain was assessed using VAS, functionality with the Lequesne questionnaire, range of motion with a universal goniometer, muscular strength using a dynamometer, and activity using WOMAC at three time points: (T1) baseline, (T2) at the end of laser therapy (three weeks) and (T3) at the end of the exercises (11 weeks).

When comparing groups, significant differences in activity were found ($p = 0.03$), but no other significant differences ($p > 0.05$) were observed in other variables. Within group analysis showed participants in the laser group had significant improvement, relative to baseline, on pain ($p = 0.001$); range of motion ($p = 0.01$); functionality ($p = 0.001$; and activity ($p < 0.001$). No significant improvement was reported in the placebo group. The findings suggested that low-intensity laser therapy associated with exercises was effective in providing pain relief, function and activity in patients with OAK.

Comment

Low-intensity laser therapy mixed with exercise makes it difficult to assess a specific response from any light-based modality. Unfortunately, the laser power density

recommended by WALT was not reported. Replicating this study would be difficult without full details.

Alghadir et al. (2014)

The Alghadir et al. (2014) study recruited 40 OAK participants aged 45 to 65 years. Twenty participants were randomised to active low-intensity laser therapy (LILT) and 20 to sham LILT. Heat packs wrapped in toweling were placed on target knees for 20 minutes followed by LILT. A GaAs 850nm 50mW laser with a beam diameter of 1mm and dosage of 6J was applied to eight points for six seconds twice a week over four weeks, giving a total dosage of 48J/cm^2 per treatment. Irradiated points included three on the medial side of the knee, three on the lateral side of the knee and two on the medial edge of the tendon of the biceps femoris muscle and semitendinosis muscle in the popliteal fossa.

Participants also were given a home-based exercise program consisting of isometric knee extension and straight leg lifting. All participants were told to maintain their activity level and continue taking 2g of paracetamol daily during the study. Outcome measures included pain intensity at rest and when moving, knee function using WOMAC and ambulation duration. Measurements were collected at baseline and post-intervention. Post-intervention timing was not stated. It is assumed that post-intervention occurred immediately after the last round of treatments and home-based exercises. No post-treatment follow-up appears to have been done.

Despite this, the results were reported as showing significant improvements in all assessment parameters in the active and placebo groups compared to baseline. The active laser group showed significant differences in pain intensity at rest and movement, knee function and ambulation duration when compared to the sham group. The study concluded that LILT appears to be effective for short-term pain relief and improving knee function affected by chronic OAK.

Comment

As convincing as these results appear, it is unclear how much the heat packs contributed to the positive outcome or whether the improvement in OAK was maintained over time. The sham device relied on a red light, which could have produced physiological effects (NASA 2005). For the inclusion criteria, only American College of Rheumatology guidelines was used. The Kellgren-Lawrence OAK diagnostic scale was not employed and neither were WALT parameters for the treatment of OAK. The number of treatments and their frequency were not clearly described. Conclusion: Mixing laser therapy with home exercises could have impacted on treatment outcomes.

Soleimanpour et al. (2014)

The Soleimanpour et al. (2014) study enrolled 33 participants in a descriptive, prospective study testing the effectiveness of two low-intensity laser therapy (LILT) wavelengths and power densities on OAK. Fifteen people were excluded due to incomplete treatment, leaving a total of 18 participants. A GaAlAs diode LILT device was used to power two laser probes. One probe had a wavelength of 810nm and an output of 50mW delivering a total dose of 6J/cm^2; the other 890nm and an output of 30mW delivering a total dose of 10J/cm^2.

No details were provided about how the 18 participants were randomised. Participants received a total of 12 treatments, delivered in pulsed mode at the rate of three times a week. No details were given about how interventions were provided to which group or which parts of the knee were irradiated. Significant reductions were reported in nocturnal pain, pain on walking and ascending steps, knee circumference, distance between the hip and heel, and knee to horizontal hip to heel distance on completion of treatments. The study did not clarify which wavelength and dosage achieved the best result. However, it did conclude that LILT was effective in reducing OAK pain.

Comment

Double-blinding was not used in this study and no placebo-control was put in place to compare against treatment outcomes. The Kellgren-Lawrence scale was not used for inclusion criteria and no WOMAC disease-specific measurement was employed to assess any improvement in OAK. Parameters were not well described. A descriptive, prospective study is not the same as a clinical trial.

Mixed Modality Study – High-intensity Laser & LILT & Exercise

Kheshie et al. (2014)

The Kheshie et al. (2014) study compared the effects of high-intensity laser therapy (HILT) and low-intensity laser therapy (LILT) on two groups suffering OAK. Participants in Group 1 received pulsed high-intensity laser therapy (HILT) with a Class 4 Nd:YAG laser. A degenerative joint disease (DJD) hand-piece was positioned in contact and perpendicular to the knee while the patient was supine with the knee flexed at 30 degrees to open the joint surfaces to the laser beam. Scanning was performed transversely and longitudinally in the anterior, medial and lateral aspects of the knee joint, with emphasis on the joint line between the tibial and femoral epicondyles.

Total energy delivered during one treatment session was 1,250J through three treatment phases. A total of 500J was applied with fast manual scanning in the initial phase when the laser fluency was set to two successive sub-phases of 710mJ/cm^2 and 810mJ/cm^2. In the intermediate phase, the hand-piece applied 25J on the joint line proximal to the medial and lateral tibial condyles at a fluence of 610mJ/cm^2 and a time of 14s for each point, providing a total dose of 250J. The final phase was the same as the initial phase except that slow manual scanning was used. Irradiation time for all three phases was reported to be about 15 minutes.

Total energy delivered to the participant during one session was 1,250J. The HILT device calculated the energy applied in each phase and the total energy delivered to

the participant during the treatment session. HILT was applied over a total of 12 weeks (two sessions per week for six weeks). Group 2 attended a physical therapy clinic twice a week for six weeks and received sham laser. For LILT treatments, a Class 3B gallium-arsenide diode (GaAs) infrared laser cluster probe with a wavelength of 830nm and an output power of 800mW was used.

Group 2 was treated twice a week over six weeks. Participants lay supine while the affected knee was slightly flexed and supported with a pillow. For all treatments, the cluster probe was directly applied and perpendicular to the affected knee. Each treatment session lasted 32 min. and 33 sec. and delivered a total energy of 1,250J. LILT was applied in a total of 12 treatment sessions over six consecutive weeks (two sessions per week).

Comment

This study provided a good baseline, with the Kellgren-Lawrence scale being used for inclusion criteria and VAS and WOMAC as outcome measures. Unfortunately, the single blinding method used was not scientifically robust. Hence, the placebo response was not standardised between the two groups. Furthermore, the inclusion of exercise as part of the treatment may have clouded the measurement of treatment outcomes.

Mixed Modality Study – LILT & MIPE

Ammar et al. (2014)

This study compared the effects of a relatively new light-based modality called monochromatic infrared photo energy (MIPE) and low-intensity laser therapy (LILT) in reducing pain and improving circulation and function in OAK. Sixty participants were randomly assigned to two groups. Group 1 (experimental, N=30) received MIPE and exercises. Group 2 (control, N=30) received LILT and exercises. Both groups received two treatments per week for six weeks (a total of 12 treatments).

Outcome measurements included pain intensity measured on VAS and physical function measured with the lower extremity functional scale before and after the 12 treatment sessions (i.e. 6 weeks after the start of intervention).

Statistically significant improvements in OAK pain intensity and lower extremity functional scale scores were recorded in the MIPE and LILT groups. However, no significant differences were reported between the groups.

Comment

No placebo, no double blinding and no long-term follow up occurred in this study. WOMAC was not used. Mixing treatment modalities with exercise may have clouded the trial results.

Mixed Modality Study – LILT & Neuromuscular Electrical Stimulation (NES)

Melo et al. (2016)

The Melo et al. (2016) study explored the effects of neuromuscular electrical stimulation (NES) and low-intensity laser therapy (LILT) on neuromuscular parameters and health status in elderly women with OAK.

A total of 45 participants were randomised into one of three intervention groups – electrical stimulation group (18–32 min. pulsed current, stimulation frequency 80 Hz, pulse duration 400 μs, stimulation intensity 40% of maximal isometric voluntary contraction); LILT group (dose 4–6J/point, 6 points at the knee joint); and combined group (electrical stimulation plus LILT).

Outcome measures included muscle thickness and anatomical cross-sectional area (ultrasonography), knee extensors' electrical activity (electromyography), torque (dynamometry) and health status (WOMAC). All groups underwent a four-week control period without intervention followed by an eight-week intervention period.

All three groups presented similar improvements in torque, electrical activity and health status. However, muscle thickness and anatomical cross-sectional area increased in the electrical stimulation and combined groups. The study concluded that electrical stimulation alone or in combination with LILT generated positive effects on all evaluated parameters. LILT increased health status and electrical activity, but had no effect on muscle mass.

Comment

The design of this study and the lack of information researchers provided makes it impossible to judge which modality or combination of modalities produced most benefit – electrical stimulation on its own or when combined with LILT. Single blinding and the lack of a placebo control did not demonstrate scientifically robust methodology. WOMAC was used, but no follow-up assessment was undertaken.

Summary

The review of these nine contemporary laser studies (see Table 35, below) demonstrated little change in laser OAK research since the initial literature review was conducted for this RCT in 2008-2010. Few of the reviewed studies were well designed; others lacked scientific vigour; some did not follow guidelines recommended by CONSORT/STRICTA or WALT and some did not strictly follow the TCM paradigm. In short, none of the reviewed studies followed the essence of the TCM paradigm, which treats the underlying causes and symptoms of disease with specific acupuncture point formulae for the presenting disease pattern. Some studies combined laser with other modalities (e.g. heat packs and exercise), or used single-blinding or dubious placebo devices. Other flaws included a lack of clear diagnostic inclusion criteria, inappropriate laser parameters, the absence of credible OAK outcome measures (i.e. WOMAC) or not clearly describing treatment programs and follow-up assessment periods.

Only five of the nine studies used randomisation (Alfredo et al. 2011, Alghadir et al. 2014, Al Rashoud et al. 2014, Kheshie et al. 2014) and (Melo et al. 2016).

In terms of placebo arrangements, only Alfredo et al. (2011) had a valid placebo. Two other studies (Al Rashoud et al. 2014 and Hinman et al. 2014) used an inappropriate red light as a placebo and Alghadir et al. (2014) did not describe the placebo method.

Only two studies (Alfredo et al. 2011, Al Rashoud et al. 2014) listed laser power densities, crucial for replication, while Al Rashoud et al. (2014) and Hinman et al. (2014) used laser doses well below WALT recommendations and generally accepted practice.

Of the nine studies, only six (Alfredo et al. 2011, Wang et al. 2013, Alghadir et al. 2014, Hinman et al. 2014, Kheshie et al. 2014, Melo et al. 2016) used the internationally recognised OAK-specific WOMAC to track treatment outcomes.

While three studies (Wang et al. 2013, Al Rashoud et al. 2014, Hinman et al. 2014) made passing references to the TCM treatment of OAK, none applied the strict disease pattern diagnosis and treatment principles typically used in TCM-based acupuncture.

Four studies that used mixed modalities to treat OAK were problematic because none provided a clear distinction between the effects of active laser and sham laser. The inclusion of other treatments in those studies (i.e. hot and cold laser, cold laser and exercise, cold laser and heat packs, and cold laser and electrical stimulation) had the potential to add confounding factors that might impact on the recognised healing effects of Class 3B lasers.

Findings

Five out of the nine contemporary studies produced positive results in varying degrees. For example, Wang et al. (2013) did not gain a positive outcome for OAK pain and stiffness. The positive findings reported by Al Rashoud et al. (2014) were questionable because they used the outcome measure, SKFS, which is not widely used and validated for clinical use. Alfredo et al. (2011) and Kheshie et al. (2014) did not design a pure placebo group for comparison because their placebo groups mixed sham treatments with exercise. The descriptive prospective study designed by Soleimanpour et al.

(2014) had no double blinding, no randomisation and no placebo arrangement. As a result, all of the reported positive findings appear to be questionable.

Conclusion

This review of the strengths, weaknesses and flaws found in previous research, coupled with expert knowledge of laser science and the TCM framework, confirmed the need for a well-designed, reliable, robust and replicable clinical trial.

Table 35– Overview of Contemporary Laser Acupuncture & Low-Intensity Laser Therapy OAK Studies Conducted Between 2011 & Mid-2016

LASER ACUPUNCTURE FOR OAK												
Study/Year	***Design***	***Placebo***	***Laser/ Wavelength***	***Power Density***	***Output Power***	***Fluence/ Joules/Point***	***Total Joules /Session***	***Acupuncture points***	***Treatment Program***	***Outcome Measures***	***Follow - up Period***	***Result***
(Wang et al. 2013)	N=52 Not randomised Allocated to 2 groups: Yang Deficient Cold: N=26 Non-Yang Deficient: N=26 No placebo Operator & assessor blinded	Combined red 650nm & thermal CO_2	650nm & 10.6μm	Not reported	36mW non-thermal red 200mW thermal CO_2	43.2J/session 120J/session	604.8.2J 1680J	ST35	20-minutes 3 x wk 1st 2 wks 2 x wk next 4 wks Total = 14 x over 6 wks	WOMAC	Wk 0 Wk 2 Wk 6 Wk 10	Only positive in function at Wk 2 & Wk 6 Not significant in pain scale
Comments	TCM differentiation incomplete. ST35 acuipuncture point provided only symptomatic relief. Cause of imbalance not addressed. Not randomised No placebo Not robust	Not strictly low intensity laser	650nm penetration depth – shallow CO_2 heat penetration depth more superficial than moxa heat	Unable to assess Not reported Not replicable	Thermal CO_2 – not low intensity laser No proper scientific explanation for combining hot & cold laser			Cause of OAK not treated Only treated cold symptoms Did not treat Liver or Kidney, origin of imbalance		Only 1 outcome measure No validation with 2nd instrument	Short-term follow up	No proper comparison 2nd group's condition not specified Yang deficiency not major OAK symptom

Study/Year	*Design*	*Placebo*	*Laser/ Wavelength*	*Power Density*	*Output Power*	*Fluence/ Joules/Point*	*Total Joules /Session*	*Acupuncture points*	*Treatment Program*	*Outcome Measures*	*Follow - up Period*	*Result*
(Al Rashoud et al. 2014)	Double-blind RCT N=49 Active=26 Sham=23	Red light on sham probe	Endolaser (GaAlAs) 830nm Spot size 0.28mm/ cm^2	4J/cm^2	30mW	1.2J/pt/40sec	6J/ session	5 acupuncture points: SP9 SP10 ST35 ST36 Xi Yan medial	9 treatments	VAS positive p=0.003 SKFS positive p=0.006	6wks 6mths	Positive
Comments	LILT + exercise	Red light on sham probe not credible placebo				Joules < than WALT recommends		No TCM rationale and disease pattern differentiation Treatments provided by physio		SKFS – not widely recognised & validated Lacks credibility No data provided to validate SKFS subscales Question-able findings		Positive (unclear part played by exercise & laser on their own) Not pure laser clinical trial TCM paradigm not followed to address disease pattern differentiation & underlying cause

Study/Year	*Design*	*Placebo*	*Laser/ Wavelength*	*Power Density*	*Output Power*	*Fluence/ Joules/Point*	*Total Joules /Session*	*Acupuncture points*	*Treatment Program*	*Outcome Measures*	*Follow - up Period*	*Result*
(Hinman et al. 2014)	Randomised Zelen-design study N=282 Inclusion criteria: Aged 50 or >, knee pain > 3mths, knee pain most days, average NRS severity 4 or > out of 10, morning stiffness < 10 min.	Acupak (purpose built)	Not reported	Not reported	10mW	0.2J/point	Not reported	Medical acupuncturists left to use any of more than 30 listed points	20-minute treatment delivered one or twice a week for 12 weeks Limited to a total of 8-12 sessions Combination of Western & Chinese medicine style of acupuncture	NRS for pain WOMAC function & pain Pain on walking & standing Activity restriction AQoL-60 SF-12 PCS SF-12 MCS	12 wks 1 year	Negative
Comments	Study drew worldwide criticism Did not comply with CONSORT & STRICTA, but claimed to be compliant	Not reported	Not reported	Not reported	Output power too low	Fluence too low	Not reported	Treatment regime not standardised	Duration and frequency of treatment not standardised		1 year f-up inappropriate for chronic degenerative OAK	Study accused of inaccurate, misleading & biased research.

LOW-INTENSITY LASER THERAPY FOR OAK												
Study/Year	**Design**	**Placebo**	**Laser/ Wavelength**	**Power Density**	**Output Power**	**Fluence/ Joules/ Point**	**Total Joules/ Session**	**Treatment Area/ Acupuncture points**	**Treatment Program**	**Outcome Measures**	**Follow - up Period**	**Result**
(Alfredo et al. 2011)	Double-blind Placebo-controlled RCT N=40 Inclusion criteria based on ACR guidelines	Inactive probe	904nm Irradia	Not reported	60mW	3J/cm^2 + exercise	27J/ session	5 points in synovial region on medial side of knee & 4 points on lateral side	Laser 3 x per week for 3 weeks + exercise 3 x per week for 8 weeks	VAS Lequesne Question-naire WOMAC universal goniometer & degree of knee flexion	6 wks 6 mths	Positive for short-term benefit
Comments				WALT recom-mendations not followed				WALT recom-mendations followed	Total number of treatments not specified			
(Alghadir et al. 2014)	Single-blinded RCT N=40 Active laser group: N=20 (heat packs + active laser + home-based exercise) Sham laser group: N=20 (hot towels + sham laser + home-based exercise)	Inactive probe	850nm Intellect laser	Not reported	100mW	6J/point/ 60sec	48J/cm^2	8 points: 3 on medial side of knee; 3 on lateral side & 2 on medial edge of biceps femoris muscle tendon & semi-tendinosis muscle in popliteal fossa	Laser 2 X per week over 4wks	VAS for pain WOMAC for pain, stiffness & physical function	Wk 4	Short-term pain relief & improved knee function
Comments	Single blind study – not robust	Sham laser method not described		WALT recom-mendations not followed		WALT recom-mendations not followed						Result inconclusive

LOW-INTENSITY LASER THERAPY FOR OAK												
Study/Year	**Design**	**Placebo**	**Laser/ Wavelength**	**Power Density**	**Output Power**	**Fluence/ Joules/ Point**	**Total Joules/ Session**	**Treatment Area/ Acupuncture points**	**Treatment Program**	**Outcome Measures**	**Follow - up Period**	**Result**
(Amar et al 2014)	Not randomised N=60 2 groups a) MIPE + exercises b) LILT+ exercises	No placebo	MIPE = 890nm 60 super luminous diodes 10mW per diode 10mW/cm^2 1.6J/cm^2 per min. Reported dosage unclear			30 min. MIPE 20 min. exercise + no dosage		5 painful points on both sides of knee (medial & lateral epicondyle of tibia & femur; medial lateral knee joint gap; medial edge of the tendon of biceps femoris muscle & semi-tendinosis muscle in popliteal fossa)	2 X week for 6 weeks (12 sessions)	VAS Lower Extremity Function Scale	Before & after 12th session (6 wks)	P < 0.05 for 2 scales – both groups No significant differences between groups
			100mW 850nm Beam diameter 1mm Continuous wave			5J/pt for 2 minutes (total 10 minutes) 5 points irradiated						
Comments	No double blinding Not robust	No placebo Not robust								No extra pain valid-ation scale		

LOW-INTENSITY LASER THERAPY FOR OAK												
Study/Year	**Design**	**Placebo**	**Laser/ Wavelength**	**Power Density**	**Output Power**	**Fluence/ Joules/ Point**	**Total Joules/ Session**	**Treatment Area/ Acupuncture points**	**Treatment Program**	**Outcome Measures**	**Follow - up Period**	**Result**
(Kheshie, Alayat & Ali 2014)	RCT N=53 3 groups a) HILT+ exercise b) LILT + exercise c) Placebo + exercise	Placebo + exercise	a) HILT-1064nm Nd:YAG b) LILT IR 830nm 800mW energy Freq. 1kHz Duty cycle 80%	a) HILT-peak power 3000W pulsed emission b) LILT density 50J/cm2	a) HILT not stated b) LILT 800mW	a) HILT not stated b) LILT not stated	a) HILT - 1,250J (3 phases) b) LILT-total energy of 1,250J/ session 32min & 32 sec per session	Joint line proximal to medial & lateral tibial condyles	12 sessions (2 sessions per week for 6 weeks)	VAS WOMAC	Before & after treat-ment (Week 6)	HILT more effective than LILT HILT & LILT more effective than placebo group
Comments	3 groups mixed with exercise No pure placebo group (exercise may cloud laser result			Scanning may not give precise energy delivery	800mW not generally regarded as LILT (500mw limit for Class 3B laser)	Scanning delivered irradiation						Range of parameters makes replication difficult

LOW-INTENSITY LASER THERAPY FOR OAK												
Study/Year	**Design**	**Placebo**	**Laser/ Wavelength**	**Power Density**	**Output Power**	**Fluence/ Joules/ Point**	**Total Joules/ Session**	**Treatment Area/ Acupuncture points**	**Treatment Program**	**Outcome Measures**	**Followup Period**	**Result**
(Soleimanpour et al. 2014)	Prospective study N=18	No placebo	a) 810nm b) 890nm	a) 0.05W/ cm^2 b) 0.017W/ cm^2	a) 50mW b) 30mW	a) 6J/cm^2 b) 10J/cm^2	46J/cm^2 per session	a) 6 areas (supra, mid and infra-patella) b) Posterior patellar area	Total 12 sessions 3 x week	VAS Knee circum-ference		Positive
Comment	Not randomised No double blinding No placebo No WOMAC No followup No sample size calculation reported											

LOW-INTENSITY LASER THERAPY FOR OAK												
Study/Year	**Design**	**Placebo**	**Laser/ Wavelength**	**Power Density**	**Output Power**	**Fluence/ Joules/ Point**	**Total Joules/ Session**	**Treatment Area/ Acupuncture points**	**Treatment Program**	**Outcome Measures**	**Followup Period**	**Result**
(Melo et al. 2016)	RCT N=45 3 groups: a) LILT = 15 b) NMES (electrical stimulation group = 15 c) LILT+NMES = 15	No placebo	a) 810nm	0.218J/cm^2	200mW	a) 30 sec/pt 6j/pt (1st 4 wks) b) 20 sec/pt 4J/pt (2nd 4 wks)	a) Total 36j/ session (1st 4 weeks) b) 24J/ session (2nd 4 weeks)	3 anteromedial and 3 antero-lateral points over inter-condylar notch	Before & after treatment at week	WOMAC Muscle strength Muscle morph-ology Muscle electrical activity		a) LILT- b) NMES c) LILT+ NMES No significant differences between groups Individual groups were positive before & after treatment
Comment	Mixed modality might cloud laser result											

Chapter 4: Method

The literature review described in the previous chapter provided valuable insights into issues associated with conducting an evidence-based RCT. Those insights, coupled with the researchers' extensive knowledge of, and experience with, laser science and TCM-based acupuncture contributed to the development of a robust methodology for this exploration of the effectiveness of TCM-based laser acupuncture on OAK.

The design elements described in this section reflect best research practice. This process began with ethics committee approval and went on to establish key elements of the trial design, such as meeting CONSORT/STRICTA clinical trial reporting requirements and WALT wavelength and dosage recommendations.

Moreover, the study design broke new ground by tracking the effects of laser acupuncture delivered in ways that remained true to TCM diagnostic and OAK treatment principles and measured factors related to the placebo effect. These and other design elements are detailed in the following section.

4.1 How Research Insights Were Applied to This Study

Information gleaned from the literature review helped improve the design of the current study. As a result, particular attention was given to: (1) Calculating a sample size based on key factors identified by Kadam (2010); (2) Using computer-generated numbers to randomise participants to active and sham treatments; (3) Double-blinding the practitioner and participants to eliminate potential bias; (4) Using a credible placebo device to avoid producing physiological effects on the condition being treated, i.e. OAK; (5) Following CONSORT/STRICTA recommendations for reporting acupuncture clinical trials to inform design elements; (6) Using appropriate laser parameters based on WALT recommendations in terms of wavelength and treatment times, and clinical knowledge of laser science, laser wavelengths, output power, power density,

fluence/dosage and treatment programs; (7) Strictly following the TCM paradigm for diagnosing and differentiating disease patterns with specific acupuncture point formulae; (8) Reflecting best practice in terms of Western medical diagnosis by using the Kellgren-Lawrence OAK grade 2-3 scale to establish strict inclusion criteria; (9) Irradiating standardised acupuncture points that were rationalised to address specific TCM disease patterns integrated with the Western diagnostic model; and (10) Assessing factors associated with placebo effects that might influence active and sham treatment outcomes. The objective was to create a study design that allows replication by future researchers seeking to explore differences that appear to exist between laser acupuncture, low-intensity laser therapy and needle acupuncture.

4.2 Ethics Approval & Study Guidelines

The UTS Human Research Ethics Committee approved the trial on 9 December 2010 (Ref. No. UTS HREC 2010-340). The RCT was subsequently registered with the Australian-New Zealand Clinical Trial Registry (Reg. No. ACTRN12613000499785) under the title, *Evaluation of the Effectiveness of Laser Acupuncture on Osteoarthritic Knee Pain: A Randomised, Double Blind, Placebo-controlled Clinical Trial*.

To comply with evidence-based requirements, this study adapted CONSORT's *Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA)* and followed World Association for Laser Therapy dose recommendations for laser treatment of OAK and the conduct of clinical trials.

4.3 Trial Design

This study was a two-armed, parallel, randomised, double-blind, placebo-controlled trial involving 40 participants, with 20 in each of two groups – active laser and sham laser. The sample size was originally estimated from the size of test groups used in

previous acupuncture trials conducted at UTS and a review of the literature. With an estimated effect size of 0.75, a standard deviation of 1, alpha of 0.05 for a two-tailed t-test, it was found 30 subjects per group resulted in a power of 0.81 (81%). Initially, it was determined that 60 participants would provide sufficient statistical power to validate trial results. Owing to recruitment difficulties, 40 participants were enrolled.

Two primary outcome measures – OA-specific WOMAC and pain-specific VAS – and four secondary outcome measures – SF-MPQ, C/E Questionnaire, WAI (C) and MHLC-C – were used over four time points at four-week intervals to assess a range of factors relating to pain, stiffness, physical function and the placebo effect associated with the practitioner-participant relationship and the power of other influences. The statistical software package, SPSS Version 23, was used to analyse results on an intention-to-treat basis.

4.4 Recruitment of Participants

Sixty-three participants were recruited over a 12-month period in 2011-2012 with the aid of media releases, radio interviews, the World Wide Web, print advertising, flyers, letters, pamphlet distribution and word of mouth. Although a sample size of 60 was originally proposed, several factors hampered recruitment. Most prospective participants had co-morbidities, such as diabetes and severe OA in other joints. Others were unable to meet the inclusion criteria or had undergone knee surgery. Because of these constraints, 40 participants (20 females and 20 males with a mean age of 62 years) were subsequently accepted (see flow chart at Figure 2).

Initially, participants were required to confirm verbally their willingness to enroll in the RCT on the basis of informed consent. A researcher then requested each participant's medical practitioner to confirm the participant met the RCT inclusion criteria. Each participant signed a consent form and completed a medical history form that identified medical conditions, contraindications and allowed for the determination of the TCM disease pattern. Participants also agreed to complete outcome measure

questionnaires as required. Each participant was provided with written information that explained the treatment rationale, treatment procedures and anticipated treatment reactions. Participants retained the right to withdraw from the study at any time.

4.5 Inclusion /Exclusion Criteria

The 40 participants enrolled in the RCT were required to meet the following inclusion criteria: be aged 40 years or more; score grade 2-3 on the Kellgren-Lawrence OA scale (knee pain and radiographic osteophytes, morning stiffness of less than 30 minutes duration, crepitus on motion); have no other serious health condition; suffer OA less than 10 years; no history of receiving laser acupuncture for OAK; speak English and be literate enough to understand and sign a treatment consent form and complete outcome measuring instruments. The taking of OA medication was noted, but not restricted.

Volunteers were excluded if laser treatments were contraindicated or they had a pacemaker or were suffering other medical conditions, such as multiple sclerosis, diabetes, asthma, dementia or kidney disease, thyroid condition, cancer or epilepsy. Other contraindications were irradiating over the thyroid, known malignant lesions, pregnancy, tattoos, the taking of photo-sensitive medication and very dark skin or hair; impaired mobility that would make participation difficult; inability to speak English or illiteracy; or a cognitive disability that might prevent understanding of study protocols and procedures.

4.6 Randomisation & Double Blinding

To randomise participants into active or sham laser groups (see Table 36, below), a co-researcher used a computer to generate 60 randomised strips of paper bearing either the number 1 or 2 and the identification number of the participant to which the

numbered probe had been assigned. These paper strips were placed in separate envelopes and sealed. The envelopes were handed in ascending numerical order to the laser operator, who opened each envelope at the initial treatment session and followed the instructions inside. The allocated probe was used on the same participant at each subsequent treatment. Double blinding was achieved in two ways because both the laser operator and participants were unaware who had been randomised to the active laser or sham laser groups. Additionally, the use of an invisible infra-red Class3B 810nm wavelength laser provided a second form of blinding. This type of laser produces neither heat nor sensation when applied to the skin. Consequently, neither the laser operator nor the participant knew whether the probe being used at any given time was active or inactive.

Table 36 – Randomisation of OAK Trial Participants to Active & Sham Laser Groups

Cohort	**Phlegm Retention in Knee Joint Group**	**Blood Stasis in Knee Joint Group**	**Total**
Active Laser Treatment Group	10	10	20
Sham Laser Treatment Group	7	13	20
Totals	**17**	**23**	**40**

4.7 Selection of Laser Parameters

Fluence or dosage is not the only factor to be considered when selecting laser parameters for the treatment of a particular medical condition. Thought needs to be given to the anatomical region being treated to correlate with the penetration depth of the wavelength being used. Other factors are a power density high enough to produce an intensity that can be absorbed by the targeted tissue and cellular substrates to achieve biomodulation; an output power sufficient to produce energy that maximises the treatment effect in the shortest time possible; and a fluence that optimises treatment effects. Many other factors may impact on treatment outcomes. Among them are the optical properties of tissue and cellular substrates (i.e. absorbability of the coloured chromophore), spot size of the laser beam, mode of

applying the laser beam (i.e. skin contact or non-skin contact), pulse frequency, treatment duration, treatment principles and techniques, and the treatment program.

To make laser studies more robust, reliable and replicable for further validation, it is evident that researchers need to understand the inter-relationship of each element within laser parameters, i.e. wavelength, power density, output power, fluence/dosage, treatment sites and treatment program. Other factors affecting laser clinical trials include the design, methodology and placebo controls. None of the 27 reviewed studies rationalised the laser parameters and nor did they understand the essence of applying laser protocols.

4.8 Interventions

An 810nm Metron Advanced Laser (GaAs) unit, model number AL 170, listed on the Australian Register of Therapeutic Goods (ARTG), was used for this RCT. The laser had two probes – one active; the other deactivated by the supplier. The active probe had an output power 100mW (+/-10mW), a pulse width of 100μS nominal, a beam diameter of 2.8mm and a power density of 1.1W/cm^2. The laser was calibrated and checked before the start of the RCT.

Because the 810nm delivers an invisible infra-red beam of light that produces no heat and sensation when applied to skin, this wavelength provided the best choice for a credible placebo arrangement. Consequently, both the laser operator and participants in the active or sham laser groups were unable to identify who was receiving treatment or not.

To eliminate potential treatment bias, blue LEDs on the two probes were covered first with Blu-Tac and then black insulation tape (see Appendix 8) so that the LEDs could not produce physiological changes when the active and sham laser probes were applied to targeted acupuncture points.

4.8.1 TCM Disease Pattern Differentiation for OAK

To ensure consistency and standardisation, one laser operator, a registered TCM practitioner, applied the TCM disease pattern differentiation diagnostic method using a TCM diagnostic history sheet (see Appendix 9) and categorised participants into the two major OAK disease patterns (i.e. Phlegm Retention or Blood Stasis) shown in the signs and symptoms check-list at Appendix 10. The acupuncture point formulae were applied to each participant's identified disease pattern (see Table 37, 38 & 39 below).

The points comprised 11 standardised points for the treatment of OAK and two extra points to address each of two specific disease patterns associated with OAK. The 11 standardised points were ST34, ST35, ST36, Xiyan, SP6, SP9, SP10, GB34, He Ding, BL40 and LIV7. The two extra points that targeted specific disease patterns were KD3 and ST43 for Phlegm Retention and to resolve Dampness and Fluid Retention, and GB31 and GB41 for Blood Stasis and to promote Blood circulation and relieve pain and stiffness.

4.9 Selection of Acupuncture Points

Each of the two sets of 13 acupuncture points was selected through a manualisation process to achieve standardisation for the RCT. The 13 points included the 11 acupuncture points (see Table 37) the literature review identified as being the most commonly used for OAK. For each syndrome, two extra points based on disease pattern differentiation were added to the 11 acupuncture points by an expert panel (see Table 38 and 39, below).

Table 37 – Acupuncture Points Most Commonly Used for OAK

Acupuncture Point	Location[1]	Effects[2]	Mentions in Literature Search
1. ST36 – Zusanli	On anterior aspect of the leg, on the line connecting ST35 with ST41, 3B-cun inferior to ST35. NB: ST36 is located on the tibialis anterior muscle	• Benefits Stomach and Spleen • Tonifies Qi and Blood • Dispels Cold • Strengthens body • Brightens eyes	11

		• Regulates Nutritive and Defensive Qi • Regulates Intestines • Raises Yang • Expels Wind and Damp • Resolves oedema	
2. ST35 – Dubi	On anterior aspect of knee, in the depression lateral to the patella ligament. NB: When knee is flexed, ST35 is located in depression lateral and inferior to patella ligaments. The lateral Xiyan is identical to ST35 Dubi.	• Expels Wind-Damp • Benefits knees	9
3. Xiyan – (Knee Eyes)	Knee eye acupuncture points are located in depressions medial and lateral to patella ligaments.	• Expels Wind-Damp • Benefits knees	9
4. SP9 – Yinlingquan	On tibial aspect of leg, in depression between inferior border of medial condyle of tibia and medial border of tibia. NB: A depression can be felt inferior to knee joint when moving proximally along medial border of tibia. SP9 is located in a depression at an angle formed by inferior border of medial condyle of tibia and posterior border of tibia.	• Resolves Dampness • Benefits urination • Removes obstructions from channel	9
5. GB34 – Yanglingquan	On the fibular aspect of the leg, in the depression anterior and distal to the head of the fibula	• Promotes smooth flow of Liver Qi • Resolves Damp-Heat • Removes obstruction from channel • Relaxes sinews • Subdues rebellious Qi	8
6. He Ding	Located above patella	• Activates vessels and alleviates knee joint pain • Relieves restricted. movement of lower extremity	6
7. BL40 – Weizhong	On posterior aspect of knee, at mid-point of popliteal crease	• Clears Heat • Resolves Dampness • Relaxes sinews • Removes obstruction from channel • Cools blood • Eliminates Blood stasis • Clears Summer Heat	4
8. SP6 – Sanyinjiao	On tibial aspect of the leg, posterior to medial border of tibia, 3B-cun superior to prominence of medial malleolus. NB: 1 B-cun superior to KD8	• Strengthens the Spleen, resolves and expels Dampness • Restores balance to the Yin and Blood, Liver and Kidneys • Improves movement in the lower extremity	4
9. ST34 – Liangqiu	On anterolateral aspect of thigh, between vastus lateralis muscle and lateral border of rectus femoris tendon, 2B-cun superior to base of patella	• Subdues rebellious Stomach Qi • Removes obstruction from channel • Expels Dampness and Wind	4
10. SP10 – Xuehai	On anteromedial aspect of thigh, on the bulge of the vastus medialis muscle, 2B-cun superior to medial end of base of patella	• Invigorates Blood • Expels Dampness	3
11. LIV7 – Xiguan*	On tibial aspect of leg, inferior to medial condyle of tibia, 1B-cun posterior to SP9.	• Local point for Painful Obstruction Syndrome of the knee, particularly from Wind and when pain is on inner aspect of knee	*

[1] World Health Organisation (2008); [2] Maciocia (1989, 1990); * Recommended by expert panel

4.10 Selection of Syndrome-specific Acupuncture points

To provide specific laser acupuncture treatments for targeted disease patterns, as is done in TCM acupuncture, two different sets of acupuncture points were added to the treatment regimens established for participants with Phlegm Retention and Blood Stasis (see Tables 38 and 39, below).

Table 38 – Extra Acupuncture Points Selected to Target Phlegm Retention, Dampness & Fluid Retention

Acupuncture Point	Location[1]	Effects[2]
KD3 – Taixi	On posteromedial aspect of ankle in depression between prominence of medial malleolus and calcaneal tendon	• Tonifies kidneys in any deficiency pattern of Kidney-Yin or Kidney-Yang • As Source point, in contact with Original Qi of body and seat of Original Qi • Goes straight to core of Original Qi • Because kidneys also store Essence, KD3 can tonify Essence, bones and Marrow
ST43 – Xiangu	On dorsum of foot, between second and third metatarsal bones, in depression proximal to second metatarsophalangeal joint	• Eliminates Wind and Heat • Removes obstruction from channel

[1] WHO Standard Acupuncture Point Locations in the Western Pacific Region (2008); [2] (Maciocia 1990).

Table 39 – Extra Acupuncture Points Selected to Target Blood Stasis, Promote Blood Circulation & Relieve Pain & Stiffness

Acupuncture point	Location[1]	Effects[2]
GB31 – Fengshi	On lateral aspect of thigh, in depression posterior to iliotibial band where tip of middle finger rests, when standing up with arms hanging alongside thigh.	• Expels Wind • Relaxes sinews • Strengthens bones • Relieves itching
GB41 – Zulingqi	On dorsum of foot, distal to function of bases of 4th and 5th metatarsal bones, in depression lateral to 5th extensor digitorum longus tendon	• Resolves Damp-Heat • Promotes smooth flow of Liver-Qi • Regulates Girdle Vessel • Influences Painful Obstruction Syndrome – particularly of knee and hip

[1] WHO Standard Acupuncture Point Locations in the Western Pacific Region (2008);.

[2] Maciocia, G, 1989. *Foundations of Chinese Medicine (Churchill Livingstone)* (Maciocia 1990).

4.11 Treatment Protocol

Although laser dosage recommendations have been provided by WALT since 2010, few studies appeared to follow them. For wavelengths of 780 to 860nm, WALT recommends a mean output of 5mW-500mW along with irradiation times of 20-300 seconds on 3-6 points and a dose of 12J delivered on 3-6 points at a minimum of 4J/point.

In the treatment of medial knee arthritis with a 780-860nm GalAlAs laser, WALT further suggests reducing dosage by 30% when inflammation is under control. Therapeutic dose windows typically range from +/- 50% of given values. This indicates that maximum dosage for knee arthritis pain should not exceed 18J, if the 12J is indeed the given value for the therapeutic dose window. WALT's recommended doses are for white/Caucasian skin types and are reportedly based on clinical trial results or extrapolation of study results with similar pathology and ultrasonographic tissue measurements.

For this RCT, a Class 3B GaAs 810nm laser supplied with two 100mW probes (one active and one deactivated by the manufacturer) was used to irradiate 13 standardised acupuncture points in the prescribed order shown in Table 40 (see below). Irradiating acupuncture points in a defined order reflects TCM-based acupuncture practice.

Treatment was administered three times a week over four weeks, i.e. a total of 12 treatments. Laser dosage was 18J for two minutes per point targeting either Blood Stasis or Phlegm Retention. The duration of each treatment was 26 minutes. This provided a laser acupuncture dose of 234J per treatment session and a total dose of 2,808J for all 12 treatments (see Table 41, below).

Table 40 – Order in Which Points Were Irradiated for Treating OAK Pain & TCM Disease Patterns

For Blood Stasis	For Phlegm Retention
1 SP6 – Sanyinjiao	1. SP6 – Sanyinjiao
2. SP9 – Yinlingquan	2. SP9 – Yinlingquan
3. ST36 – Zusanli	3. ST36 – Zusanli
4. GB34 – Yanglingquan	4. GB34 – Yanglingquan
5. LIV7 – Xiguan	5. LIV7 – Xiguan
6. SP10 – Xuehai	6. SP10 – Xuehai
7. ST34 – Liangqiu	7. ST34 – Liangqiu
8. He ding	8. He ding
9 . Xi Yan	9. Xi Yan
10. ST35 – Dubi	10. ST35 – Dubi
11. GB31 – Fengshi	11. KD3 – Taixi
12. GB41 – Zulingqi	12. ST43 – Xiangu
13. BL40 – Weizhong	13. BL40 – Weizhong

Note: Total time for irradiating the presenting disease pattern on one knee affected by OA at each treatment session was 26 minutes.

Table 41 **– Parameters Laser Acupuncture RCT Used for OAK**

Laser Type	**Output Power**	**CW**	**Spot size**	**Dose**	**Power Density**	**Application Mode**	**Treatment Area**	**Treatment Time**	**No. of Treatment Sessions**	**Assessment Intervals**
Metron Advanced Laser GaAs 810nm IR (TGA listed)	100 mW	✔	Approx. 3.08mm (elliptical beam)	18J per point Total energy per treatment session 234J or 2,808J over 12 weeks	*1.1W/ cm^2	Direct skin contact	13 points based on presenting syndrome	2 min per point Total time 26 min per session	3 x week for 4 weeks Total treatments = 12	Baseline (Time Point 1) At Week 4 (Time Point 2) Follow-up at Week 8 (Time Point 3) Follow/up at Week 12 (Time Point 4)

4.12 Treatment Setting

For each laser acupuncture treatment, participants were supine on a treatment couch. To comply with laser eye safety requirements, participants wore blind goggles and the laser operator wavelength-specific safety goggles during each treatment. It should be noted that Australian and New Zealand laser safety standards stipulate that laser operators should be required to complete a recognised laser safety course before administering any light-based treatment. Particular attention should be given to the need for the laser operator, participants and support staff to wear appropriate eye protection during any laser treatment and to follow laser safety protocols at all times. Participants were advised to inform the practitioner if they felt any discomfort during the treatment. No adverse events occurred.

Participants completed six outcome measures – at the initial treatment to establish a baseline and again at Week 4 (Time Point 2), Week 8 (Time Point 3) and Week 12 (Time Point 4).

Treatments were provided at two private clinics by one qualified acupuncturist and TCM practitioner registered with the Australian Health Practitioner Regulation Agency (AHPRA). The practitioner holds a Bachelor of Applied Science (Acupuncture) and a Master Degree of Traditional Chinese Medicine. The practitioner/operator also holds a laser safety qualification and has extensive experience in using Class 3B and Class 4 lasers for therapeutic and cosmetic treatments.

4.13 Treatment Outcome Measures

As mentioned earlier, six instruments were used to measure treatment outcomes. The two primary measures were WOMAC (short for Western Ontario and McMasters Universities' Index) and a Visual Analogue Scale (VAS). The four secondary measures were McGill Pain Questionnaire (SF-MPQ), Credibility/Expectancy Questionnaire (C/E),

Working Alliance Inventory – Short Form (WAI-C) and Multi-dimensional Health Locus of Control – C (MHLC-C).

WOMAC, VAS and SF-MPQ are well regarded among researchers and are recognised internationally as reliable measures of pain in RCTs.

4.13.1 WOMAC: OA-specific Treatment Assessment

WOMAC is a self-administered and assesses three dimensions of pain, disability and joint stiffness in knee and hip OA using 24 questions.

The version used in this RCT, WOMAC 3.1, is available in more than 100 languages and in five-point Likert or 10cm visual analogue format. The instrument has been linguistically validated and is widely used in the evaluation of knee and hip OA. As such, WOMAC is a valid, reliable and responsive measure of outcome. It has been used in diverse clinical and interventional environments and has been subjected to numerous validation studies.

WOMAC is described as a disease-specific, purpose-built, high-performance instrument for evaluative research in OA clinical trials. The pain, stiffness and physical function sub-scale in WOMAC fulfils convention criteria for face, content and construct validity, reliability, responsiveness and relative efficiency (Bellamy et al. 1988).

WOMAC comprises three sections – Section A Question 1-5 VAS Pain Scale from zero (no pain) to 10 cm (extreme pain); Section B Question 6-7 VAS Stiffness Scale from zero (no stiffness) to 10cm (extreme stiffness); and Section C Question 8-24 VAS Physical Function Scale (difficulty performing daily activities) from zero (no difficulty) to 10cm (extreme difficulty). The higher the score the worse the condition.

4.13.2 Visual Analogue Scale (VAS)

The Visual Analogue Scale (VAS) is a commonly used 11-point assessment instrument for pain intensity and proven to be reliable and valid (Crossley et al. 2004). VAS for pain consists of a 10cm line with two end-points representing “no distress” (i.e. no pain) and “unbearable distress” (i.e. agonising pain). Before and after each treatment, participants rated their pain by placing a mark on the line corresponding to their presenting pain level. The distance along the line from the “no distress” marker was then measured with a ruler to give a pain score from zero out of 10. The higher the number the greater the pain intensity.

VAS has been shown to be valid and comparable to other methods and offers several advantages. VAS has been found to provide greater sensitivity and greater statistical power to data collection and analysis by allowing a broader range of responses than traditional categorical responses (Flandry et al. 1991). It removes bias introduced by examiner questioning, and it allows graphic temporal comparisons. Most importantly, participant affinity is higher for this type of subjective evaluation than other methods.

4.13.3 Secondary Outcome Measures

A further four instruments – Short Form McGill Pain Questionnaire (SF-MPQ), Credibility/Expectancy Questionnaire (C/E), Working Alliance Inventory Short Form C (WAI-C) and Multi-dimensional Health Locus of Control Form C (MHLC-C) – examined other important aspects of the OAK pain study, including psychometric properties, the practitioner-participant relationship and placebo effect. The four instruments also provided Insights into the way participants perceive and react to this new approach to laser acupuncture therapy.

4.13.4 Short Form McGill Pain Questionnaire (SF-MPQ)

Short Form McGill Pain Questionnaire (SF-MPQ), which assesses multi-dimensional experience of pain, was used to validate the pain findings of the two primary outcome measures – WOMAC and VAS. The 17 questions in SF-MPQ gauged the sensory and affective dimensions of pain, a Visual Analogue Scale and a Present Pain Intensity Scale.

SF-MPQ uses 15 descriptors – Questions 1-11 represent the sensory dimension of pain experience and Questions 12-15 represent the affective dimension. The 15 pain descriptors range from throbbing through to shooting, stabbing, sharp, cramping, gnawing, hot-burning, aching, heavy, tender, splitting, tiring-exhausting, sickening, fearful and punishing-cruel. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe.

SF-MPQ Question 16 – VAS pain scale runs from zero (no pain) to 10cm (worst possible pain). Question 17 – Present Pain Intensity (PPI) ranges from zero to 5 (no pain through to mild, discomforting, distressing, horrible and excruciating).

As with other primary outcome measures of pain, the higher the score in SF-MPQ the worse the pain.

4.13.5 Credibility/Expectancy Questionnaire (C/E)

The psychometric properties of the Credibility/Expectancy Questionnaire (C/E) provide a quick and easy scale for measuring treatment expectancy and rationale credibility for use in clinical outcome trials (Devilly & Borkovec 2000). Credibility has been defined as "how believable, convincing and logical the treatment is" whereas expectancy refers to "improvements that clients believe will be achieved" (Kazdin 1979).

C/E derives two predicted factors – cognitively-based "creditability" and relatively more affected-based "expectancy". The expectancy factor predicts outcome on some measures whereas the credibility factor is unrelated to outcome.

During administration of the questionnaire, the participant sees two sections – one related to "thinking" and one related to "feeling". However, the two factors derived are not grouped into those questions. Instead, credibility has been found to be derived from the first three "think" questions and expectancy from the fourth "think" question and the two "feel" questions. C/E therefore helps identify or measure the psychometric perception of participants receiving treatments.

C/E comprises six questions using a scale ranging from 1 to 9 (1 being not at all, 5 being somewhat logical/useful, 9 being very logical/useful/total improvement/very much). The higher the score the greater the participant's faith in the belief, credibility or expectancy of the treatment.

4.13.6 Working Alliance Inventory Short Form C (WAI – C)

The Working Alliance Inventory Short Form C (WAI – C), defined as the extent to which the client and practitioner work collaboratively and purposefully and connect emotionally, is conceptualised as a common or generic factor in that it is believed to cut across various treatment approaches (Horvath & Greenberg 1994).

For this RCT, the 12-item/question self-report measure, WAI (C), was used. Like the long-form WAI, WAI (C) has three sub-scales – Goals, Tasks and Bond.

The Goals sub-scale (Q4, 6, 10 & 11) measures the extent to which a client and therapist agree on the goals or outcomes targeted by the intervention (Horvath & Greenberg 1994). The Tasks sub-scale (Q1, 2, 8 & 12) measures the extent to which a client and therapist agree on the behaviours and cognitions forming the substance of the intervention process, while the Bond sub-scale (Q3, 5, 7 & 9) measures the extent to which a client and therapist possess mutual trust, acceptance and confidence.

Each WAI (C) sub-scale is scored on a seven-point Likert-type scale ranging from 1 (never), 2 (rarely), 3 (occasionally), 4 (sometimes), 5 (often), 6 (very often) and 7 (always). Sub-scale scores can range from 4 to 28 and can, if desired, be summed to obtain a total score. Thus, total scores can range from 12 to 84. Higher scores reflect more positive ratings of WAI.

According to Hanson's study of the *Reliability Generalisation of Working Alliance Inventory Scale Scores* (2002), WAI and WAI (C) score uniformly high reliability estimates. These estimates easily meet professional standards of acceptability (Cicchetti 1994).

4.13.7 Multi-dimensional Health Locus of Control Short Form C

The Multi-dimensional Health Locus of Control Short Form C (MHLC-C) assesses the participants' perception of health by providing data on how they view themselves, the practitioner delivering treatments and the impact of sheer chance and the influential power of doctors and others involved in their illness and treatment outcomes.

MHLC consists of three scales (A, B, and C). Forms A & B are the "general" health locus of control scales. Each of these two "equivalent" forms contains three six-item sub-scales: internality; powerful others externality; and chance externality.

For the current study, the "condition-specific" Form C was used in place of Form A/B to study people with an existing health/medical condition.

Like Forms A/B, Form C also has 18 items/questions. But, instead of a single six-item powerful others sub-scale, Form C has five sub-scales: internal belief (Q1, 6, 8, 12, 13 & 17), chance (Q2, 4, 9, 11, 15 & 16), powerful others (Q3, 5, 7, 10, 14 & 18), doctors (Q3, 5 & 14) and other people (Q7, 10 & 18). The questionnaires are formatted with a Likert-type scale from 1 (strongly disagree), 2 (moderately disagree), 3 (slightly disagree), 4 (slightly agree), 5 (moderately agree) and 6 (strongly agree). The higher

the score, the more the participant agrees with the statement. This implies the higher the score, the stronger the belief and the greater the influence of a particular factor.

The inclusion of MHLC-C as an outcome measure for this study helped identify the above-listed variables likely to occur in investigating the effects of laser acupuncture on OAK pain.

4.14 Statistical Methods

The statistical software, SPSS Ver. 23, was used to analyse treatment outcomes while a General Linear Model with repeated measures tested the hypothesis of the RCT. A univariate variance of analysis and t-test comparison assessed differences between each time point. A p value of less than 0.05 was considered statistically significant for all comparisons. A qualified statistician provided advice on the collection, sorting and analyses of research data. Data on 40 participants were analysed on an intention-to-treat basis with the last scores carried forward to the end to avoid statistical bias.

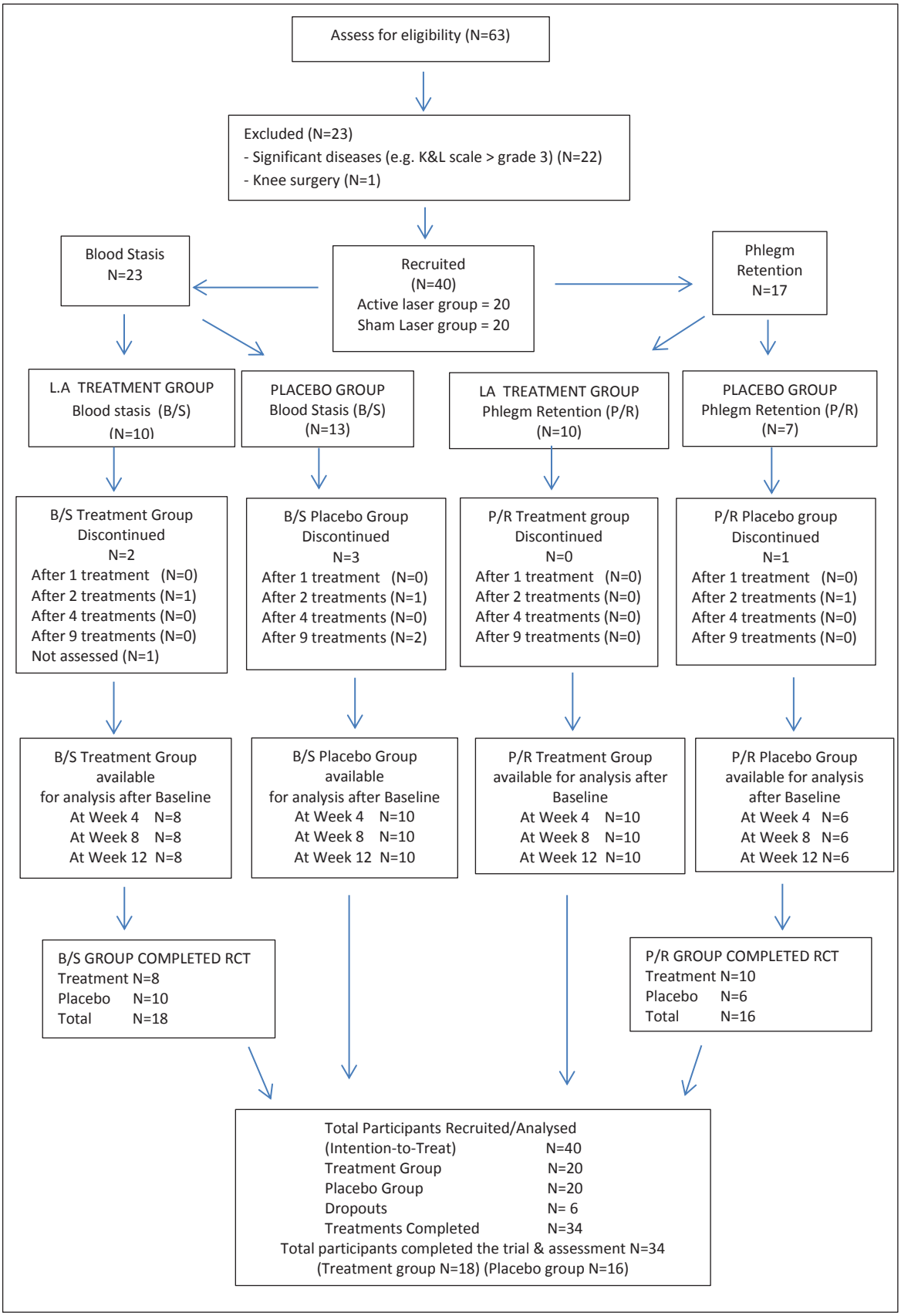

Figure 2 – Flow Chart of Laser Acupuncture RCT Procedures

Chapter 5 Results

This chapter presents the results from the trial. Demographic data including the mean scores for all outcome measures is followed by data relating to each of the two primary outcome measures – WOMAC and VAS – and secondary outcome measures – Short Form McGill Pain Questionnaire (SF-MPQ), Credibility/Expectancy Questionnaire (C/E), Working Alliance Inventory Short Form C (WAI-C) and the Multi-dimensional Health Locus of Control Form C (MHLC-C). The statistical software package, SPSS Version 23, was used to analyse treatment outcomes. A General Linear Model with repeated measures tested the null hypothesis of the RCT, which was consequently rejected. A univariate of analysis and T-test comparison assessed differences between each time point. A p value of < 0.05 was considered statistically significant for all comparisons. Data for the 40 participants enrolled in the RCT were analysed on an intention-to-treat basis. This allowed data for the six participants who dropped out to be carried forward from their last visit, thus limiting statistical bias.

5.1 Participant Demographics

Table 42 (below) shows the participant demographics for the study, including baseline outcome measure scores. Following random allocation to the two groups, no significant differences for the participant demographics were found between the two groups for WOMAC, SF-MPQ, C/E, WAI (C) and MHLC-C.

Table 42 – Baseline Demographic Scores for Active & Sham Laser Groups

Participant Description	**Mean Score**		**Significance Level (p) at Baseline**
	Active (SD)	Sham (SD)	
Age (years)	61.3 (11.36)	63.0 (10.11)	0.620
	No. Active	**No. Sham**	
Gender (male/female)	10/10	10/10	N/A

Location of Pain (Knee)	**Mean Score Active**	**Mean Score Sham**	**Significance Level (p) at Baseline**
Left knee (24)	13	11	N/A
Right knee (16)	7	9	N/A
Outcome Measures			
WOMAC	**Mean Score**	**Mean Score**	**Significance Level (p) at Baseline**
Total score	106.29	116.99	0.417
Pain Q 1-5	19.99	21.63	0.569
Stiffness Q 6-7	9.42	10.23	0.632
Physical function Q 8-24	76.88	85.14	0.410
Visual Analogue Scale (Pain)	4.88 (2.10)	4.88 (1.15)	1.000
Secondary Outcome Measures	**Mean Score**	**Mean Score**	**Significance Level (p) at Baseline**
1) McGill Pain Questionnaire Short Form	**Active (SD)**	**Sham (SD)**	
a) Sensory pain Q 1-11	11.40 (6.99)	12.00 (6.99)	0.772
b) Affective pain Q 12-15	3.25 (3.52)	3.00 (2.38)	0.794
Overall sensation (Sensory/Affective) pain Q 1-15	14.65 (9.86)	15.15 (8.12)	0.862
c) VAS pain scale Q 16	5.44 (2.12)	4.79 (2.20)	0.349
d) Pain intensity PPI	2.75 (1.02)	2.60 (0.99)	0.640
2) Credibility/Expectancy Questionnaire	**Active (SD)**	**Sham (SD)**	**Significance Level (p) at Baseline**
a) Thinking component - Q 1-4	27.40 (5.88)	28.05 (5.37)	0.717
b) Feeling aspect - Q 5-6	13.90 (2.90)	13.80 (2.91)	0.914
Total score Q 1-6	41.30 (8.39)	41.85 (7.88)	0.832
3) Working Alliance Inventory Short Form C	**Active (SD)**	**Sham (SD)**	**Significance Level (p) at Baseline**
a) Task (Q1, 2, 8 & 12)	24.80 (3.29)	23.60 (4.08)	0.312
b) Bonding (Q3, 5, 7 & 9)	25.10 (3.11)	23.50 (4.29)	0.185
c) Goals (Q4, 6, 10 & 11)	18.45 (3.02)	18.70 (4.31)	0.833
Total score (Q1-12)	68.35 (6.68)	65.80 (10.71)	0.372

4) Multi-dimensional Health Locus of Control Form C		Active (SD)	Sham (SD)	Significance Level (p) at Baseline
a)	Internal belief Q1, 6, 8, 12, 13 & 17	22.00 (8.75)	22.25 (6.63)	0.919
b)	Chance Q2, 4, 9, 11, 15 & 16	15.20 (7.58)	14.90 (5.54)	0.887
c)	Powerful others Q3, 5, 7, 10, 14 &18	21.65 (5,99)	21.50 (4.05)	0.927
d)	Doctor Belief Q3, 5 & 14	12.40 (2.93)	13.70 (2.54)	0.142
e)	Other People Q7, 10 & 18	9.25 (4.08)	7.80 (3.29)	0.223

5.2 WOMAC All Scales (Q1-24)

5.2.1 Comparison Within Each Group

Table 43 and Figure 3 (below) show the WOMAC All Scales (Q1-24) mean total scores at four time points (baseline, week 4, week 8 and week 12) for both the active and sham laser interventions. Active laser mean scores were significantly reduced, indicating an improvement over time. Mean scores for the four time points were 106.29 (week 0); 28.36 (week 4); 24.65 (week 8); and 24.48 (week 12). Table 44 (below) shows that the changes were significant ($p < 0.05$), indicating an improvement in WOMAC scores from baseline at all three successive time points.

When compared to baseline, a similar situation occurred for the sham laser group with the mean decreasing from 116.99 (baseline) to 72.17 (week 4); 79.13 (week 8) and 71.38 (week 12). For all three successive time points the changes were statistically significant ($p < 0.05$ at all times), indicating an improvement in WOMAC scores from baseline for the sham laser group.

In summary, both the active laser and sham laser groups showed significant changes over all three successive time points when compared to the baseline score for each group.

Table 43 – WOMAC All Scales (Q1-24) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

Group	Time	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	106.29 (44.52)	89.76	122.82
	4 weeks (T2)	28.36 (27.73)	11.83	44.89
	8 weeks (T3)	24.65 (35.79)	8.12	41.18
	12 weeks (T4)	24.48 (38.44)	7.95	41.01
Sham laser (N=20)	Baseline week 0 (T1)	116.99 (37.78)	97.41	136.58
	4 weeks (T2)	72.17 (41.16)	52.58	91.75
	8 weeks (T3)	79.13 (47.70)	59.54	98.71
	12 weeks (T4)	71.38 (48.40)	51.79	90.97

Table 44 – WOMAC All Scales (Q1-24) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WOMAC All Scales (Q1-24) Group	Time point Baseline Week 0 (T1)	Time Points	Mean Difference Compared to Baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	77.93	.000*	54.55	101.30
		8 weeks (T3)	81.65	.000*	58.27	105.02
		12 weeks (T4)	81.81	.000*	58.44	105.19
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	44.83	.002*	17.13	72.53
		8 weeks (T3)	37.87	.008*	10.17	65.57
		12 weeks (T4)	45.61	.002*	17.91	73.32

*p-value < 0.05 significant

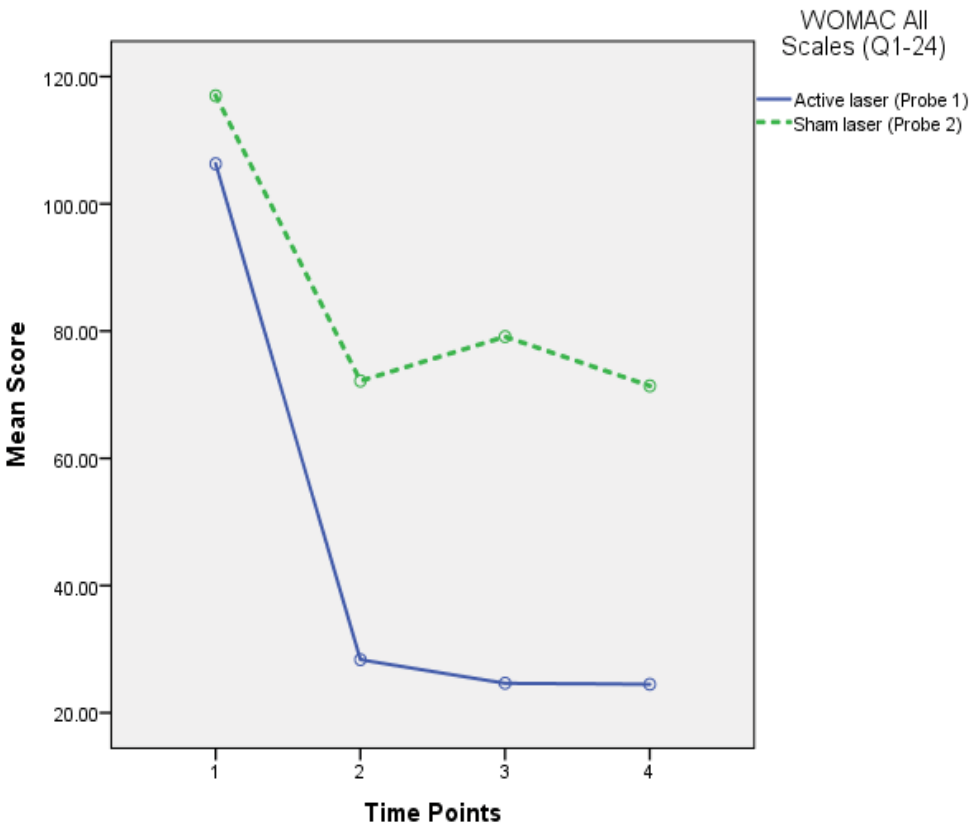

Figure 3 – WOMAC All Scales (Q1-24) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.2.2 Comparison Between Groups at Each Time Point

Table 45 (below) shows that when comparing between the two groups (WOMAC All Scales Q1-24 pairwise comparisons), the mean difference scores for the active laser WOMAC scores were statistically significantly greater than the sham laser scores at week 4, 8 and 12 (-43.80, $p < 0.001$; -54.48, $p < 0.001$; -46.91, $p = 0.002$).

Table 45 – WOMAC All Scales (Q1-24) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WOMAC All Scales (Q1-24) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	**Mean difference between active and sham laser**	**P-value**	Lower Bound	Upper Bound
Baseline (week 0)(T1)	-10.71	.417	-37.14	15.73
4 weeks (T2)	-43.80	.000*	-66.27	-21.34
8 weeks (T3)	-54.48	.000*	-81.48	-27.49
12 weeks (T4)	-46.91	.002*	-74.88	-18.93

*p-value < 0.05 significant

5.2.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 46 (below) shows that when the mean differences between the two groups were compared to the baseline mean in the WOMAC All Scales Q1-24, the active laser was significantly different from the sham laser at all three successive time points. At time point 2, the mean difference was -33.10 ($p = 0.032$), for time point 3 it was -43.78 ($p = 0.011$) and for time point 4 the mean difference was 36.20 ($p = 0.045$). Overall comparison effect mean difference was -38.97 ($p < 0.001$), showing statistically significant difference between two groups.

Table 46 – WOMAC All Scales (Q1-24) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WOMAC All Scales (Q1-24) Between Group Comparison from baseline week 0 (time point 1) over time point 2, 3 & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower	Upper
Time point 1 Vs Time point 2	-33.10	.032*	-63.15	-3.04
Time point 1 Vs Time point 3	-43.78	.011*	-77.02	-10.54
Time point 1 Vs Time point 4	36.20	.045*	0.92	71.48
Overall comparison effect	-38.97	.000*	-58.21	-19.74

*p-value < 0.05 significant

5.3 WOMAC Pain Scale Component (Q1-5)

5.3.1 Comparison Within Each Group

Table 47 and Figure 4 (below) show the WOMAC Pain Scale component scores for both the active and sham laser at four time points (baseline, week 4, week 8 and week 12). For the active laser, the mean scores reduced significantly, indicating an improvement over time. Mean scores for the four time points were 19.99 (week 0); 5.03 (week 4); 4.30 (week 8) and 4.63 (week 12). Table 48 shows that the changes were significant ($p < 0.001$ at all times), indicating a significant improvement in WOMAC pain scale scores from baseline at all three successive time points.

This also occurred for the sham laser WOMAC Pain Scale component scores with participants reporting mean scores of 21.63 (week 0); 12.45 (week 4); 14.34 (week 8); and 12.43 (week 12). At each time point, the differences from the baseline scores were statistically significant ($p < 0.05$ at all times).

Table 47 – WOMAC Pain Scale (Q1-5) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

WOMAC Pain Scale (Q1-5) Group	Time point	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser N=20	Baseline week 0 (T1)	19.99 (9.55)	16.66	23.32
	4 weeks (T2)	5.03 (5.41)	1.69	8.36
	8 weeks (T3)	4.30 (6.03)	0.97	7.63
	12 weeks (T4)	4.63 (8.18)	1.30	7.96
Sham laser N=20	Baseline (T1 week 0)	21.63 (8.50)	17.21	26.05
	4 weeks (T2)	12.45 (9.36)	8.02	16.87
	8 weeks (T3)	14.34 (11.07)	9.92	18.77
	12 weeks (T4)	12.43 (10.59)	8.01	16.86

Table 48 – WOMAC Pain Scale (Q1-5) Mean Difference Scores 2 Groups Compared to Baseline at Each of 3 Time Points

WOMAC Pain Scale (Q1-5) Group	Time point Baseline week 0 (T1)	Time points	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	14.96	.000*	10.25	19.67
		8 weeks (T3)	15.69	.000*	10.98	20.40
		12 weeks (T4)	15.36	.000*	10.65	20.07
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	9.18	.005*	2.93	15.44
		8 weeks (T3)	7.29	.023*	1.03	13.54
		12 weeks (T4)	9.20	.004*	2.94	15.45

*p-value < 0.05 significant

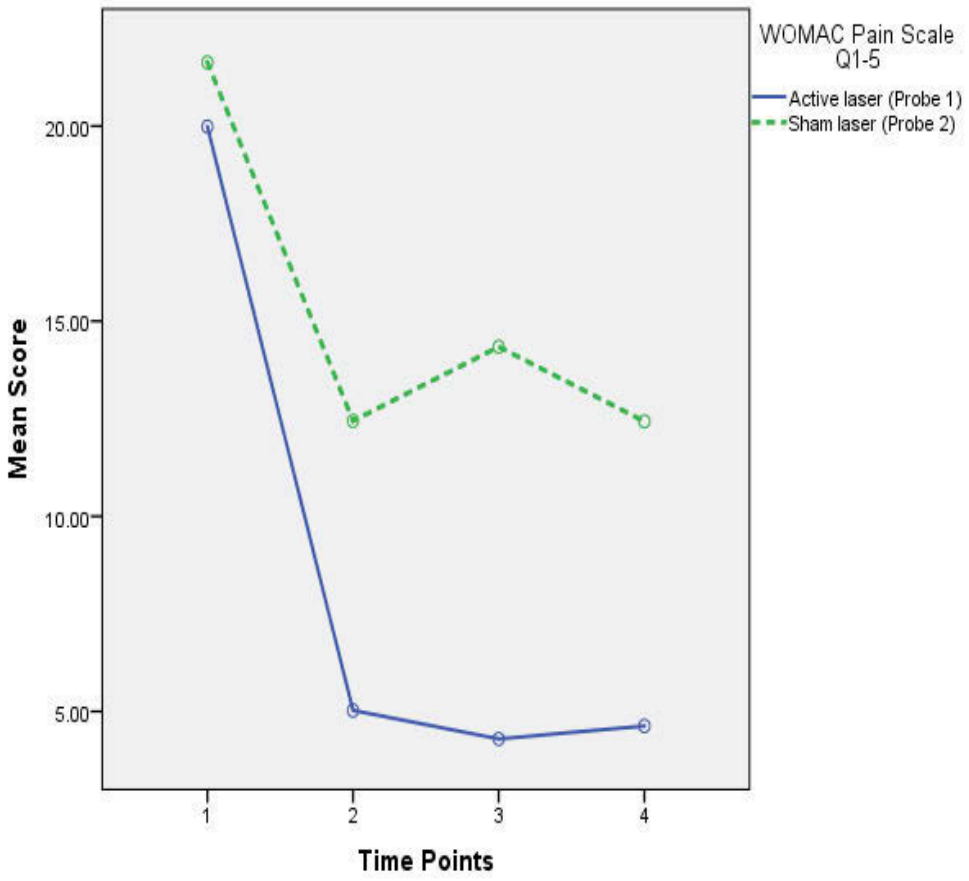

Figure 4 – WOMAC Pain Scale (Q1-5) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.3.2 Comparison Between Groups at Each Time Point

Table 49 (below) shows that, when comparing between the two groups (pairwise comparison), the mean difference scores for the active laser WOMAC Pain Scale (Q1-5) scores were statistically significantly greater than the sham laser scores at week 4, 8 and 12 (-7.42 p = 0.004; -10.05 p = 0.001; -7.81 p = 0.13).

Table 49 – WOMAC Pain Scale (Q1-5) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WOMAC Pain Scale (Q1-5) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-1.64	.569	-7.43	4.15
4 weeks (T2)	-7.42	.004*	-12.32	-2.53
8 weeks (T3)	-10.05	.001*	-15.75	-4.34
12 weeks (T4)	-7.81	.013*	-13.86	-1.75

*p-value < 0.05 significant

5.3.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 50 (below) shows that, when the mean differences between the two groups were compared to the baseline mean in WOMAC Pain Scale (Q1-5), only time point 3 with a mean difference of -8.41 was significantly different (p value, < 0.05), but not at time point 2 and 4, which recorded mean differences of -5.78 (p, value > 0.05) and -6.16 (p value > 0.05) respectively. However, the overall comparison effect was statistically significantly different with a mean difference of -6.73 (p value < 0.05).

Table 50 – WOMAC Pain Scale (Q1-5) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WOMAC Pain Scale (Q1-5) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-5.78	.095	-12.61	1.05
Time point 1 Vs Time point 3	-8.41	.029*	-15.92	-0.90
Time point 1 Vs Time point 4	-6.16	.133	-14.28	1.95
Overall comparison effect	-6.73	.002*	-10.79	-2.67

*p-value < 0.05 significant

5.4 WOMAC Stiffness Scale Component (Q6-7)

5.4.1 Comparison Within Each Group

Table 51 and Figure 5 (below) show the WOMAC Stiffness Scale (Q6-7) mean scores at the four time points (baseline, week 4, week 8 and week 12) for both the active and sham laser interventions. The active laser mean scores were significantly reduced, indicating an improvement over time. Mean scores for the four time points were 9.42 (week 0); 2.70 (week 4); 2.50 (week 8); 3.12 (week 12). Table 52 (below) shows that, at all time points, the changes were significant ($p < 0.001$), indicating a significant improvement in WOMAC Stiffness Scale (Q6-7) scores from baseline at all three successive time points.

For the sham laser group, the mean scores were 10.23 (week 0), 5.67 (week 4), 7.24 (week 8) and 6.47 (week 12). The mean differences between baseline and the three successive time points were 4.56, 2.99 and 3.76 respectively. Sham laser showed significant changes at time point 2 and 4 (p value < 0.05), but not at time point 3 (p value = 0 .056).

Table 51 – WOMAC Stiffness Scale (Q6-7) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

WOMAC Stiffness Scale (Q6-7) Group	Time	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	9.42 (5.21)	7.04	11.80
	4 weeks (T2)	2.70 (2.88)	1.05	4.35
	8 weeks (T3)	2.50 (2.81)	0.66	4.35
	12 weeks (T4)	3.12 (4.35)	1.05	5.19
Sham laser (N=20)	Baseline week 0 (T1)	10.23 (5.30)	7.85	12.60
	4 weeks (T2)	5.67 (4.29)	4.01	7.32
	8 weeks (T3)	7.24 (5.03)	5.40	9.08
	12 weeks (T4)	6.47 (4.80)	4.40	8.54

Table 52 – WOMAC Stiffness Scale (Q6-7) Mean Difference Scores for 2 Groups Compared To Baseline At Each Of 3 Time Points

WOMAC Stiffness Scale (Q6-7) Group	Time point Baseline week 0 (T1)	Time points	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	6.72	.000*	4.24	9.21
		8 weeks (T3)	6.92	.000*	4.44	9.40
		12 weeks (T4)	6.31	.000*	3.82	8.79
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	4.56	.004*	1.49	7.63
		8 weeks (T3)	2.99	.056	-0.08	6.05
		12 weeks (T4)	3.76	.017*	0.69	6.82

*p-value < 0.05 significant

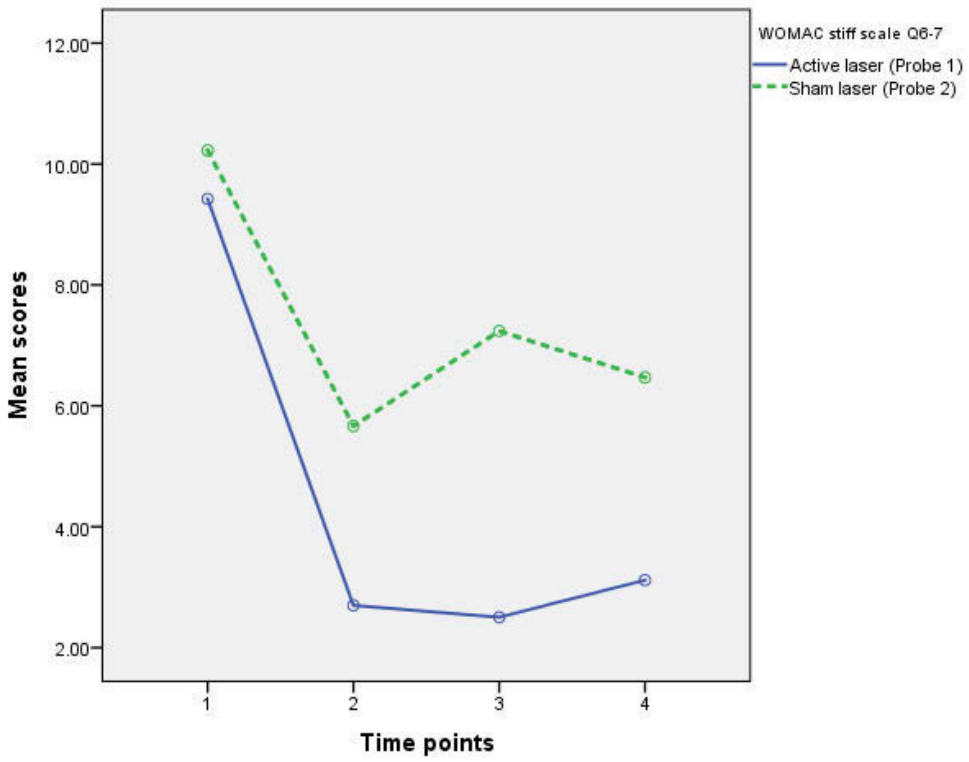

Figure 5 – WOMAC Stiffness Scale (Q6-7) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.4.2 Comparison Between Groups at Each Time Point

Table 53 (below) shows that, when comparing between the two groups (pairwise comparison), the mean differences for the active laser WOMAC Stiffness Scale (Q6-7) scores were statistically significantly greater than sham laser scores at week 4, 8 and 12 (-2.97, p =0.014 < 0.05; -4.74, p =0.001 < 0.05; -3. 35, p= 0.026 <0.05) respectively.

Table 53 – WOMAC Stiffness Scale (Q6-7) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WOMAC Stiffness Scale (Q6-7) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0)(T1)	-.802	.632	-4.17	2.56
4 weeks (T2)	-2.97	.014*	-5.31	-0.63
8 weeks (T3)	-4.74	.001*	-7.34	-2.13
12 weeks (T4)	-3.35	.026*	-6.28	-0.42

*p-value < 0.05 significant

5.4.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) and Time Point 4 (12 Weeks)

Table 54 (below) shows that when the mean differences between the two groups were compared to the baseline mean in the WOMAC Stiffness Scale (Q6-7), the active laser was only significantly different from sham laser at time point 3, where the mean difference was 3.93 (p = 0.034). However no significant difference occurred at time point 2 and 4, with mean differences of -2.16 (p=0.217) and -2.55 (p=0.192) respectively.

Overall comparison effect mean difference was -2.96 (p = 0.008 < 0.05), showing statistically significant difference between two groups.

Table 54 – WOMAC Stiffness Scale (Q6-7) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WOMAC Stiffness Scale (Q6-7) Between groups comparison from baseline week 0 (time point1) over time point 2, 3 & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-2.16	.217	-5.65	1.32
Time point 1 Vs Time point 3	3.93	.034*	-7.54	-.32
Time point 1 Vs Time point 4	-2.55	.192	-6.43	1.33
Overall comparison effect	-2.96	0.008*	-5.11	-.817

*p-value < 0.05 significant

5.5 WOMAC Physical Function Scale (Q8-24)

5.5.1 Comparison Within Each Group

Table 55 and Figure 6 (below) show the WOMAC Physical Function Scale (Q8-24) mean scores at four time points (baseline, week 4, week 8 and week 12) for both the active and sham laser interventions.

The active laser mean scores were significantly reduced, indicating an improvement over time. The mean scores for the four time points were 76.88 (week 0); 17.85 (week 4); 16.73 (week 8); 20.64 (week 12). Table 56 (below) shows the mean differences between baseline and the three successive time points were 59.04, 60.15 and 56.24 respectively for the WOMAC Physical Function Scale (Q8-24). The changes were significant ($p < 0.001$), indicating a significant improvement in WOMAC Physical Function Scale scores from baseline at all three successive time points.

For the sham laser group, the mean scores were 85.14 (week 0), 57.54 (week 4), 52.48 (week 8) and 54.05 (week 12). Mean differences between the baseline and the

successive three time points were 27.60, 32.66 and 31.09 respectively. Sham laser showed significant changes at all time points with a p value < 0.05.

Table 55 – WOMAC Physical Function Scale (Q8-24) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

WOMAC Physical Function Scale (Q8-24) Group	Time	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	76.88 (35.14)	64.37	89.39
	4 weeks (T2)	17.85 (27.54)	5.34	30.36
	8 weeks (T3)	16.73 (26.56)	4.22	29.24
	12 weeks (T4)	20.64 (21.37)	8.13	33.15
Sham laser (N=20)	Baseline week 0 (T1)	85.14 (27.07)	70.93	99.35
	4 weeks (T2)	57.54 (34.90)	43.34	71.75
	8 weeks (T3)	52.48 (34.69)	38.27	66.69
	12 weeks (T4)	54.05 (30.27)	39.85	68.26

Table 56 – WOMAC Physical Function Scale (Q8-24) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WOMAC Physical Function Scale (Q8-24) Group	Time point Baseline week 0 (T1)	Time points	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	59.04	.000*	41.35	76.73
		8 weeks (T3)	60.15	.000*	42.46	77.84
		12 weeks (T4)	56.24	.000*	38.55	73.93
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	27.60	.008*	7.51	47.69
		8 weeks (T3)	32.66	.002*	12.57	52.75
		12 weeks (T4)	31.09	.003*	11.00	51.18

*p-value < 0.05 significant

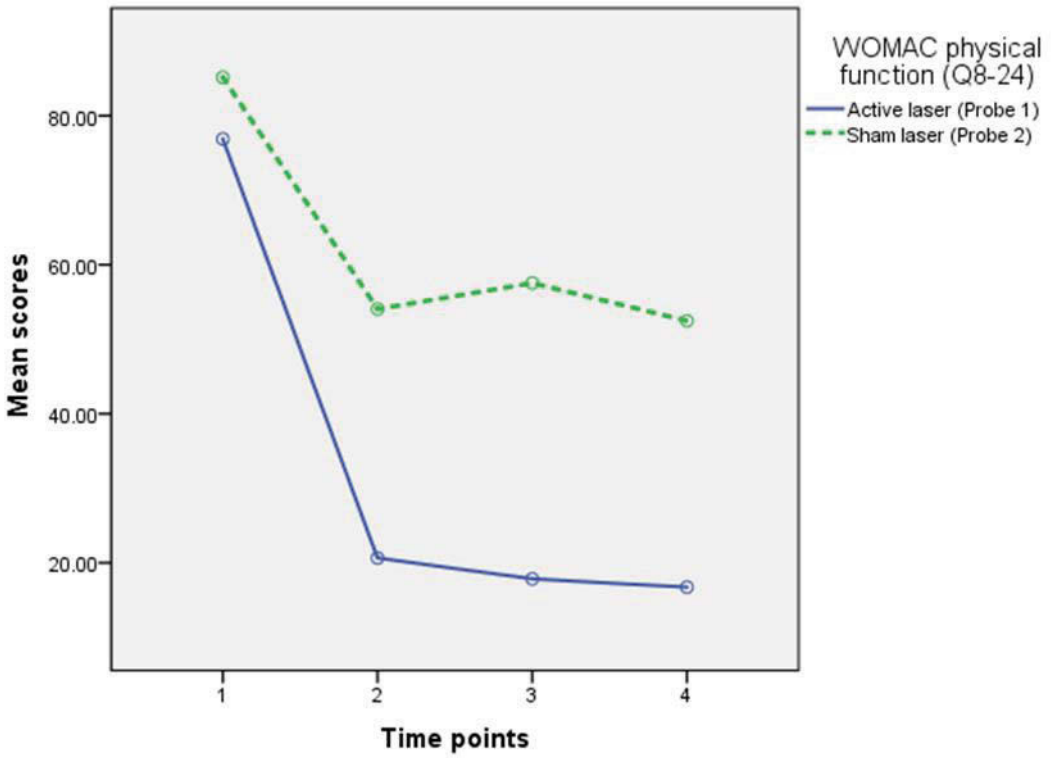

Figure 6 – WOMAC Physical Function Scale (Q8-24) Total Mean Scores for Active Laser and Sham Laser Groups at All 4 Time Points

5.5.2 Comparison Between Groups at Each Time Point

Table 57 shows that, when comparing between two groups (pairwise comparison), mean difference scores for the active laser WOMAC Physical Function (Q8-24) scores were statistically significantly greater than the sham laser scores at week 4, 8 and 12 (-39.70, $p < 0.001$; -35.75, $p < 0.005$; -33.41, $p < 0.001$).

Table 57 – WOMAC Physical Function Scale (Q8-24) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WOMAC Physical Function Scale (Q8-24) Pairwise Comparisons				
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	95% Confidence Interval for Difference	
			Lower Bound	Upper Bound
Baseline (week 0) (T1)	-8.26	.410	-28.34	11.82
4 weeks (T2)	-39.70	.000*	-59.82	-19.57
8 weeks (T3)	-35.75	.001*	-55.52	-15.97
12 weeks (T4)	-33.41	.000*	-50.19	-16.64

*p-value < 0.05 significant

5.5.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 weeks), Time Point 3 (8 weeks) & Time Point 4 (12 weeks)

Table 58 (below) shows that, when mean differences between the two groups were compared to the baseline mean, active laser was significantly different from sham laser at all three successive time points in the WOMAC Physical Function Scale (Q8-24). For time point 2, the mean difference was -25.15 ($p = 0.028$); for time point 3 it was -31.44 ($p = 0.014$); and for time point 4 it was -27.49 ($p = 0.035$). Overall comparison effect mean difference was -29.28 ($p < 0.001$), showing statistically significant difference between two groups.

Table 58 – WOMAC Physical Function Scale (Q8-24) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WOMAC Physical Function Scale (Q8-24) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-25.15	.028*	-47.45	-2.86
Time point 1 Vs Time point 3	-31.44	.014*	-56.23	-6.65
Time point 1 Vs Time point 4	-27.49	.035*	-52.91	-2.06
Overall comparison effect	-29.28	.000*	-43.48	-15.08

*p-value < 0.05 significant

5.6 VAS Pain Scale

5.6.1 Comparison Within Each Group

Table 59 and Figure 7 (below) show the VAS Pain Scale mean scores at four time points (baseline, week 4, week 8 and week 12) for both active and sham laser interventions.

Active laser mean scores were significantly reduced, indicating an improvement over time. Mean scores for the four time points were 4.88 (week 0); 0.28 (week 4); 0.44 (week 8); 0.98 (week 12).

Table 60 (below) shows that mean differences between baseline and the three successive time points were 4.60, 4.44 and 3.90 respectively. The changes were ($p < 0.001$), indicating a significant improvement in VAS scores from baseline at all three successive time points.

For the sham laser group, mean scores were 4.88 (week 0), 2.67 (week 4), 3.39 (week 8) and 2.85 (week 12). Mean differences between baseline and the three successive

time points were 2.21, 1.49 and 2.03 respectively. Sham laser showed significant changes at all time points with a p value < 0.05.

Table 59 – VAS Pain Scale Mean, Standard Deviation and Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

VAS Pain Scale Group	Time	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	4.88 (2.10)	4.16	5.60
	4 weeks (T2)	0.28 (0.75)	-.45	1.00
	8 weeks (T3)	0.44 (1.13)	-.28	1.16
	12 weeks (T4)	0.98 (2.06)	.26	1.70
Sham laser (N=20)	Baseline week 0 (T1)	4.88 (1.15)	3.97	5.78
	4 weeks (T2)	2.67 (2.14)	1.76	3.58
	8 weeks (T3)	3.39 (2.15)	2.48	4.29
	12 weeks (T4)	2.85 (2.46)	1.94	3.75

Table 60– VAS Pain Scale Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

VAS Pain Scale Group	Time point Baseline week 0 (T1)	Time points	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	4.60	.000*	3.58	5.62
		8 weeks (T3)	4.44	.000*	3.42	5.45
		12 weeks (T4)	3.90	.000*	2.88	4.91
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	2.21	.001*	.92	3.49
		8 weeks (T3)	1.49	.023*	.21	2.77
		12 weeks (T4)	2.03	.002*	.75	3.31

*p-value < 0.05 significant

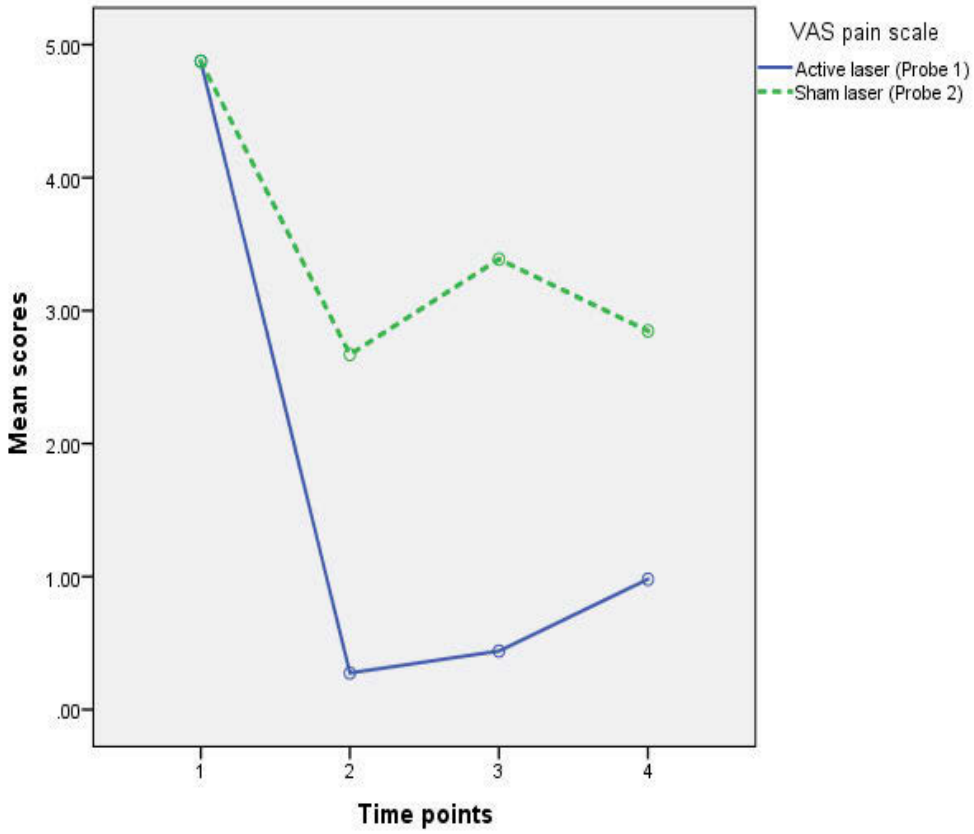

Figure 7 – VAS Pain Scale Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.6.2 Comparison Between Groups at Each Time Point

Table 61 (below) shows that, when comparing between two groups (pairwise comparison), the mean difference scores for active laser VAS scores were statistically significantly greater than sham laser scores at week 4, 8 and 12 respectively (-2.40, $p < 0.001$; -2.95 , $p < 0.001$; -1.87, $p = 0.013$).

Table 61 – VAS Pain Scale Mean Difference Scores Between 2 Groups at Each of 4 Time Points

VAS Pain Scale Pairwise Comparisons				
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	95% Confidence Interval for Difference	
			Lower Bound	Upper Bound
Baseline (week 0) (T1)	0.00	1.000	-1.08	1.08
4 weeks (T2)	-2.40	0.000*	-3.42	-1.37
8 weeks (T3)	-2.95	0.000*	-4.05	-1.85
12 weeks (T4)	-1.87	0.013*	-3.32	-0.42

*p-value < 0.05 significant

5.6.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 weeks)

Table 62 (below) shows that, when the mean differences between the two groups were compared to the baseline mean in the VAS Pain Scale, active laser was significantly different from sham laser at all three successive time points. For time point 2, the mean difference was -2.40 ($p = 0.001$); for time point 3 it was -2.95 ($P < 0.001$); and for time point 4 it was -1.87 ($p = 0.038$). Overall comparison effect mean difference was -1.80 ($p < 0.001$), a statistically significant difference between two groups.

Table 62 – VAS Pain Scale Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

VAS Pain Scale Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-2.40	.001*	-3.76	-1.03
Time point 1 Vs Time point 3	-2.95	.000*	-4.40	-1.49
Time point 1 Vs Time point 4	-1.87	.038*	-3.63	-.10
Overall comparison effect	-1.80	.000*	-2.66	-.94

*p-value < 0.05 significant

5.7 McGill Pain Questionnaire Short Form (SF-MPQ) – McGill Sensory Scale (Q1-11)

5.7.1 Comparison Within Each Group

Table 63 and Figure 8 (below) show the McGill Pain Questionnaire Sensory Scale mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores were significantly reduced, indicating an improvement over time. Mean scores for the four time points were 11.40 (week 0); 4.35 (week 4); 3.40 (week 8); 3.95 (week 12).

Table 64 (below) shows that the mean differences between baseline and the three successive time points were 7.05, 8.00 and 7.45 respectively. The changes were significant ($p < 0.001$), indicating improvement in McGill Sensory Scale scores from baseline at all three successive time points.

For the sham laser group, mean scores were 12.00 (week 0), 7.85 (week 4), 7.70 (week 8) and 7.50 (week 12). Mean differences between baseline and the three successive

time points were 4.15, 4.30 and 4.50 respectively. Sham laser only showed significant changes at time points 3 and 4 with respective p values of 0.043 and 0.034.

Table 63 – McGill Sensory Scale (Q1-11) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

McGill Sensory Scale Q1-11 Group	Time	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	11.40 (6.99)	9.11	13.69
	4 weeks (T2)	4.35 (4.38)	2.06	6.64
	8 weeks (T3)	3.40 (3.41)	1.11	5.69
	12 weeks (T4)	3.95 (5.08)	1.66	6.24
Sham laser (N=20)	Baseline week 0 (T1)	12.00 (6.99)	9.06	14.94
	4 weeks (T2)	7.85 (4.38)	4.91	10.79
	8 weeks (T3)	7.70 (3.41)	4.76	10.64
	12 weeks (T4)	7.50 (5.08)	4.56	10.44

Table 64 – McGill Sensory Scale (Q1-11) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

McGill Sensory Scale (Q1-11) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	7.05	.000*	3.82	10.29
		8 weeks (T3)	8.00	.000*	4.77	11.24
		12 weeks (T4)	7.45	.000*	4.22	10.69
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	4.15	.051	-0.01	8.31
		8 weeks (T3)	4.30	.043*	0.14	8.46
		12 weeks (T4)	4.50	.034*	0.34	8.66

*p-value < 0.05 significant

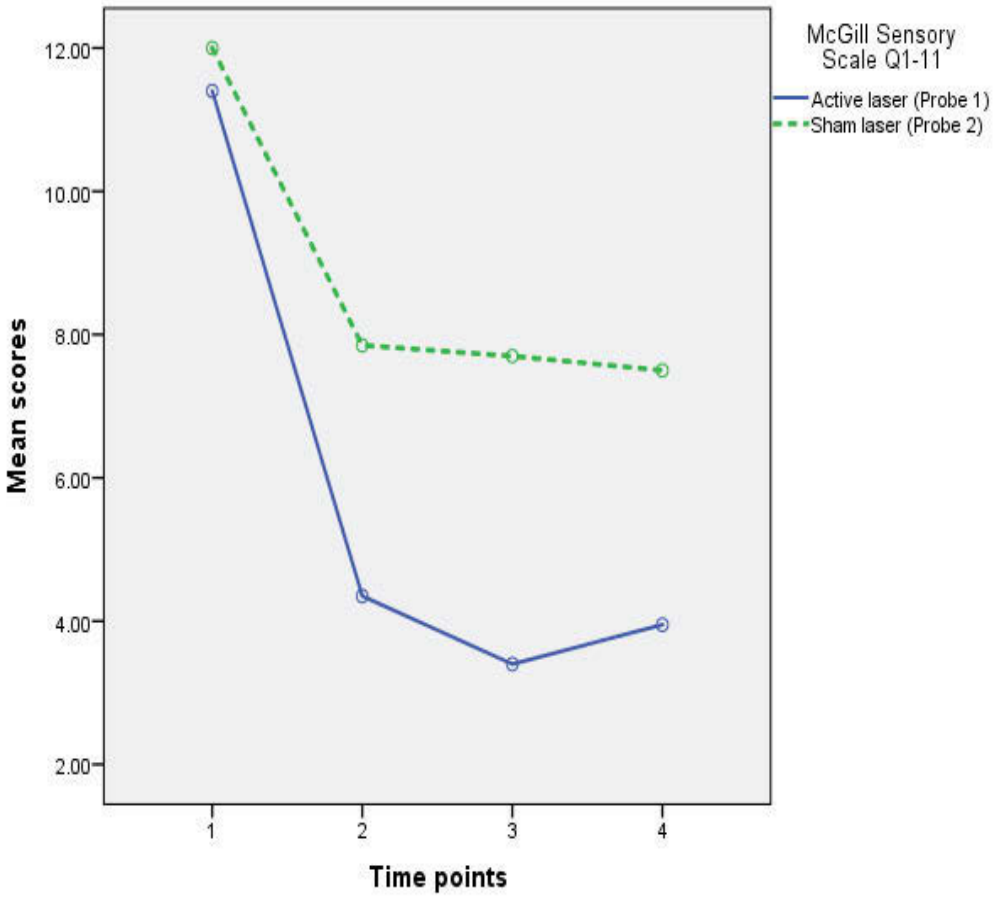

Figure 8 – McGill Sensory Scale (Q1-11) Total Mean Scores for Active Laser and Sham Laser Groups at All 4 Time Points

5.7.2 Comparison Between Groups at Each Time Point

Table 65 (below) shows that, when comparing between two groups (pairwise comparison), mean difference scores for active laser in the McGill Sensory Scale were statistically significantly greater than sham laser scores at week 4 and 8, but not at week 12. The mean differences for week 4 and week 8 were -3.50 (p =0.037) and -4.30 (P = 0.016) respectively, while the mean difference for week 12 was -3.55 (p = 0.092).

Table 65 – McGill Sensory Scale (Q1-11) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

McGill Sensory Scale (Q1-11) Pairwise Comparisons				
Between active laser & sham laser groups - Time point	**Mean difference between active and sham laser**	**P-value**	**95% Confidence Interval for Difference**	
			Lower Bound	**Upper Bound**
Baseline (week 0) (T1)	-0.60	.772	-4.77	3.57
4 weeks (T2)	-3.50	.037*	-6.78	-0.22
8 weeks (T3)	-4.30	.016*	-7.77	-0.84
12 weeks (T4)	-3.55	.092	-7.71	0.61

*p-value < 0.05 significant

5.7.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 weeks)

Table 66 (below) shows that, when the mean differences between the two groups were compared to the baseline mean, active laser was not significantly different from sham laser at all three successive time points in the McGill Sensory Scale (Q1-11). For time point 2, the mean difference was -2.90 ($p = 0.201$); for time point 3 it was -3.70 ($p = 0.114$); and for time point 4 it was -2.95 ($p = 0.281$). However, the overall comparison effect mean difference was -2.99 ($p = 0.037 < 0.05$), showing a statistically significant difference between two groups.

Table 66 – McGill Sensory Scale (Q1-11) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

McGill Sensory Scale (Q1-11) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower	Upper
Time point 1 Vs Time point 2	-2.90	.201	-7.41	1.61
Time point 1 Vs Time point 3	-3.70	.114	-8.33	0.93
Time point 1 Vs Time point 4	-2.95	.281	-8.41	2.51
Overall comparison effect	-2.99*	.037*	-5.78	-0.20

*p-value < 0.05 significant

5.8 McGill Pain Questionnaire – Affective Scale (Q12-15)

5.8.1 Comparison Within Each Group

Table 67 and Figure 9 (below) show the McGill Affective Scale mean scores at four time points (baseline, week 4, week 8 and week 12) for both active and sham laser interventions.

Active laser mean scores were significantly reduced, indicating an improvement over time. Mean scores for the four time points were 3.25 (week 0); 0.70 (week 4); 0.65 (week 8); 0.25 (week 12).

Table 68 (below) shows that the mean differences between baseline and the three successive time points were 2.55, 2.60 and 3.00 respectively. The changes recorded a p-value < 0.001, indicating a significant improvement in McGill Affective Scale scores from baseline at all three successive time points.

For the sham laser group, mean scores were 3.00 (week 0), 1.40 (week 4), 2.00 (week 8) and 1.75 (week 12). Mean differences between baseline and the successive three time points were 1.60 (p = 0.015); 1 (p = 0.124); and 1.25 (p = 0.056) respectively.

Sham laser only showed significant change at time point 1 with a p value < 0.05, but not at time point 3 and 4.

Table 67 – McGill Affective Scale (Q12-15) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

McGill Affective Scale (Q12-15) Group	Time Points	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	3.25 (3.52)	2.32	4.18
	4 weeks (T2)	.70 (1.81)	-0.23	1.63
	8 weeks (T3)	.65 (1.23)	-0.28	1.58
	12 weeks (T4)	.25 (.64)	-0.68	1.18
Sham laser (N=20)	Baseline week 0 (T1)	3.00 (2.38)	2.09	3.91
	4 weeks (T2)	1.40 (1.64)	0.49	2.31
	8 weeks (T3)	2.00 (2.18)	1.09	2.91
	12 weeks (T4)	1.75 (1.86)	0.84	2.66

Table 68 – McGill Affective Scale (Q12-15) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

McGill Affective Scale (Q12-15) Group	Time point Baseline week 0 (T1)	Time Points	Mean Difference compared to baseline	P value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	2.55	.000*	1.23	3.87
		8 weeks (T3)	2.60	.000*	1.28	3.92
		12 weeks (T4)	3.00	.000*	1.68	4.32
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	1.60	.015*	0.32	2.88
		8 weeks (T3)	1.00	.124	-0.28	2.28
		12 weeks (T4)	1.25	.056	-0.03	2.53

*p-value < 0.05 significant

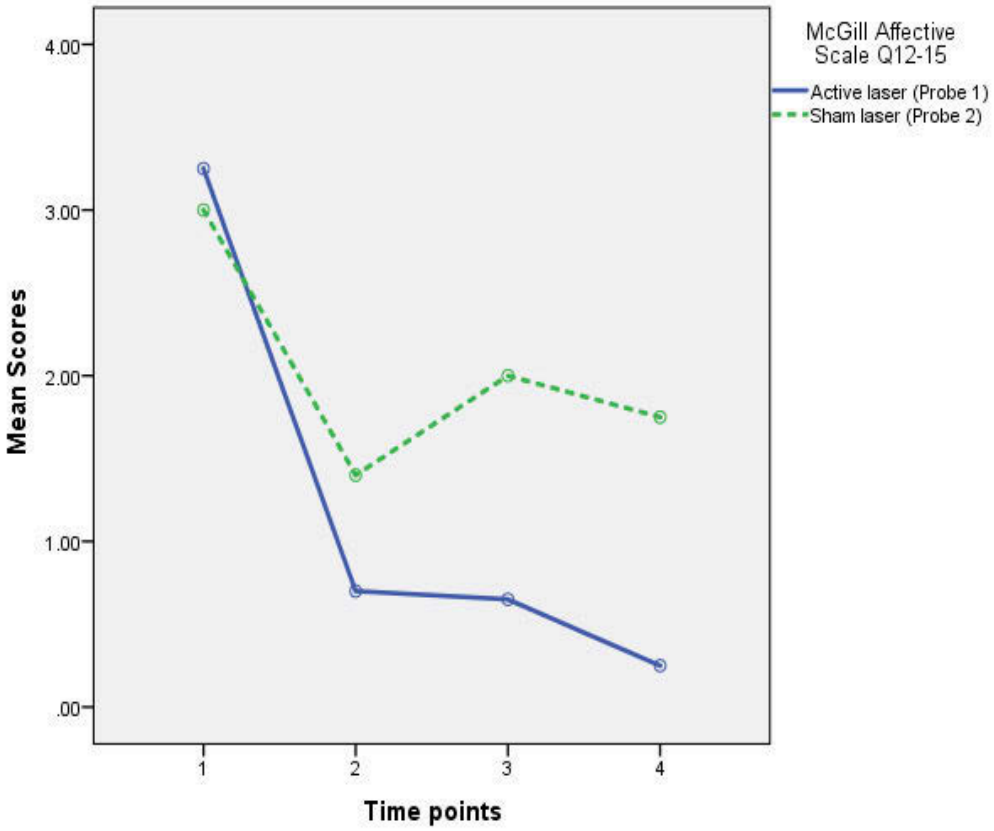

Figure 9 – McGill Affective Scale (Q12-15) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.8.2 Comparison Between Groups at Each Time Point

Table 69 (below) shows that, when comparing between two groups (pairwise comparison), the mean difference scores for active laser McGill Affective Scale scores were not significantly different at baseline (week 0) or time point 1 (week 2) and at time point 2 (4 weeks).

However, the active laser group showed statistically significant difference at 4 weeks (time point 2) and 8 weeks (time point 3) with a mean difference of -1.35 ($p = 0.02$) and -1.50 ($p < 0.001$) respectively.

Table 69 – McGill Affective Scale (Q12-15) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

McGill Affective Scale (Q12-15) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	.25	0.79	-1.68	2.18
4 weeks (T2)	-.70	0.21	-1.80	.40
8 weeks (T3)	-1.35	0.02*	-2.48	-.22
12 weeks (T4)	-1.50	0.00*	-2.39	-.61

*p-value < 0.05 significant

5.8.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 weeks)

Table 70 (below) shows that when the mean differences between the two groups were compared to the baseline mean in the McGill Affective Scale (Q12-15), active laser was not significantly different from sham laser at all three successive time points. For time point 1, the mean difference was -0.95 ($p = 0.252$); for time point 3 it was -1.60 ($p = 0.124$); and for time point 3 it was -1.75 ($p = 0.094$). Overall comparison effect mean difference was -0.825 ($p < 0.070$), indicating that McGill Affective Scale scores were not statistically significantly different between two groups.

Table 70 – McGill Affective Scale (Q12-15) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

McGill affective scale (Q12-15) Between groups comparison from baseline week 0 (Time point 1) over Time Point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-0.95	0.252	-2.60	.70
Time point 1 Vs Time point 3	-1.60	.124	-3.66	.46
Time point 1 Vs Time point 4	-1.75	.094	-3.81	.31
Overall comparison effect	-.825	.070	-1.72	.07

*p-value < 0.05 significant

5.9 McGill Pain Questionnaire – Sensory & Affective Scale (Q1-15)

5.9.1 Comparison Within Each Group

Table 71 and Figure 10 (below) show the McGill Sensory and Affective Scale mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

The active laser mean scores were significantly reduced, indicating improvement over time. The mean scores for the four time points were 14.65 (week 0); 5.05 (week 4); 4.05 (week 8); and 4.20 (week 12).

Table 72 (below) shows the mean differences between baseline and the successive three time points were 9.60, 10.60 and 10.45 respectively. The changes were significant ($p < 0.001$), indicating improvement in McGill Sensory and Affective Scale scores from baseline at all three successive time points.

For the sham laser group, the mean scores were 15.15 (week 0), 9.25 (week 4), 9.70 (week 8) and 9.25 (week 12). The mean differences between baseline and the

successive three time points were 5.90, 5.45 and 5.90 respectively. Sham laser showed significant changes at all time points with a p value < 0.05.

Table 71 – McGill Sensory & Affective (Q1-15) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

McGill Sensory & Affective Scale (Q1-15) Group	Time Points	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	14.65 (9.86)	11.75	17.55
	4 weeks (T2)	5.05 (5.26)	2.15	7.95
	8 weeks (T3)	4.05 (3.80)	1.15	6.95
	12 weeks (T4)	4.20 (5.47)	1.30	7.10
Sham laser (N=20)	Baseline week 0 (T1)	15.15 (8.12)	11.47	18.83
	4 weeks (T2)	9.25 (6.91)	5.57	12.93
	8 weeks (T3)	9.70 (8.62)	6.02	13.38
	12 weeks (T4)	9.25 (9.24)	5.57	12.93

Table 72 – McGill Sensory & Affective (Q1-15) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

McGill Sensory & Affective (Q1-15) Group	Time point Baseline week 0 (T1)	Time Points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	9.60	.000*	5.50	13.70
		8 weeks (T3)	10.60	.000*	6.50	14.70
		12 weeks (T4)	10.45	.000*	6.35	14.55
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	5.90	.027*	0.69	11.11
		8 weeks (T3)	5.45	.040*	0.24	10.66
		12 weeks (T4)	5.90	.027*	0.69	11.11

*p-value < 0.05 significant

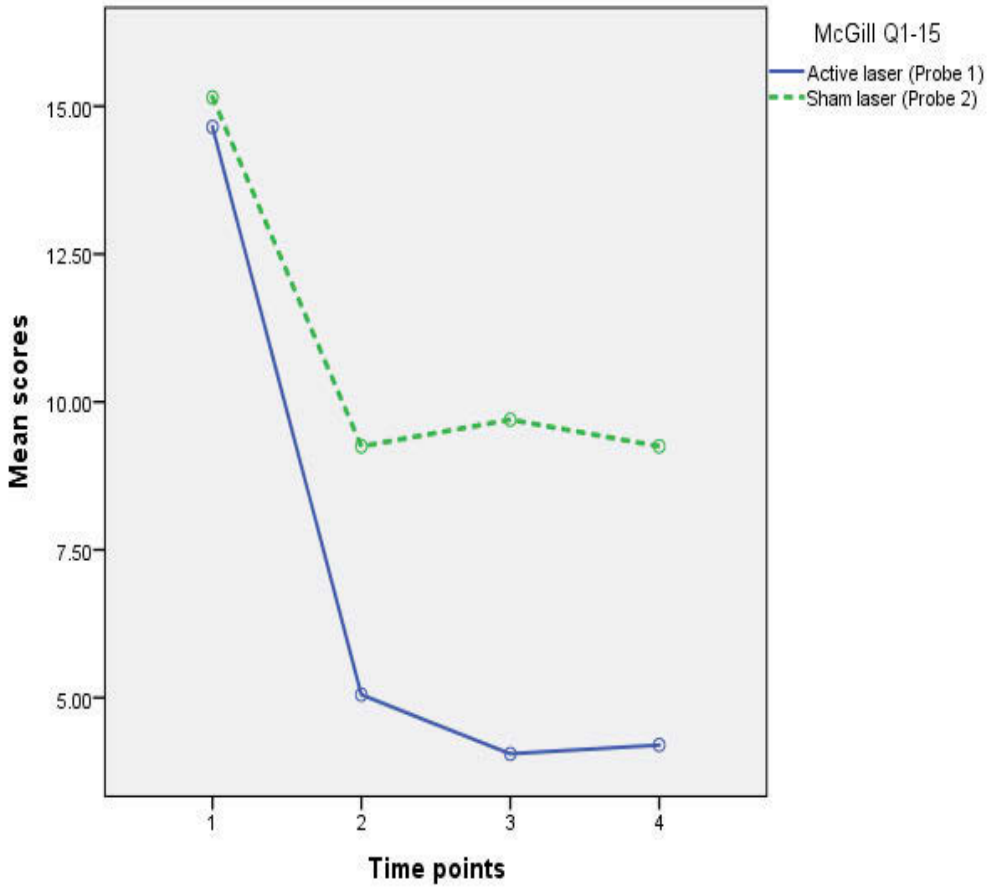

Figure 10 – McGill Sensory & Affective (Q1-15) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.9.2 Comparison Between Groups at Each Time Point

Table 73 (below) shows that, when comparing between two groups (pairwise comparison) on the McGill Sensory and Affective Scale (Q1-15), the mean difference scores for the active laser scores were statistically significantly greater than the sham laser scores at week 4, 8 and 12. The mean difference for week 4, week 8 and week 12 were -4.20 (p =0.037), -5.65 (P = 0.011) and -5.05 (P = 0.042) respectively, showing statistically significant difference between two groups at week 4, week 8 and week 12.

Table 73 – McGill Sensory & Affective Scale (Q1-15) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Pairwise Comparisons				
McGill Sensory & Affective (Q1-15)			**95% Confidence Interval for Difference**	
Between active laser & sham laser groups - Time point	**Mean difference between active and sham laser**	**P-value**	**Lower Bound**	**Upper Bound**
Baseline (week 0) (T1)	-.50	.862	-6.28	5.28
4 weeks (T2)	-4.20	.037*	-8.13	-0.27
8 weeks (T3)	-5.65	.011*	-9.91	-1.39
12 weeks (T4)	-5.05	.042*	-9.91	-0.19

*p-value < 0.05 significant

5.9.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 74 (below) shows that when the mean differences between the two groups were compared to the baseline mean on the McGill Sensory and Affective Scale, active laser was not significantly different from sham laser at all three successive time points. For time point 2, the mean difference was -3.70 ($p = 0.206$); for time point 3 it was -5.15 ($p = 0.105$); and for time point 4 it was -4.55 ($p = 0.201$). However, overall comparison effect mean difference was -3.85 ($p = 0.030 < 0.05$), showing statistically significant difference between two groups.

Table 74 – McGill Sensory & Affective Scale (Q1-15) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

McGill Sensory & Affective (Q1-15) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	**-3.70**	.206	-9.52	2.12
Time point 1 Vs Time point 3	-5.15	.105	-11.422	1.12
Time point 1 Vs Time point 4	-4.55	.201	-11.64	2.54
Overall comparison effect	-3.850	.030*	-7.31	-.38

*p-value < 0.05 significant

5.10 McGill Pain Questionnaire Short Form – VAS (Q16)

5.10.1 Comparison Within Each Group

Table 75 and Figure 11 (below) show the McGill VAS (Q16) Scale mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. The active laser mean scores were significantly reduced, indicating improvement over time. The mean scores for the four time points were 5.44 (week 0); 0.90 (week 4); 0.57 (week 8) and 0.69 (week 12).

Table 76 (below) shows that the mean differences between baseline and the three successive time points were 4.55, 4.88 and 4.75 respectively. The changes were significant ($p < 0.001$), indicating improvement in the McGill Q16 VAS pain score from baseline at all three successive time points.

For the sham laser group, the mean scores were 4.79 (week 0) to 2.96 (week 4), but rose to 3.57 at week 8 and dropped slightly to 3.08 at week 12. Mean differences between baseline and the three successive time points were 1.83, 1.23 and 1.71 respectively. This indicated significant improvement at week 4 (time point 2) and week 12 (time point 4),with p-values of 0.015 and 0.023 respectively, i.e. $p < 0.05$.

However, there was no significant difference at time point 3 with a p-value 0.100 > 0.05.

Table 75 – McGill VAS (Q16) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

McGill Pain Questionnaire - VAS Q16 Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	5.44 (2.12)	4.76	6.12
	4 weeks (T2)	.90 (1.23)	0.21	1.58
	8 weeks (T3)	.57 (1.44)	-0.12	1.25
	12 weeks (T4)	.69 (1.17)	0.01	1.38
Sham laser (N=20)	Baseline week 0 (T1)	4.79 (2.20)	3.76	5.83
	4 weeks (T2)	2.96 (2.09)	1.93	4.00
	8 weeks (T3)	3.57 (2.49)	2.53	4.60
	12 weeks (T4)	3.08 (2.50)	2.05	4.12

Table 76 – McGill VAS (Q16) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

McGill Pain Questionnaire - VAS (Q16) Group	Time Point Baseline week 0 (T1)	Time Points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	4.55	.000*	3.58	5.51
		8 weeks (T3)	4.88	.000*	3.91	5.84
		12 weeks (T4)	4.75	.000*	3.78	5.71
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	1.83	.015*	0.37	3.30
		8 weeks (T3)	1.23	.100	-0.24	2.69
		12 weeks (T4)	1.71	.023*	0.25	3.18

*p-value < 0.05 significant

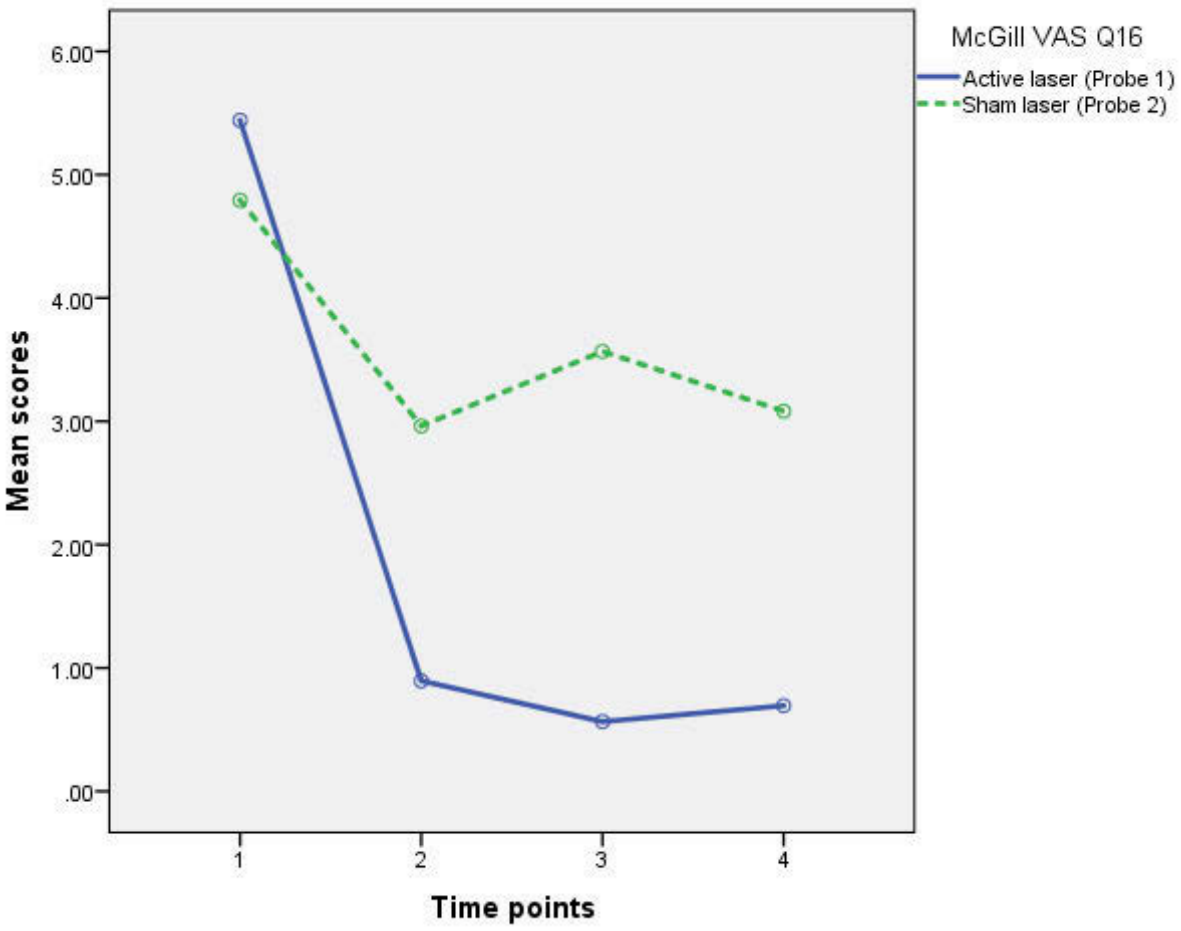

Figure 11 – McGill VAS (Q16) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.10.2 Comparison Between Groups at Each Time Point

Table 77 (below) shows that, when comparing between two groups (pairwise comparison) on the McGill VAS (Q16) scale, mean difference scores for active laser were statistically significantly greater than sham laser scores at week 4, 8 and 12. Mean differences for week 4, week 8 and week 12 were -2.07 (p = 0.000) and -3.00 (p = 0.000) and -2.39 (p = 0.000) respectively, showing statistically significant difference between two groups at week 4, week 8 and week 12 with a p value < 0.001.

Table 77 – McGill VAS (Q16) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

McGill VAS (Q16) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	0.65	.349	-0.73	2.03
4 weeks (T2)	-2.07	.000*	-3.16	-0.97
8 weeks (T3)	-3.00	.000*	-4.30	-1.70
12 weeks (T4)	-2.39	.000*	-3.64	-1.14

*p-value < 0.05 significant

5.10.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 78 (below) shows that when the mean differences between two groups were compared to the baseline mean on the McGill VAS (Q16) Scale, active laser was significantly different from sham laser at all three successive time points. For time point 2, the mean difference was -2.71 ($p = 0.001$); for time point 3 it was -3.65 ($p = 0.000$); and for time point 4 it was 3.04 ($p = 0.003$). The overall comparison effect mean difference was -1.70 ($p = 0.000 < 0.05$), showing statistically significant difference between two groups.

Table 78 **– McGill VAS (Q16) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect**

McGill VAS (Q16) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-2.71	.001*	-4.31	-1.12
Time point 1 Vs Time point 3	-3.65	.000*	-5.59	-1.71
Time point 1 Vs Time point 4	3.04	.003*	1.11	4.96
Overall comparison effect	-1.70	.000*	-2.55	-.86

*p-value < 0.05 significant

5.11 McGill Pain Questionnaire Present Pain Intensity (PPI) – (Q17)

5.11.1 Comparison Within Each Group

Table 79 and Figure 12 (below) show the McGill Present Pain Intensity (PPI) Scale – (Q17) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores were significantly reduced, indicating improvement over time. Mean scores for the four time points were 2.75 (week 0); 0.75 (week 4); 0.55 (week 8) and 0.65 (week 12).

Table 80 (below) shows that the mean differences between baseline and the three successive time points were 2.00, 2.20 and 2.10 respectively. The changes were significant ($p < 0.001$), indicating improvement in the McGill Present Pain Intensity (PPI) – (Q.17) score from baseline at all three successive time points. For the sham laser group, mean scores were 2.60 (week 0) to 2.10 (week 4), but reduced to 1.95 at week 8 and dropped slightly to 1.80 at week 12.

Mean differences between baseline and the successive three time points were 0.50, 0.65 and 0.80 respectively. This indicated there was no significant improvement at week 4 (time point 2) and week 8 (time point 3) with p values of 0.143 and 0.058

respectively, i.e. p > 0.05. However, there was statistically significant difference at week 12 (time point 4), with a p value of 0.020 < 0.05.

Table 79 – McGill Pain Questionnaire Present Pain Intensity (PPI) (Q17) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

McGill Pain Questionnaire - Present Pain Intensity (PPI) Q17 Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	2.75 (1.02)	2.34	3.16
	4 weeks (T2)	.75 (.79)	0.34	1.16
	8 weeks (T3)	.55 (.94)	0.14	0.96
	12 weeks (T4)	.65 (.93)	0.24	1.06
Sham laser (N=20)	Baseline week 0 (T1)	2.60 (.99)	2.12	3.08
	4 weeks (T2)	2.10 (1.17)	1.62	2.58
	8 weeks (T3)	1.95 (1.05)	1.47	2.43
	12 weeks (T4)	1.80 (1.06)	1.32	2.28

Table 80 – McGill Pain Questionnaire Present Pain Intensity (PPI) (Q17) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

McGill Pain Questionnaire - Q17 Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	2.00	.000*	1.42	2.58
		8 weeks (T3)	2.20	.000*	1.62	2.78
		12 weeks (T4)	2.10	.000*	1.52	2.68
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	0.50	.143	-0.17	1.17
		8 weeks (T3)	0.65	.058	-0.02	1.32
		12 weeks (T4)	0.80	.020*	0.13	1.47

*p-value < 0.05 significant

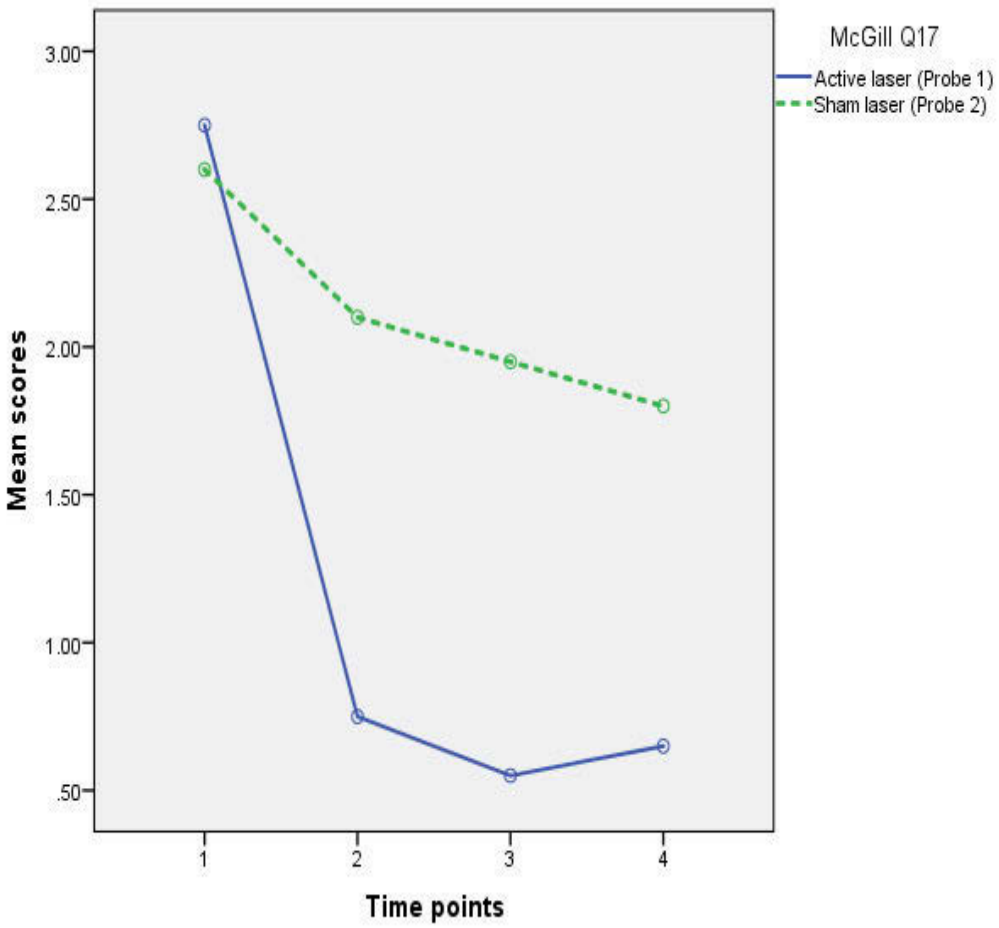

Figure 12 – McGill Pain Questionnaire Present Pain Intensity (PPI) (Q17) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.11.2 Comparison Between Groups at Each Time Point

Table 81 (below) shows that, when comparing between two groups (pairwise comparison) on the McGill PPI scale, mean difference scores for the active laser were statistically significantly greater than sham laser at week 4, 8 and 12. The mean difference for week 4, week 8 and week 12 were -1.35 ($p = 0.000$) and -1.40 ($p = 0.000$) and -1.15 ($p = 0.001$) respectively, showing statistically significant difference between two groups at week 4, week 8 and week 12 with p values < 0.005.

Table 81 – McGill Pain Questionnaire Present Pain Intensity (PPI) (Q17) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

McGill Pain Questionnaire Present Pain Intensity (PPI) Q17 Pairwise Comparisons				
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	95% Confidence Interval for Difference	
			Lower Bound	Upper Bound
Baseline (week 0) (T1)	.15	.640	-0.50	0.80
4 weeks (T2)	-1.35	.000*	-1.99	-0.71
8 weeks (T3)	-1.40	.000*	-2.04	-0.76
12 weeks (T4)	-1.15	.001*	-1.79	-0.51

*p-value < 0.05 significant

5.11.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 82 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on McGill PPI (Q17), active laser was significantly different from sham laser at all three successive time points. For time point 2, the mean difference was -1.50 ($p = 0.000$); for time point 3 it was -1.55 ($P = 0.001$); and for time point 4 it was -1.30 ($p = 0.003$). The overall comparison effect mean difference was -0.94 ($p < 0.001$), showing statistically significant difference between two groups.

Table 82 – McGill Pain Questionnaire Present Pain Intensity (PPI) (Q17) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

McGill Pain Questionnaire - Present Pain Intensity (PPI) Q17 Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-1.50	.000*	-2.27	-0.73
Time point 1 Vs Time point 3	-1.55	0.001*	-2.40	-0.70
Time point 1 Vs Time point 4	-1.30	0.003*	-2.14	-0.46
Overall comparison effect	-.94	0.000*	-1.38	-.49

*p-value < 0.05 significant

5.12 Credibility/Expectancy Questionnaire – Cognitively-based Credibility Scale (Q1-3)

5.12.1 Comparison Within Each Group

Table 83 and Figure 13 (below) show the Credibility/Expectancy Questionnaire – Cognitively-based Credibility Scale (Q1-3) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores were slightly increased. Mean scores for the four time points were 20.45 (week 0); 22.10 (week 4); 21.80 (week 8); 22.70 (week 12).

Table 84 (below) shows that on the Credibility/Expectancy Cognitively-based Credibility Scale (Q1-3), the mean differences between baseline and the three successive time points were -1.65, -1.35 and -2.25 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 20.75 (week 0), 19.10 (week 4), 18.50 (week 8) and 18.75 (week 12). Mean differences between baseline and the successive three time points were 1.65, 2.25 and 2.00 respectively. Sham laser did not show

statistically significant differences at all time points with p values > 0.05. This outcome showed that the blinding and placebo methods worked, producing a placebo effect that was the same between groups for C/E (Questions 1-3).

Table 83 – Credibility/Expectancy Cognitively Based Credibility Scale (Q1-3) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 and 12)

Credibility/Expectancy Questionnaire – Cognitively- based Credibility Scale (Q1-3) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	20.45(4.70)	-3.25	2.65
	4 weeks (T2)	22.10(4.42)	-0.65	6.65
	8 weeks (T3)	21.80(4.13)	-0.38	6.98
	12 weeks (T4)	22.70(4.63)	0.30	7.59
Sham laser (N=20)	Baseline week 0 (T1)	20.75(4.50)	18.66	22.83
	4 weeks (T2)	19.10(6.75)	16.51	21.68
	8 weeks (T3)	18.50(7.00)	15.89	21.10
	12 weeks (T4)	18.75(6.59)	16.17	21.33

Table 84 – Credibility/Expectancy Cognitively-Based Credibility Scale (Q1-3) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Credibility/ Expectancy Questionnaire – Cognitively-based Credibility Scale (Q1-3) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-1.65	.248	-4.47	1.17
		8 weeks (T3)	-1.35	.344	-4.17	1.47
		12 weeks (T4)	-2.25	.116	-5.07	0.57
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	1.65	.410	-2.32	5.62
		8 weeks (T3)	2.25	.262	-1.72	6.22
		12 weeks (T4)	2.00	.318	-1.97	5.97

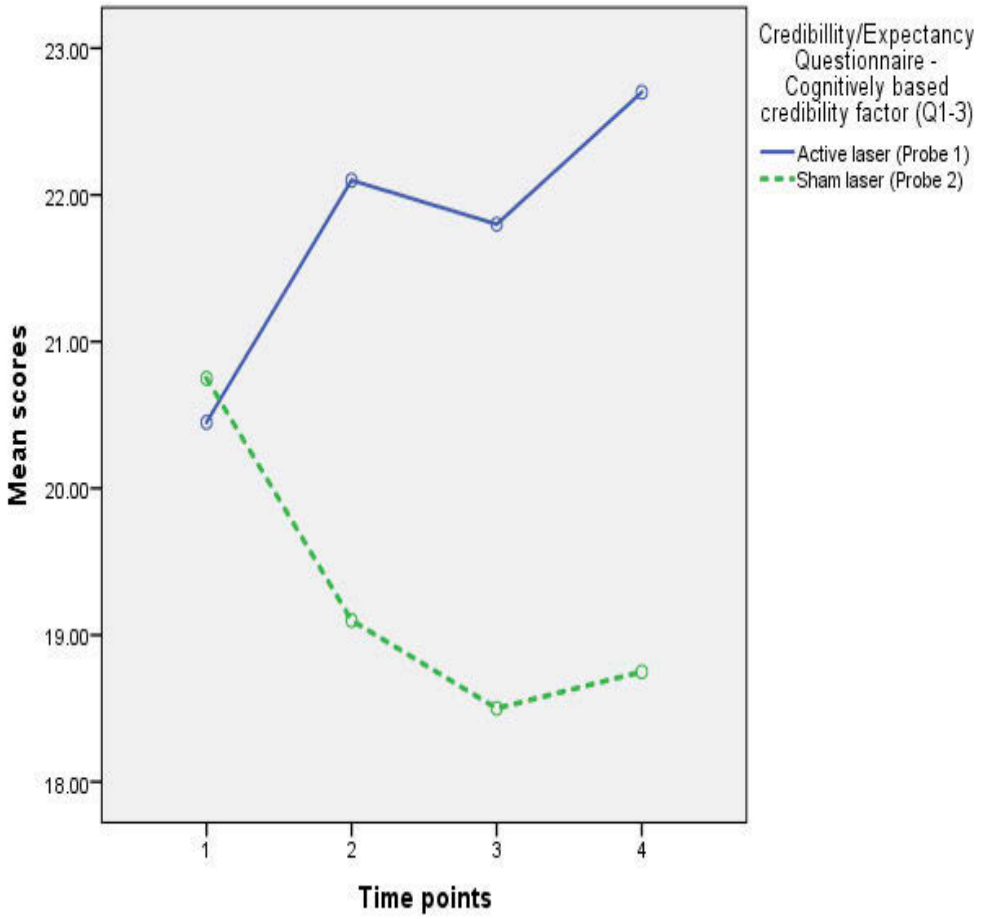

Figure 13 – Credibility/Expectancy Cognitively-Based Credibility Scale (Q1-3) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.12.2 Comparison Between Groups at Each Time Point

Table 85 (below) shows that, when comparing between two groups (pairwise comparison), mean difference scores for active laser on the C/E Cognitively-based Credibility Scale (Q1-3) were significantly different from sham laser scores at week 12, but not at weeks 4 and 8. Mean differences for week 4 and week 8 were 3.00 ($p = 0.105$) and 3.30 ($p = 0.078$) respectively. However, the mean differences for week 12 was 3.95 ($p = 0.035$) with a p value < 0.05.

Table 85 – Credibility/Expectancy Cognitively-Based Credibility Scale (Q1-3) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Credibility/Expectancy Questionnaire – Cognitively-based Credibility Scale (Q1-3) - Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-0.30	.838	-3.25	2.65
4 weeks (T2)	3.00	.105	-0.66	6.66
8 weeks (T3)	3.30	.078	-0.38	6.98
12 weeks (T4)	3.95	.035*	0.30	7.60

*p-value < 0.05 significant

5.12.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 86 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on the C/E Cognitively-based Credibility Scale (Q1-3), active laser was not significantly different from sham laser at all time points. The mean difference for time point 2 was 3.30 ($p = 0.129$); for time point 3 it was 3.60 ($p = 0.123$); for time point 4 it was 4.25 ($p = 0.075$); and the overall comparison effect mean difference was 3.67 ($p = 0.062$).

Table 86 – Credibility/Expectancy Cognitively-Based Credibility Scale (Q1-3) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Credibility/Expectancy Questionnaire –Cognitively-based Credibility Scale (Q1-3) Between Groups Comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P value	Lower	Upper
Time point 1 Vs Time point 2	3.30	.129	-1.01	7.61
Time point 1 Vs Time point 3	3.60	.123	-1.024	8.224
Time point 1 Vs Time point 4	4.25	.075	-0.45	8.95
Overall comparison effect	3.67	.062	-0.14	5.11

5.13 Credibility/Expectancy Affectively-based Expectancy Scale (Q4-6)

5.13.1 Comparison Within Each Group

Table 87 and Figure 14 (below) show the C/E Affectively-based Expectancy Scale (Q4-6) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 20.85 (week 0); 21.75 (week 4); 21.65 (week 8); 22.00 (week 12). Table 88 (below) shows that mean differences between baseline and three successive time points were -0.90, -0.80 and -1.15 respectively. Active laser did not show statistically significant differences at all time points, with p values > 0.05.

For the sham laser group, mean scores were 21.10 (week 0), 17.60 (week 4), 15.90 (week 8) and 15.80 (week 12). Mean differences between baseline and the successive three time points were 3.50, 5.20 and 5.30 respectively. Sham laser showed statistically significant differences at time points 3 and 4 with p values of 0.16 and 0.14 respectively, being < 0.05.

Table 87 – Credibility Expectancy Affectively-Based Expectancy Scale (Q4-6) Mean, Standard Deviation & Confidence Interval for Active Laser &Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

Credibility/Expectancy-Affectively-based Expectancy Scale (Q4-6) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	20.85 (4.20)	-2.92	2.42
	4 weeks (T2)	21.75 (4.48)	0.33	7.96
	8 weeks (T3)	21.65 (4.88)	1.69	9.80
	12 weeks (T4)	22.00 (5.04)	2.20	10.19
Sham laser (N=20)	Baseline week 0 (T1)	21.10 (4.14)	19.21	22.99
	4 weeks (T2)	17.60 (7.14)	14.89	20.30
	8 weeks (T3)	15.90 (7.51)	13.03	18.76
	12 weeks (T4)	15.80 (7.23)	12.97	18.62

Table 88 – Credibility/Expectancy Affectively-Based Expectancy Scale (Q4-6) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Credibility Expectancy-Affectively-based Expectancy Scale (Q4-6) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	- 0.90	.544	- 3.84	2.04
		8 weeks (T3)	- 0.80	.589	- 3.74	2.14
		12 weeks (T4)	- 1.15	.438	- 4.09	1.79
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	3.50	.100	- 0.69	7.69
		8 weeks (T3)	5.20	.016*	1.01	9.39
		12 weeks (T4)	5.30	.014*	1.11	9.49

*p-value < 0.05 significant

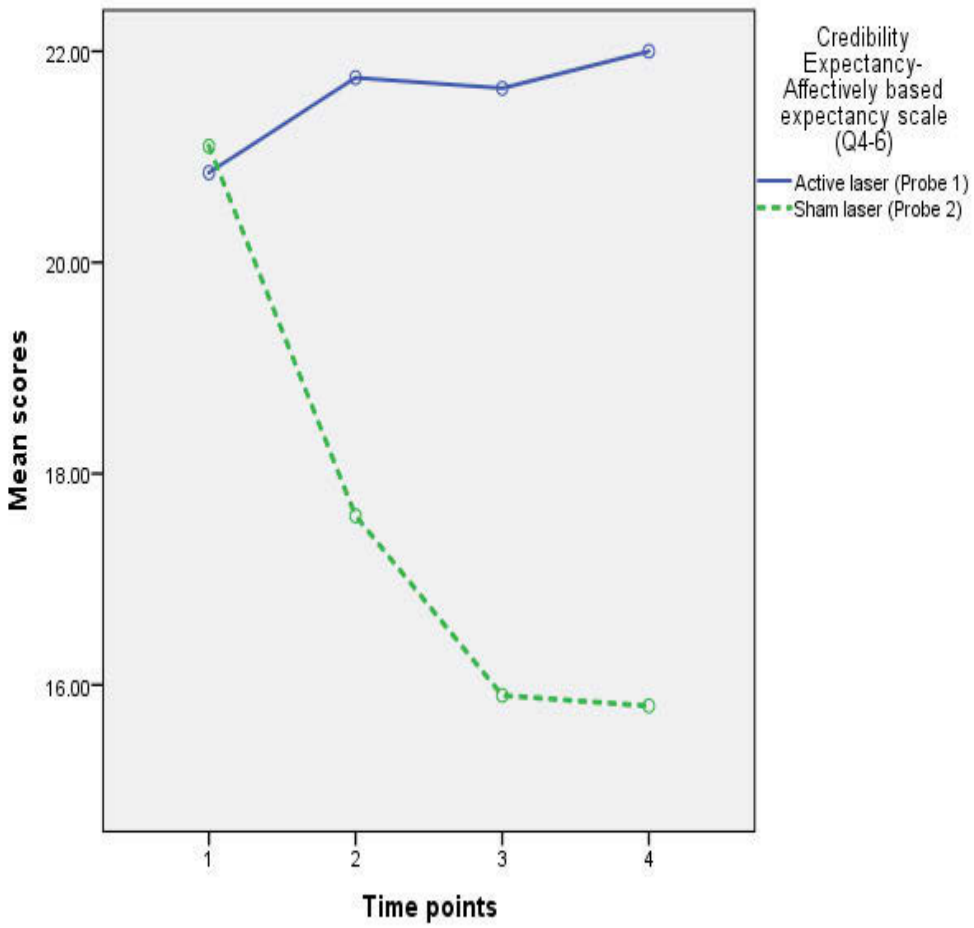

Figure 14 – Credibility/Expectancy Affectively-Based Expectancy Scale (Q4-6) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.13.2 Comparison Between Groups at Each Time Point

Table 89 (below) shows that, when comparing between two groups (pairwise comparison) on the C/E Affectively-based Expectancy Scale (Q4-6), mean difference scores for active laser were statistically significantly different from sham laser at time points 2, 3 and 4. Mean differences for time points 2, 3 and 4 were 4.15 ($p = 0.034$), 5.75 ($p = 0.007$) and 6.20 ($p = 0.003$) respectively with p values < 0.05.

Table 89 – Credibility/Expectancy Affectively Based Expectancy Scale (Q4-6) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Credibility Expectancy- Affectively based expectancy scale (Q4-6) - Pairwise Comparisons				
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	95% Confidence Interval for Difference	
			Lower Bound	Upper Bound
Baseline (week 0) (T1)	-0.25	.851	-2.92	2.42
4 weeks (T2)	4.15	.034*	0.33	7.97
8 weeks (T3)	5.75	.007*	1.69	9.81
12 weeks (T4)	6.20	.003*	2.21	10.19

*p-value < 0.05 significant

5.13.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 90 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on the C/E Affectively-based Expectancy Scale (Q4-6), active laser was statistically significantly different from sham laser at all time points. Mean difference for time point 2 was 4.40 ($p = 0.046$); for time point 3 it was 6.00 ($p = 0.011$); and for time point 4 it was 6.45 ($p = 0.005$). The overall comparison effect mean difference was 3.96 ($p = 0.008 < 0.05$).

Table 90 – Credibility/Expectancy Affectively-Based Expectancy Scale (Q4-6) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Credibility/Expectancy Affectively-based Expectancy Scale (Q4-6) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower	Upper
Time point 1 Vs Time point 2	4.40	.046	0.08	8.72
Time point 1 Vs Time point 3	6.00	.011*	1.47	10.53
Time point 1 Vs Time point 4	6.45	.005*	2.04	10.86
Overall comparison effect	3.96	.008*	1.097	6.828

*p-value < 0.05 significant

5.14 Credibility Expectancy (Q 1-6) – Think & Feel Scale Cognitively-based Credibility (Q1-3) & Affectively-based Expectancy Scale (Q4-6)

5.14.1 Comparison Within Each Group

Table 91 and Figure 15 (below) show the Credibility/Expectancy Questionnaire Think & Feel Scale (Q1-6) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores for the four time points were 41.30 (time point 1); 43.85 (time point 2); 43.45 (time point 3); and 44.70 (time point 4).

Table 92 (below) shows that the mean differences between baseline and the three successive time points were -2.55, -2.15 and -3.40 respectively. Active laser did not show statistically significant differences at all time points, with p values > 0.05.

For the sham laser group, mean scores were 41.85 (time point 1), 36.70 (time point 2), 34.40 (time point 3) and 34.55 (time point 4). Mean differences between baseline and the three successive time points were 5.15, 7.45 and 7.30 respectively. Sham laser did not show statistically significant differences at all time points, with p values > 0.05.

Table 91 – Credibility/Expectancy Think & Feel Scale (Q 1-6) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 and 12)

Credibility/Expectancy - Think & Feel Scale (Q 1-6) Group	Time Point (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	41.30 (8.39)	37.45	45.16
	4 weeks (T2)	43.85 (8.33)	40.00	47.71
	8 weeks (T3)	43.45 (8.78)	39.60	47.31
	12 weeks (T4)	44.70 (9.10)	40.85	48.56
Sham laser (N=20)	Baseline week 0 (T1)	41.85 (7.88)	36.31	47.39
	4 weeks (T2)	36.70 (13.39)	31.16	42.24
	8 weeks (T3)	34.40 (14.14)	28.86	39.94
	12 weeks (T4)	34.55 (13.32)	29.01	40.09

Table 92 – Credibility/Expectancy Think & Feel Scale (Q 1-6) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Credibility Expectancy- Think & Feel Scale (Q 1-6) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-2.55	.788	-9.74	4.64
		8 weeks (T3)	-2.15	.861	-9.34	5.04
		12 weeks (T4)	-3.40	.602	-10.59	3.79
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	5.15	.560	-5.18	15.48
		8 weeks (T3)	7.45	.239	-2.88	17.78
		12 weeks (T4)	7.30	.256	-3.03	17.63

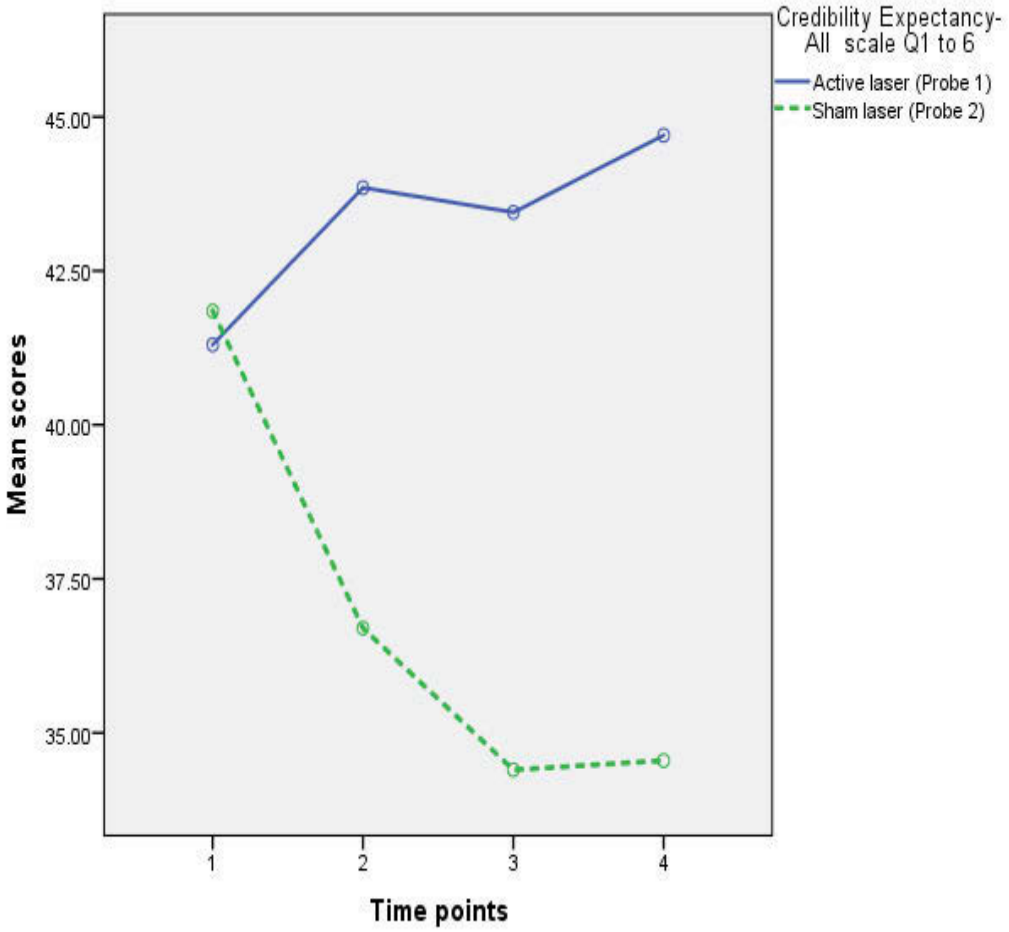

Figure 15 – Credibility/Expectancy All-Scale – Think & Feel Scale (Q1-6) Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.14.2 Comparison Between Groups at Each Time Point

Table 93 (below) shows that, when comparing between two groups (pairwise comparison) on the Think & Feel Scale (Q1-6), mean difference scores for active laser were not statistically significantly different from sham laser at time point 2, but were statistically different at time points 3 and 4. Mean differences for time points 2, 3 and 4 were 7.15 ($p = 0.050$), 9.05 ($p = 0.020$) and 10.15 ($p = 0.008$) respectively.

Table 93 – Credibility/Expectancy Think & Feel Scale (Q1-6) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Credibility/Expectancy Think & Feel Scale (Q1-6) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-0.55	.832	-5.76	4.66
4 weeks (T2)	7.15	.050	0.01	14.29
8 weeks (T3)	9.05	.020*	1.51	16.59
12 weeks (T4)	10.15	.008*	2.85	17.45

*p-value < 0.05 significant

5.14.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 94 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on the C/E Think & Feel Scale (Q1-6), active laser was statistically significantly different from sham laser at time points 3 and 4, but not at time point 2. The mean difference for time point 2 was 7.70 (p = 0.066); for time point 3 it was 9.60 (p = 0.032); and for time point 4 it was 10.70 (p = 0.016). The overall comparison effect mean difference was 6.45 (p = 0.018).

Table 94 – Credibility/Expectancy Think & Feel Scale (Q 1-6) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Credibility Expectancy- Think & feel scale (Q 1-6)		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	7.70	.066	-0.55	15.95
Time point 1 Vs Time point 3	9.60	.032*	0.85	18.35
Time point 1 Vs Time point 4	10.70	.016*	2.07	19.33
Overall comparison effect	6.45	.018*	1.18	11.72

*p-value < 0.05 significant

5.15 Working Alliance Inventory (WAI) Short Form (C) – Task (Q1, 2, 8, 12)

5.15.1 Comparison Within Each Group

Table 95 and Figure 16 (below) show the WAI Short Form (C) Task (Q1, 2, 8, 12) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores for the four time points were 24.80 (time point 1); 25.40 (time point 2); 25.55 (time point 3); and 26.05 (time point 4).

Table 96 (below) shows that the mean differences between the baseline and the successive three time points were -0.60, -0.75 and -1.25 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group the mean scores were 23.60 (time point 1), 22.20 (time point 2), 22.45 (time point 3) and 22.65 (time point 4). The mean differences between the baseline and the successive three time points were 1.40, 1.15 and 0.95 respectively. Sham laser did not show statistically significant differences at all time points with p values > 0.05.

Table 95 – WAI (C) Task (Q1, 2, 8, 12) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 and 12)

WAI (C) Task (Q1, 2, 8, 12) Group	Time Point (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	24.80 (3.29)	23.49	26.11
	4 weeks (T2)	25.40 (2.66)	24.09	26.71
	8 weeks (T3)	25.55 (3.24)	24.24	26.86
	12 weeks (T4)	26.05 (2.48)	24.74	27.36
Sham laser (N=20)	Baseline week 0 (T1)	23.60 (4.08)	21.49	25.71
	4 weeks (T2)	22.20 (5.77)	20.09	24.31
	8 weeks (T3)	22.45 (4.39)	20.34	24.56
	12 weeks (T4)	22.65 (4.56)	20.54	24.76

Table 96 – WAI (C) Task (Q1, 2, 8, 12) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WAI (C) Task (Q1, 2, 8, 12) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.60	.520	-2.45	1.25
		8 weeks (T3)	-0.75	.422	-2.60	1.10
		12 weeks (T4)	-1.25	.182	-3.10	0.60
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	1.40	.354	-1.59	4.39
		8 weeks (T3)	1.15	.446	-1.84	4.14
		12 weeks (T4)	0.95	.529	-2.04	3.94

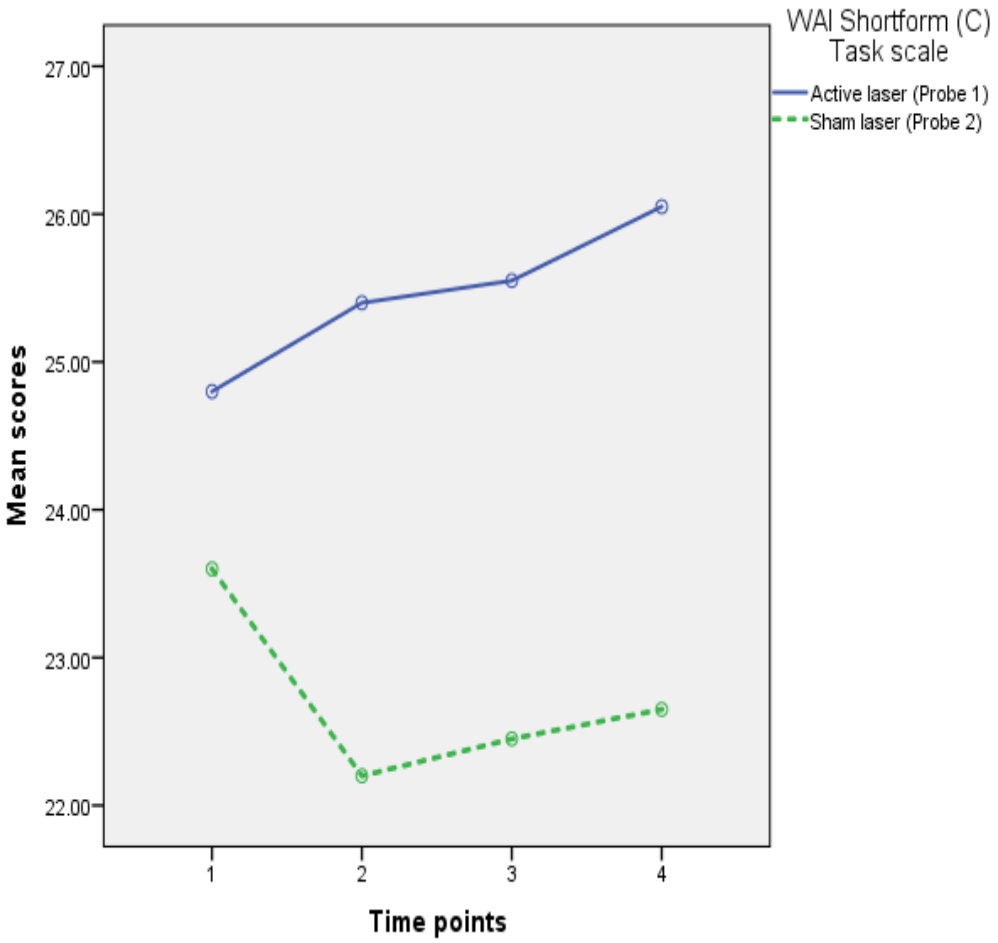

Figure 16 – WAI (C) Task (Q1, 2, 8, 12) Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.15.2 Comparison Between Groups at Each Time Point

Table 97 (below) shows that when comparing between two groups (pairwise comparison) on WAI (C) Task (Q1, 2, 8, 12), mean difference scores for active laser were statistically significantly different from sham laser at time points 2, 3 and 4. Mean differences for time points 2, 3 and 4 were 3.20 ($p = 0.030$), 3.10 ($p = 0.015$) and 3.40 ($p = 0.006$) respectively with p values < 0.05.

Table 97 – WAI (C) Task (Q1, 2, 8, 12) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WAI Short Form (C) Task (Q1, 2, 8, 12) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	1.20	.312	-1.17	3.57
4 weeks (T2)	3.20	.030*	0.32	6.08
8 weeks (T3)	3.10	.015*	0.63	5.57
12 weeks (T4)	3.40	.006*	1.05	5.75

*p-value < 0.05 significant

5.15.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks)

Table 98 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on WAI (C) Task (Q1, 2, 8, 12), active laser was only statistically significantly different from sham laser for the overall comparison effect, , but not at time points 2, 3 and 4. The mean difference for time point 2 was 2.00 ($p = 0.202$); for time point 3 it was 1.90 ($p = 0.117$); and for time point 4 it was 2.20 ($p = 0.089$). Overall comparison effect mean difference was 2.73 ($p = 0.013 < 0.05$), which is statistically significantly different between two groups.

Table 98 – WAI (C) Task (Q1, 2, 8, 12) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WAI (C) Task (Q1, 2, 8, 12) Between groups comparison from baseline week 0 (Time Point 1) over Time Point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	2.00	0.202	-1.12	5.12
Time point 1 Vs Time point 3	1.90	0.117	-0.50	4.30
Time point 1 Vs Time point 4	2.20	0.089	-0.35	4.75
Overall comparison effect	2.73	0.013*	0.62	4.83

*p-value < 0.05 significant

5.16 Working Alliance Inventory Short Form (WAI-C) – Bond Scale Q3, 5, 7 & 9

5.16.1 Comparison Within Each Group

Table 99 and Figure 17 (below) show the WAI (C) Bond Scale (Q3, 5, 7 & 9) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores for the four time points were 25.10 (time point 1); 25.95 (time point 2); 26.30 (time point 3); and 26.55 (time point 4).

Table 100 (below) shows that the mean differences between baseline and three successive time points were -0.85, -1.20 and -1.45 respectively. Active laser did not show statistically significant differences at all time points, with p values > 0.05.

For the sham laser group, mean scores were 23.50 (time point 1), 24.40 (time point 2), 23.15 (time point 3) and 23.60 (time point 4). Mean differences between baseline and the three successive time points were -0.90, 0.35 and -0.10 respectively. Sham laser did not show statistically significant differences at all time points with p values > 0.05.

Table 99 – WAI (C) Bond Scale (Q3, 5,7 & 9) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Weeks 0, 4, 8 & 12)

WAI (C) - Bond Scale (Q3, 5, 7 & 9) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	25.10 (3.11)	23.83	26.37
	4 weeks (T2)	25.95 (3.03)	24.68	27.22
	8 weeks (T3)	26.30 (2.64)	25.03	27.57
	12 weeks (T4)	26.55 (2.63)	25.28	27.82
Sham laser (N=20)	Baseline week 0 (T1)	23.50 (4.29)	21.60	25.41
	4 weeks (T2)	24.40 (4.39)	22.50	26.31
	8 weeks (T3)	23.15 (4.26)	21.25	25.06
	12 weeks (T4)	23.60 (4.17)	21.70	25.51

Table 100 – WAI (C) Bond Scale (Q3, 5, 7 & 9) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WAI (C) Bond Scale (Q3, 5,7 & 9) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.85	.350	-2.65	0.95
		8 weeks (T3)	-1.20	.189	-3.00	0.60
		12 weeks (T4)	-1.45	.113	-3.25	0.35
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.90	.508	-3.60	1.80
		8 weeks (T3)	0.35	.797	-2.35	3.05
		12 weeks (T4)	-0.10	.941	-2.80	2.60

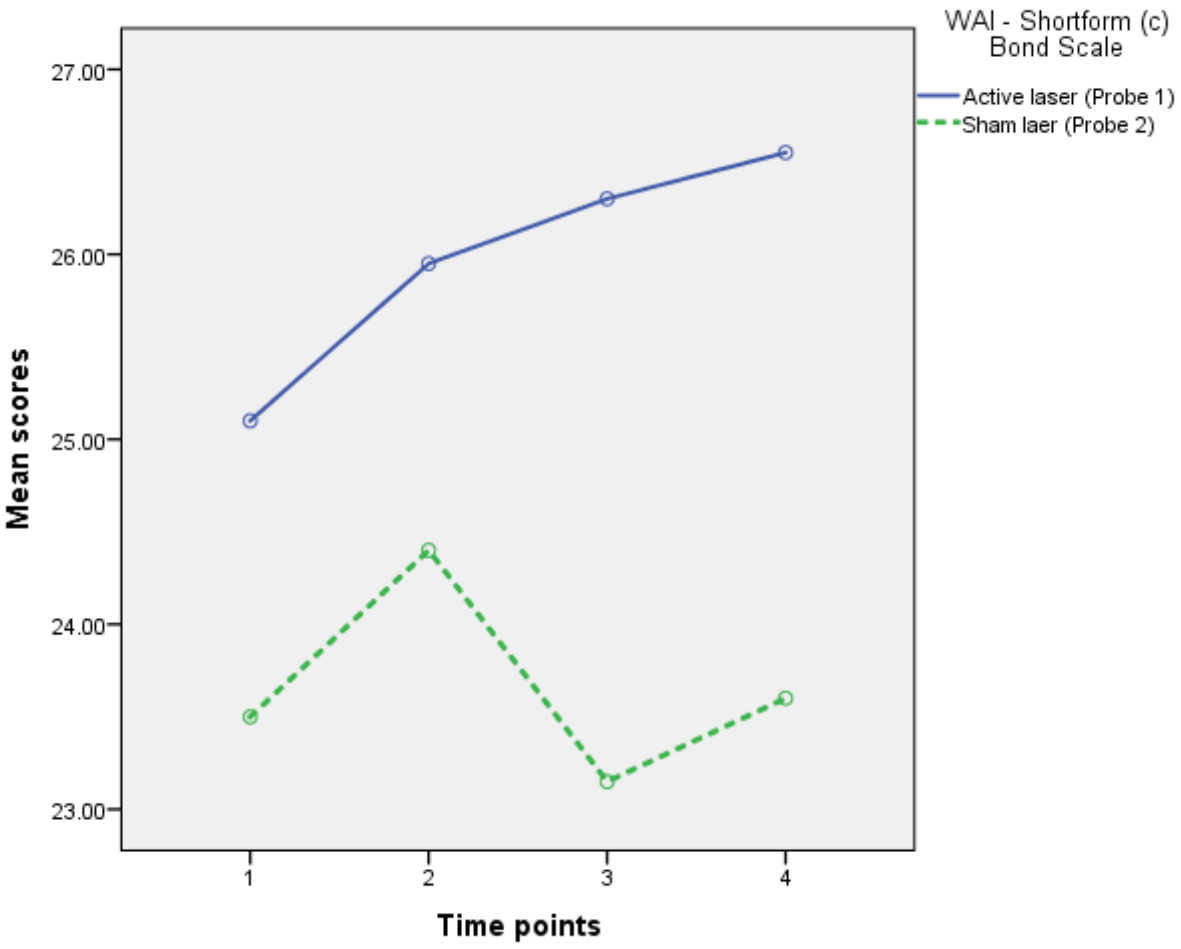

Figure 17 – WAI (C) Bond Scale (Q3, 5,7 & 9) Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.16.2 Comparison Between Groups at Each Time Point

Table 101 (below) shows that there was no statistically significant difference at baseline on the WAI (C) Bond Scale Q3, 5, 7 and 9). When comparing between two groups (pairwise comparison), mean difference scores for active laser were statistically significantly different from sham laser at time points 3 and 4, but not at time point 2. Mean differences for time points 2, 3 and 4 were 1.55 ($p = 0.202$), 3.15 ($p = 0.008$) and 2.95 ($p = 0.011$) respectively.

Table 101 – WAI (C) Bond Scale (Q3, 5, 7 & 9) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WAI -Short Form (C) Bond Scale (Q3, 5,7 & 9) - Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	1.60	.185	-0.80	4.00
4 weeks (T2)	1.55	.202	-0.87	3.97
8 weeks (T3)	3.15	.008*	0.88	5.42
12 weeks (T4)	2.95	.011*	0.72	5.18

*p-value < 0.05 significant

5.16.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 102 (below) shows that, when the mean differences between the two groups were compared to the baseline mean on the WAI (C) Bond Scale (Q3, 5, 7 & 9), active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was -0.05 ($p = 0.957$); for time point 3 it was 1.55 ($p = 0.100$); and for time point 4 it was 1.35 ($p = 0.145$). The overall comparison effect mean difference was 2.31 ($p = 0.032 < 0.05$), which is statistically significantly different between two groups.

Table 102 – Wai (C) Bond Scale Q3, 5, 7 & 9 Mean Difference Scores Between 2 Groups From Baseline Week 0 (Time Point 1) Over Time Points 2, 3 & 4 And Overall Comparison Effect

WAI (C) Bond Scale (Q3, 5, 7 & 9) Between groups comparison from baseline week 0 (Time point 1) over time points 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-0.05	0.957	-1.93	1.83
Time point 1 Vs Time point 3	1.55	0.100	-0.31	3.41
Time point 1 Vs Time point 4	1.35	0.145	-.49	3.19
Overall comparison effect	2.31	0.032*	0.21	4.42

*p-value < 0.05 significant

5.17 Working Alliance Inventory Short Form (WAI-C) – Goals (Q4, 6, 10 & 11)

5.17.1 Comparison Within Each Group

Table 103 and Figure 18 (below) show the WAI (C) – Goals (Q4, 6, 10 & 11) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores for the four time points were 18.45 (time point 1); 17.90 (time point 2); 18.65 (time point 3); and 18.50 (time point 4).

Table 104 (below) shows the mean differences between baseline and three successive time points were 0.55, -0.20 and -0.05 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 18.70 (time point 1), 16.45 (time point 2), 17.70 (time point 3) and 17.25 (time point 4). Mean differences between baseline and the three successive time points were 2.25, 1.00 and 1.45 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 103 – WAI (C) Goals (Q4, 6, 10 & 11) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

WAI Short Form (C) - Goals (Q4, 6, 10 & 11) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	18.45 (3.02)	17.00	19.90
	4 weeks (T2)	17.90 (2.47)	16.45	19.35
	8 weeks (T3)	18.65 (3.72)	17.20	20.10
	12 weeks (T4)	18.50 (3.69)	17.05	19.95
Sham laser (N=20)	Baseline week 0 (T1)	18.70 (4.31)	17.14	20.26
	4 weeks (T2)	16.45 (2.93)	14.89	18.01
	8 weeks (T3)	17.70 (2.90)	16.14	19.26
	12 weeks (T4)	17.25 (3.65)	15.69	18.81

Table 104 – WAI (C) Goals (Q4, 6, 10 & 11) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WAI Short Form (C) Goals (Q4, 6, 10 & 11) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	0.55	0.60	-1.51	2.61
		8 weeks (T3)	-0.20	0.85	-2.26	1.86
		12 weeks (T4)	-0.05	0.96	-2.11	2.01
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	2.25	0.05	0.05	4.45
		8 weeks (T3)	1.00	0.37	-1.20	3.20
		12 weeks (T4)	1.45	0.19	-0.75	3.65

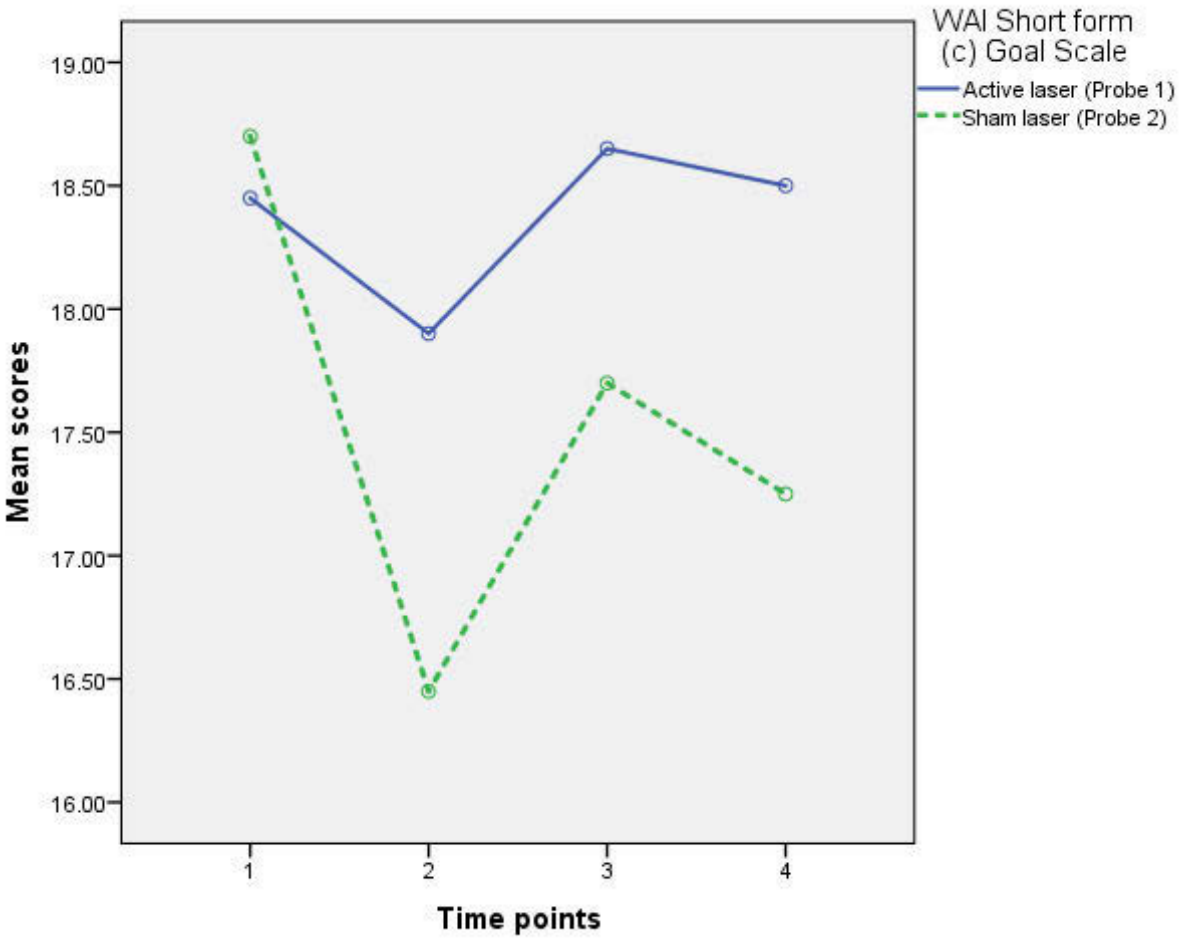

Figure 18 – WAI (C) Goals (Q4, 6, 10 & 11) Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.17.2 Comparison Between Groups at Each Time Point

Table 105 (below) shows that there was no statistically significant difference at baseline between two groups WAI (C) Goals (Q4, 6, 10 & 11) Scale. When comparing between two groups (pairwise comparison) the mean difference scores for active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were 1.45 (p = 0.099), 0.95 (p = 0.373) and 1.25 (p = 0.289) respectively.

Table 105 – WAI (C) Goals (Q4, 6, 10 & 11) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WAI Short Form (C) Goals (Q4, 6, 10 & 11) - Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-0.25	.833	-2.63	2.13
4 weeks (T2)	1.45	.099	-0.28	3.18
8 weeks (T3)	0.95	.373	-1.19	3.09
12 weeks (T4)	1.25	.289	-1.10	3.60

5.17.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 106 (below) shows that when the mean differences between the two groups were compared to the baseline mean on the WAI (C) Goal Scale, active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was 1.70 ($p = 0.148$); for time point 3 it was 1.20 ($p = 0.284$); and for time point 4 it was -1.00 ($p = 0.609$). The overall comparison effect mean difference was 0.85 ($p = 0.304$).

Table 106 – WAI (C) Goals (Q 4, 6, 10 & 11) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WAI Short Form (C) Goal (Q4, 6, 10 & 11) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower	Upper
Time point 1 Vs Time point 2	1.70	0.148	-0.63	4.03
Time point 1 Vs Time point 3	1.20	0.284	-1.04	3.44
Time point 1 Vs Time point 4	-1.00	0.609	-4.92	2.92
Overall comparison effect	0.85	0.304	-0.80	2.50

5.18 Working Alliance Inventory Short Form (WAI-C) – All Scales (Tasks, Goals & Bond) (Q1-12)

5.18.1 Comparison Within Each Group

Table 107 and Figure 19 (below) show the WAI (C) – All scales (Tasks, Goals & Bond) (Q1-12) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points. Active laser mean scores for the four time points were 68.35 (time point 1); 69.25 (time point 2); 70.50 (time point 3); and 71.10 (time point 4).

Table 108 (below) shows the mean differences between baseline and three successive time points were -0.90, -2.15, and -2.75 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, the mean scores were 65.80 (time point 1), 63.05 (time point 2), 63.30 (time point 3) and 63.50 (time point 4). Mean differences between baseline and the three successive time points were 2.75, 2.50 and 2.30 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 107 – WAI (C) All Scales (Task, Goal & Bond) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

WAI Short Form (C) - All Scales (Task, Goal & Bond) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	68.35 (6.67)	65.22	71.48
	4 weeks (T2)	69.25 (6.46)	66.12	72.38
	8 weeks (T3)	70.50 (7.82)	67.37	73.63
	12 weeks (T4)	71.10 (7.05)	67.97	74.23
Sham laser (N=20)	Baseline week 0 (T1)	65.80 (10.71)	61.30	70.30
	4 weeks (T2)	63.05 (10.25)	58.55	67.55
	8 weeks (T3)	63.30 (9.44)	58.80	67.80
	12 weeks (T4)	63.50 (9.93)	59.00	68.00

Table 108 – WAI (C) All Scales (Task, Goal & Bond) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

WAI Short Form (C) - All Scales (Task, Goal & Bond) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.90	.686	-5.32	3.52
		8 weeks (T3)	-2.15	.336	-6.57	2.27
		12 weeks (T4)	-2.75	.219	-7.17	1.67
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	2.75	.392	-3.61	9.11
		8 weeks (T3)	2.50	.436	-3.86	8.86
		12 weeks (T4)	2.30	.473	-4.06	8.66

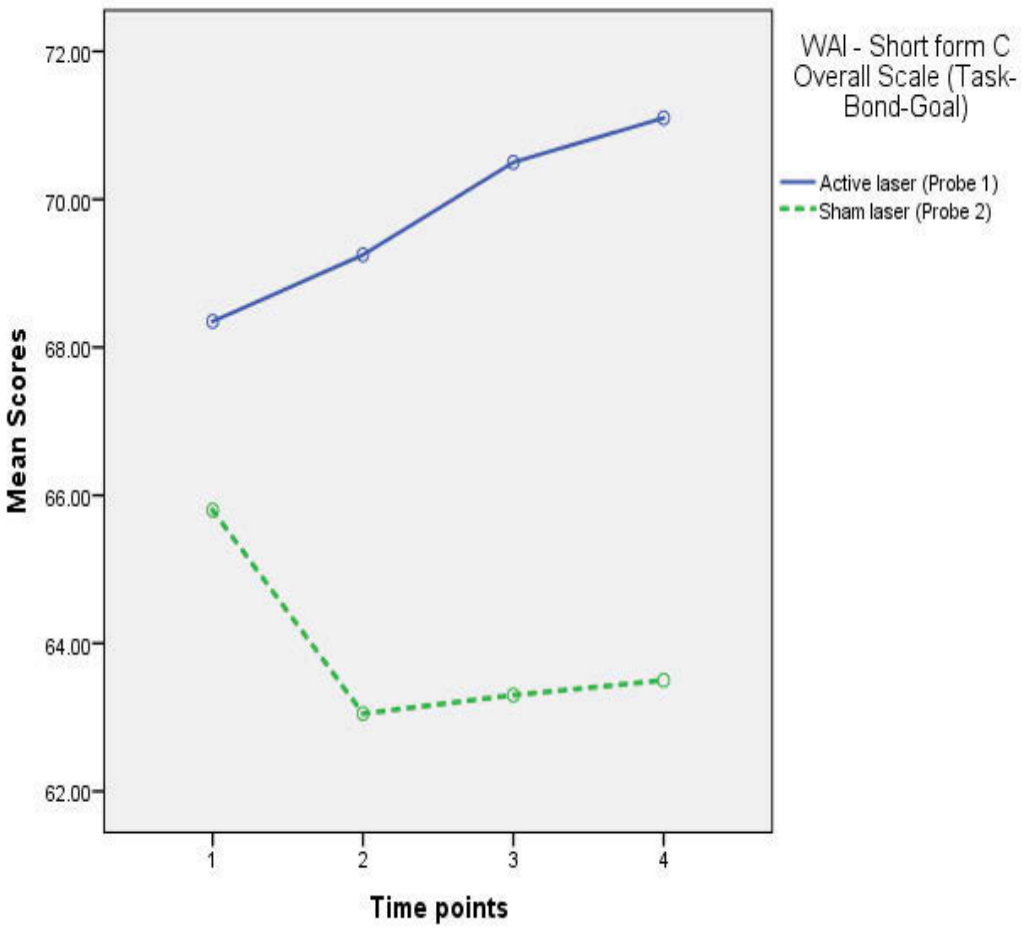

Figure 19 – WAI (C) All Scales (Task, Goal & Bond) Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.18.2 Comparison Between Groups at Each Time Point

Table 109 (below) shows there was no statistically significant difference at baseline between two groups in WAI (C) All Scales (Task, Goal & Bond). When comparing between two groups (pairwise comparison), mean difference scores for active laser were statistically significantly different from sham laser at all successive time points. The mean differences for time points 2, 3 and 4 were 6.20 ($p = 0.028$), 7.20 ($p = 0.12$) and 7.60 ($p = 0.008$) respectively, with all p values < 0.05.

Table 109 – WAI (C) All Scales (Task, Goal & Bond) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

WAI Short Form (C) - All Scales (Task, Goal & Bond) - Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	2.55	.372	-3.16	8.26
4 weeks (T2)	6.20	.028*	0.72	11.68
8 weeks (T3)	7.20	.012*	1.65	12.75
12 weeks (T4)	7.60	.008*	2.09	13.11

*p-value < 0.05 significant

5.18 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 110 (below) shows that, when the mean differences between the two groups were compared to the baseline mean in WAI (C) All Scales (Task, Goal & Bond), active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was 3.65 ($p = 0.188$); for time point 3 it was 4.65 ($p = 0.074$); and for time point 4 it was 5.05 ($p = 0.088$). However, the overall comparison effect mean difference was 5.89 ($p = 0.017 < 0.05$), indicating a statistically significant difference.

Table 110 – WAI (C) All Scales (Task, Goal & Bond) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

WAI Short Form (C) - All scales (task, goal & bond) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	3.65	0.188	-1.89	9.19
Time point 1 Vs Time point 3	4.65	0.074	-0.47	9.77
Time point 1 Vs Time point 4	5.05	0.088	5.05	2.85
Overall comparison effect	5.89	0.017*	1.12	10.65

*p-value < 0.05 significant

5.19 Multi-dimensional Health Locus of Control Short Form C (MHLC-C) – Internal Belief (Q1, 6, 8, 12, 13, 17)

5.19.1 Comparison Within Each Group

Table 111 and Figure 20 (below) show the Multi-dimensional Health Locus of Control (MHLC-C) – Internal Belief (Q1, 6, 8, 12, 13, 17) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 22.00 (time point 1); 22.60 (time point 2); 24.45 (time point 3); 24.20 (time point 4).

Table 112 (below) shows that the mean differences between baseline and three successive time points were -0.60, -2.45, and -2.20 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, the mean scores were 22.25 (time point 1), 22.30 (time point 2), 23.60 (time point 3) and 23.65 (time point 4). Mean differences between baseline and the three successive time points were -0.05, -1.35 and -1.40 respectively. Sham

laser showed no statistically significant differences at all time points with p values > 0.05.

Table 111 – Multi-Dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

Multi-dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	22.00 (8.75)	18.53	25.47
	4 weeks (T2)	22.60 (7.91)	19.13	26.07
	8 weeks (T3)	24.45 (6.16)	20.98	27.92
	12 weeks (T4)	24.20 (8.10)	20.73	27.67
Sham laser (N=20)	Baseline week 0 (T1)	22.25 (6.63)	19.58	24.92
	4 weeks (T2)	22.30 (6.62)	19.63	24.97
	8 weeks (T3)	23.60 (5.93)	20.93	26.27
	12 weeks (T4)	23.65 (4.53)	20.98	26.32

Table 112 – Multi-Dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8,12, 13, 17) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Multi-dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.60	.808	-5.51	4.31
		8 weeks (T3)	-2.45	.323	-7.36	2.46
		12 weeks (T4)	-2.20	.375	-7.11	2.71
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.05	.979	-3.82	3.72
		8 weeks (T3)	-1.35	.478	-5.12	2.42
		12 weeks (T4)	-1.40	.462	-5.17	2.37

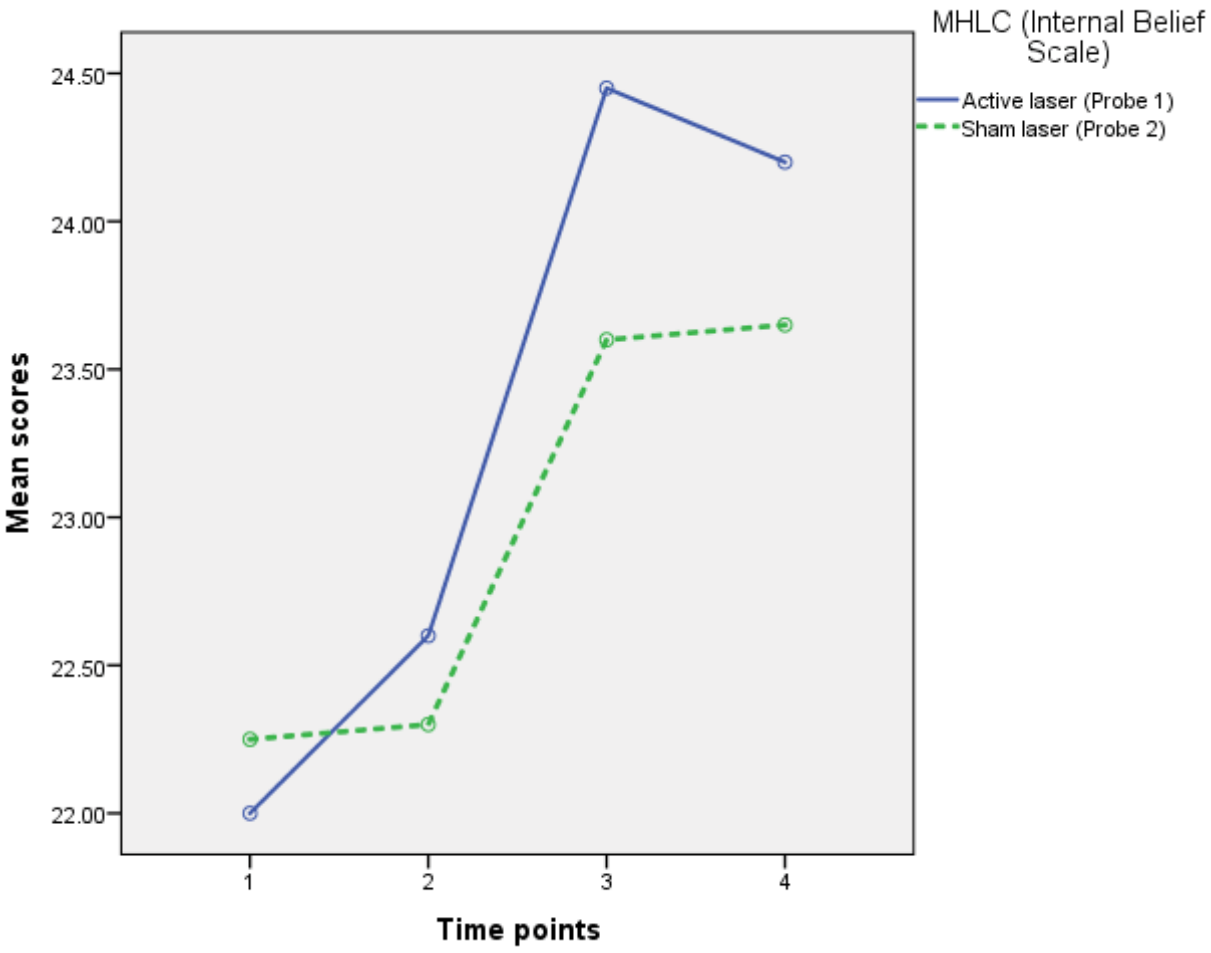

Figure 20 – Multi-Dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.19.2 Comparison Between Groups at Each Time Point

Table 113 (below) shows there was no statistically significant difference at baseline between two groups for the MHLC-C Internal Belief score. When comparing between two groups (pairwise comparison), mean difference scores for active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were -7.36 (p = 0.897), -7.11 (p = 0.659) and -3.82 (p = 0.792) respectively.

Table 113 – Multi-Dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Multi-dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-5.51	.919	-5.22	4.72
4 weeks (T2)	-7.36	.897	-4.37	4.97
8 weeks (T3)	-7.11	.659	-3.02	4.72
12 weeks (T4)	-3.82	.792	-3.65	4.75

5.19.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 114 (below) shows that when the mean differences between the two groups were compared to the baseline mean in the MHLC-C Internal Belief score, active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was 0.55 ($p = 0.819$); for time point 3 it was 1.10 ($p = 0.615$); and for time point 4 it was 0.80 ($p = 0.729$). The overall comparison effect mean difference was 0.36 ($p = 0.840$).

Table 114 – Multi-Dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Points 2, 3 & 4 & Overall Comparison Effect

Multi-dimensional Health Locus of Control (Form C) – Internal Belief (Q1, 6, 8, 12, 13, 17) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	0.55	0.819	-4.29	5.39
Time point 1 Vs Time point 3	1.10	0.615	-3.29	5.49
Time point 1 Vs Time point 4	0.80	0.729	-3.85	5.45
Overall comparison effect	0.36	0.840	-3.25	3.98

5.20 Multi-dimensional Health Locus of Control Form C (MHLC-C) – Chances (Q2, 4, 9, 11, 15, 16)

5.20.1 Comparison Within Each Group

Table 154 and Figure 21 (below) show the Multi-dimensional Health Locus of Control Form C (MHLC-C) – Chances (Q2, 4, 9, 11, 15, 16) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 15.20 (time point 1); 16.40 (time point 2); 17.15 (time point 3); and 16.70 (time point 4). Table 116 (below) shows that the mean differences between baseline and three successive time points were -1.20, -1.95 and -1.50 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 14.90 (time point 1), 13.75 (time point 2), 14.30 (time point 3) and 15.10 (time point 4). Mean differences between baseline and

the three successive time points were 1.15, 0.60 and -0.20 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 115 – MHLC-C Chances (Q2, 4, 9, 11, 15,16) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Weeks 0, 4, 8 & 12)

Multi-dimensional Health Locus of Control (Form C) – Chances (Q2, 4, 9, 11, 15, 16) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	15.20 (7.58)	11.66	18.75
	4 weeks (T2)	16.40 (8.05)	12.86	19.95
	8 weeks (T3)	17.15 (8.25)	13.61	20.70
	12 weeks (T4)	16.70 (7.94)	13.16	20.25
Sham laser (N=20)	Baseline week 0 (T1)	14.90 (5.54)	11.67	18.13
	4 weeks (T2)	13.75 (6.63)	10.52	16.98
	8 weeks (T3)	14.30 (7.97)	11.07	17.53
	12 weeks (T4)	15.10 (8.53)	11.87	18.33

Table 116 – MHLC-C – Chances (Q2, 4, 9, 11, 15, 16) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Multi-dimensional Health Locus of Control (Form C) – Chances (Q2, 4, 9, 11, 15, 16) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-1.20	.635	-6.21	3.81
		8 weeks (T3)	-1.95	.441	-6.96	3.06
		12 weeks (T4)	-1.50	.553	-6.51	3.51
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	1.15	.618	-3.42	5.72
		8 weeks (T3)	0.60	.795	-3.97	5.17
		12 weeks (T4)	-0.20	.931	-4.77	4.37

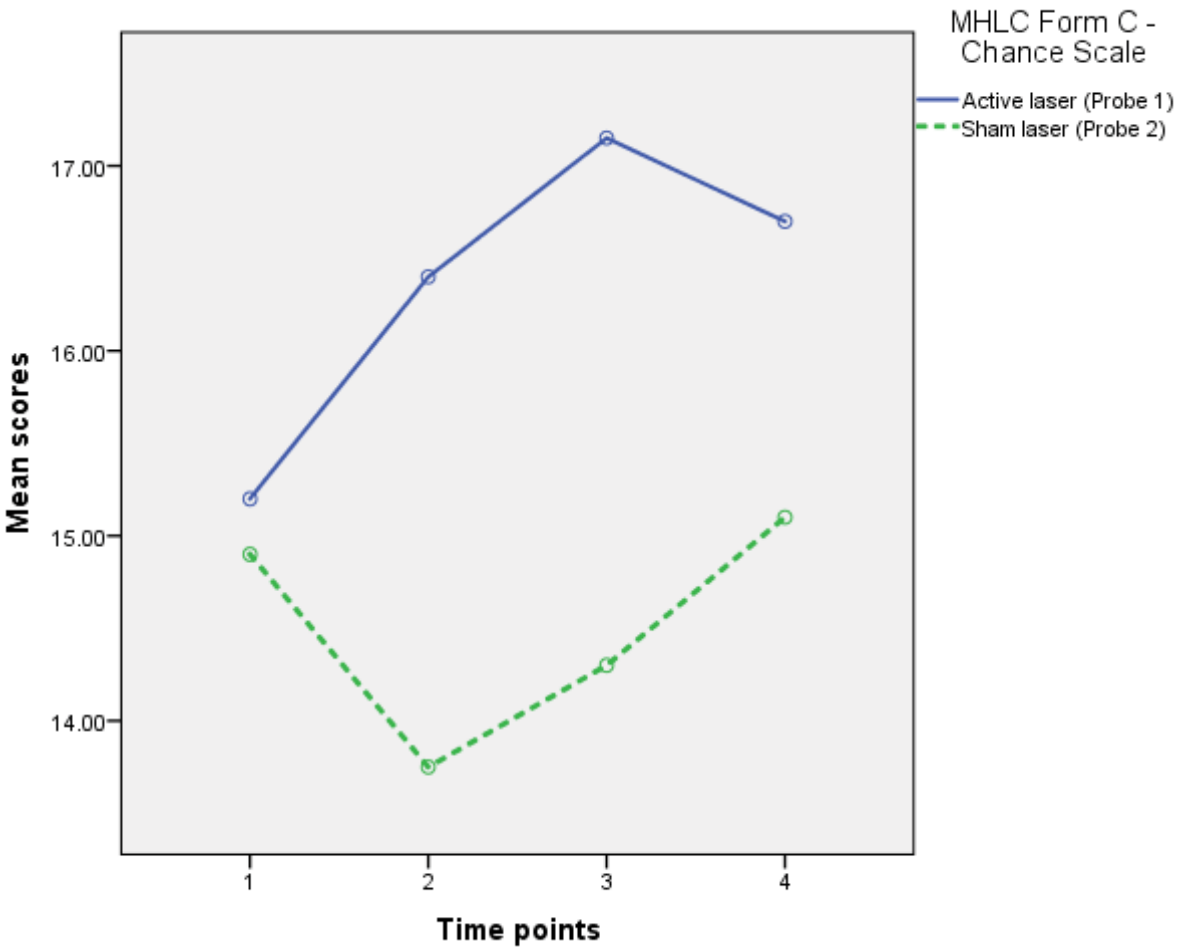

Figure 21 – MHLC-C – Chances (Q2, 4, 9, 11, 15, 16) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.20.2 Comparison Between Groups at Each Time Point

Table 117 (below) shows there was no statistically significant difference at baseline between two groups in the MHLC-C Chances scores. When comparing between two groups (pairwise comparison), mean difference scores for active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were 2.65 (p = 0.263), 2.85 (p = 0.274) and 1.60 (p = 0.543) respectively.

Table 117 – MHLC-C Chances (Q2, 4, 9, 11, 15, 16) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Multi-dimensional Health Locus of Control (Form C) – Chances (Q2, 4, 9, 11, 15, 16) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	0.30	.887	-3.95	4.55
4 weeks (T2)	2.65	.263	-2.07	7.37
8 weeks (T3)	2.85	.274	-2.34	8.04
12 weeks (T4)	1.60	.543	-3.68	6.88

5.20.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 118 (below) shows that when the mean differences between the two groups were compared to the baseline mean in the MHLC-C Chances scores, active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was 2.35 ($p = 1.000$); for time point 3 it was 2.55 ($p = 0.151$); and for time point 4 it was 1.30 ($p = 0.469$). The overall comparison effect mean difference was 1.85 ($p = 0.413$).

Table 118 – MHLC-C – Chances (Q2, 4, 9, 11, 15, 16) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Multidimensional Health Locus of Control (Form C) – Chances (Q2, 4, 9, 11, 15 & 16) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	2.35	0.100	-0.47	5.17
Time point 1 Vs Time point 3	2.55	0.151	-0.97	6.07
Time point 1 Vs Time point 4	1.30	0.469	-2.30	4.90
Overall comparison effect	1.85	0.413	-2.67	6.37

5.21 Multi-dimensional Health Locus of Control Form C (MHLC-C) – Powerful Others (Q3, 5, 7, 10, 14, 18)

5.21.1 Comparison Within Each Group

Table 119 and Figure 22 (below) show the Multi-dimensional Health Locus of Control Form C (MHLC-C) – Powerful Others (Q3, 5, 7, 10, 14, 18) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 21.65 (time point 1); 22.70 (time point 2); 23.35 (time point 3); and 23.55 (time point 4). Table 120 (below) shows that the mean differences between baseline and three successive time points were -1.05, -1.70, and -1.90 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 21.50 (time point 1), 21.35 (time point 2), 22.60 (time point 3) and 22.10 (time point 4). Mean differences between baseline and

the three successive time points were 0.15, -1.10 and -0.60 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 119 – MHLC-C – Powerful Others (Q3, 5,7, 10, 14, 18) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Weeks 0, 4, 8 & 12)

Multi-dimensional Health Locus of Control (Form C) –Powerful Others (Q3, 5, 7, 10, 14, 18) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	21.65 (5.99)	18.79	24.51
	4 weeks (T2)	22.70 (6.33)	19.84	25.56
	8 weeks (T3)	23.35 (7.01)	20.49	26.21
	12 weeks (T4)	23.55 (6.33)	20.69	26.41
Sham laser (N=20)	Baseline week 0 (T1)	21.50 (4.05)	19.53	23.47
	4 weeks (T2)	21.35 (4.69)	19.38	23.32
	8 weeks (T3)	22.60 (4.51)	20.63	24.57
	12 weeks (T4)	22.10 (4.44)	20.13	24.07

Table 120 – Powerful Others (Q3, 5, 7, 10, 14, 18) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Multi=dimensional Health Locus of Control (Form C) – - Powerful Others (Q3, 5, 7, 10, 14, 18) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-1.05	0.607	-5.10	3.00
		8 weeks (T3)	-1.70	0.405	-5.75	2.35
		12 weeks (T4)	-1.90	0.353	-5.95	2.15
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	0.15	0.915	-2.64	2.94
		8 weeks (T3)	-1.10	0.435	-3.89	1.69
		12 weeks (T4)	-0.60	0.670	-3.39	2.19

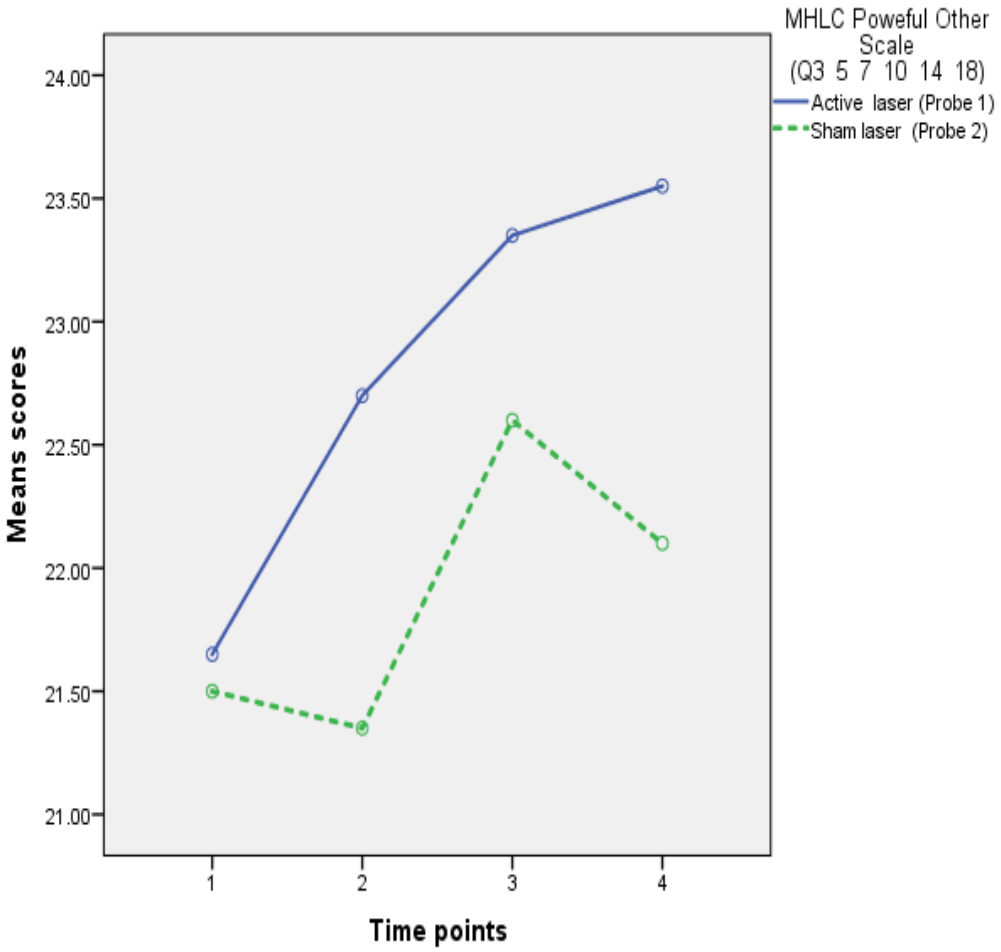

Figure 22 – MHLC-C – Powerful Others (Q3, 5, 7, 10, 14, 18) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.21.2 Comparison Between Groups at Each Time Point

Table 121 (below) shows there was no statistically significant difference at baseline between two groups in the MHLC-C Powerful Others' scores. When comparing between two groups (pairwise comparison), the mean difference scores for active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were 1.35 (p = 0.448), 0.75 (p = 0.69) and 1.45 (p = 0.407) respectively.

Table 121 – MHLC-C – Powerful Others (Q3, 5, 7, 10, 14, 18) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Multi-dimensional Health Locus of Control (Form C) – Powerful Others (Q3, 5, 7, 10, 14, 18) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	0.15	0.927	-3.12	3.42
4 weeks (T2)	1.35	0.448	-2.22	4.92
8 weeks (T3)	0.75	0.69	-3.02	4.52
12 weeks (T4)	1.45	0.407	-2.05	4.95

5.21.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 122 (below) shows that when the mean differences between the two groups were compared to the baseline mean, active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was 1.20 (p = 0.438); for time point 3 it was 0.60 (p = 0.689); and for time point 4 it was 1.30 (p = 0.368). The overall comparison effect mean difference was 0.93 (p = 0.548).

Table 122 – MHLC-C – Powerful Others (Q3, 5, 7, 10, 14, 18) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Multi-dimensional Health Locus of Control (Form C) –Powerful Others(Q3; 5, 7, 10, 14, 18) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	1.20	.438	-1.90	4.30
Time point 1 Vs Time point 3	0.60	.689	-2.41	3.61
Time point 1 Vs Time point 4	1.30	.368	-1.59	4.19
Overall comparison effect	0.93	.548	-2.16	4.01

5.22 Multi-dimensional Health Locus of Control Form C (MHLC-C) – Doctor Scale (Q3, 5, 14)

5.22.1 Comparison Within Each Group

Table 123 and Figure 23 (below) show the MHLC-C – Doctor Scale (Q3, 5, 14) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 12.40 (time point 1); 13.05 (time point 2); 13.65 (time point 3); and 13.80 (time point 4). Table 124 (below) shows that the mean differences between baseline and three successive time points were -0.65, -1.25, and -1.40 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 13.70 (time point 1), 13.05 (time point 2), 13.35 (time point 3) and 13.60 (time point 4). Mean differences between baseline and the three successive time points were 0.65, 0.35 and 0.10 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 123 – MHLC-C – Doctor Scale (Q3, 5, 14) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

Multi-dimensional Health Locus of Control (Form C) – Doctor Scale (Q3, 5, 14) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	12.40 (2.93)	10.93	13.87
	4 weeks (T2)	13.05 (3.41)	11.58	14.52
	8 weeks (T3)	13.65 (3.52)	12.18	15.12
	12 weeks (T4)	13.80 (3.33)	12.33	15.27
Sham laser (N=20)	Baseline week 0 (T1)	13.70 (2.54)	12.55	14.85
	4 weeks (T2)	13.05 (2.95)	11.90	14.20
	8 weeks (T3)	13.35 (2.21)	12.20	14.50
	12 weeks (T4)	13.60 (2.56)	12.45	14.75

Table 124 – MHLC-C – Doctor Scale (Q3, 5, 14) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Multi-dimensional Health Locus of Control (Form C) - Doctor Scale (Q3, 5, 14) Group	Time point Baseline Week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.65	.536	-2.73	1.43
		8 weeks (T3)	-1.25	.236	-3.33	0.83
		12 weeks (T4)	-1.40	.185	-3.48	0.68
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	0.65	.427	-0.97	2.27
		8 weeks (T3)	0.35	.669	-1.27	1.97
		12 weeks (T4)	0.10	.903	-1.52	1.72

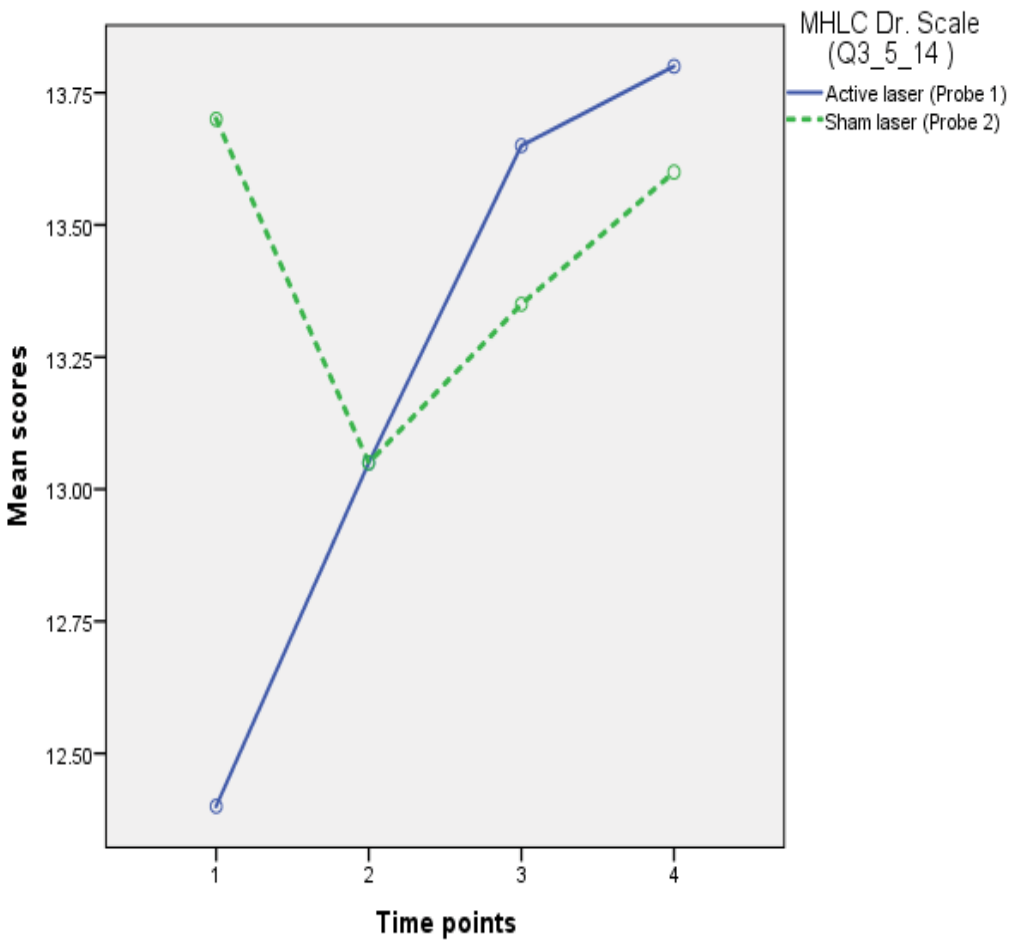

Figure 23 – MHLC-C – Doctor Scale (Q3, 5, 14) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.22.2 Comparison Between Groups at Each Time Point

Table 125 (below) shows there was no statistically significant difference at baseline between two groups in the MHLC-C Doctor Scale scores. When comparing between two groups (pairwise comparison), mean difference scores for active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were 0.00 (p = 1.00), 0.30 (p = 0.749) and 0.20 (p = 0.833) respectively.

Table 125 – MHLC-C – Doctor Scale (Q3, 5, 14) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Multi-dimensional Health Locus of Control (Form C) - Doctor Scale (Q3, 5, 14) Pairwise Comparisons				
			95% Confidence Interval for Difference	
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	Lower Bound	Upper Bound
Baseline (week 0) (T1)	-1.30	0.142	-3.05	0.45
4 weeks (T2)	0.00	1.000	-2.04	2.04
8 weeks (T3)	0.30	0.749	-1.58	2.18
12 weeks (T4)	0.20	0.833	-1.70	2.10

5.22.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 126 (below) shows that, when the mean differences between the two groups were compared to the baseline mean in the MHLC-C Doctor Scale scores, active laser was statistically significantly different from sham laser only at time point 3, but not at time points 2 and 4. The mean difference for time point 2 was 1.30 (p = 0.230); for time point 3 it was 1.60 (p = 0.041); and for time point 4 it was 1.50 (p = 0.102). The overall comparison effect mean difference was 0.925 (p = 0.548).

Table 126 – MHLC-C – Doctor Scale (Q3, 5, 14) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Points 2, 3 & 4 & Overall Comparison Effect

Multi-dimensional Health Locus of Control (Form C) - Doctor Scale (Q3, 5, 14) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	1.30	0.230	-0.86	3.46
Time point 1 Vs Time point 3	1.60	0.041*	0.073	3.13
Time point 1 Vs Time point 4	1.50	0.102	-.312	3.31
Overall comparison effect	0.925	0.548	-2.16	4.01

*p-value < 0.05 significant

5.23 Multi-dimensional Health Locus of Control Form C (MHLC-C) – Other People Scale (Q7, 10 , 18)

5.23.1 Comparison Within Each Group

Table 127 and Figure 24 (below) show the Multi-dimensional Health Locus of Control Form C (MHLC-C) – Other People Scale (Q7, 10, 18) mean, standard deviation and confidence interval for active laser and sham laser groups over four time points.

Active laser mean scores for the four time points were 9.25 (time point 1); 9.65 (time point 2); 9.70 (time point 3); and 9.75 (time point 4). Table 128 (below) shows that mean differences between baseline and three successive time points were -0.40, -0.45, and -0.50 respectively. Active laser did not show statistically significant differences at all time points with p values > 0.05.

For the sham laser group, mean scores were 7.80 (time point 1), 8.30 (time point 2), 9.25 (time point 3) and 8.50 (time point 4). Mean differences between baseline and the three successive time points were -0.50, -1.45 and -0.70 respectively. Sham laser showed no statistically significant differences at all time points with p values > 0.05.

Table 127 – MHLC-C – Other People Scale (Q7, 10, 18) Mean, Standard Deviation & Confidence Interval for Active Laser & Sham Laser Over 4 Time Points (Week 0, 4, 8 & 12)

Multi-dimensional Health Locus of Control (Form C) – Other People Scale (Q7, 10, 18) Group	Time (T)	Mean (SD)	95% Confidence Interval	
			Lower Bound	Upper Bound
Active laser (N=20)	Baseline week 0 (T1)	9.25 (4.08)	7.41	11.09
	4 weeks (T2)	9.65 (3.84)	7.81	11.49
	8 weeks (T3)	9.70 (4.38)	7.86	11.54
	12 weeks (T4)	9.75 (4.19)	7.91	11.59
Sham laser (N=20)	Baseline week 0 (T1)	7.80 (3.29)	6.39	9.21
	4 weeks (T2)	8.30 (2.68)	6.89	9.71
	8 weeks (T3)	9.25 (3.40)	7.84	10.66
	12 weeks (T4)	8.50 (3.28)	7.09	9.91

Table 128 – MHLC-C - Other People Scale (Q7, 10, 18) Mean Difference Scores for 2 Groups Compared to Baseline at Each of 3 Time Points

Multi-dimensional Health Locus of Control (Form C) - Other People Scale (Q7, 10, 18) Group	Time point Baseline week 0 (T1)	Time points (T)	Mean Difference compared to baseline	P-value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Active laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.40	0.760	-3.00	2.20
		8 weeks (T3)	-0.45	0.731	-3.05	2.15
		12 weeks (T4)	-0.50	0.703	-3.10	2.10
Sham laser (N=20)	Baseline (week 0) (T1)	4 weeks (T2)	-0.50	0.620	-2.50	1.50
		8 weeks (T3)	-1.45	0.153	-3.45	0.55
		12 weeks (T4)	-0.70	0.488	-2.70	1.30

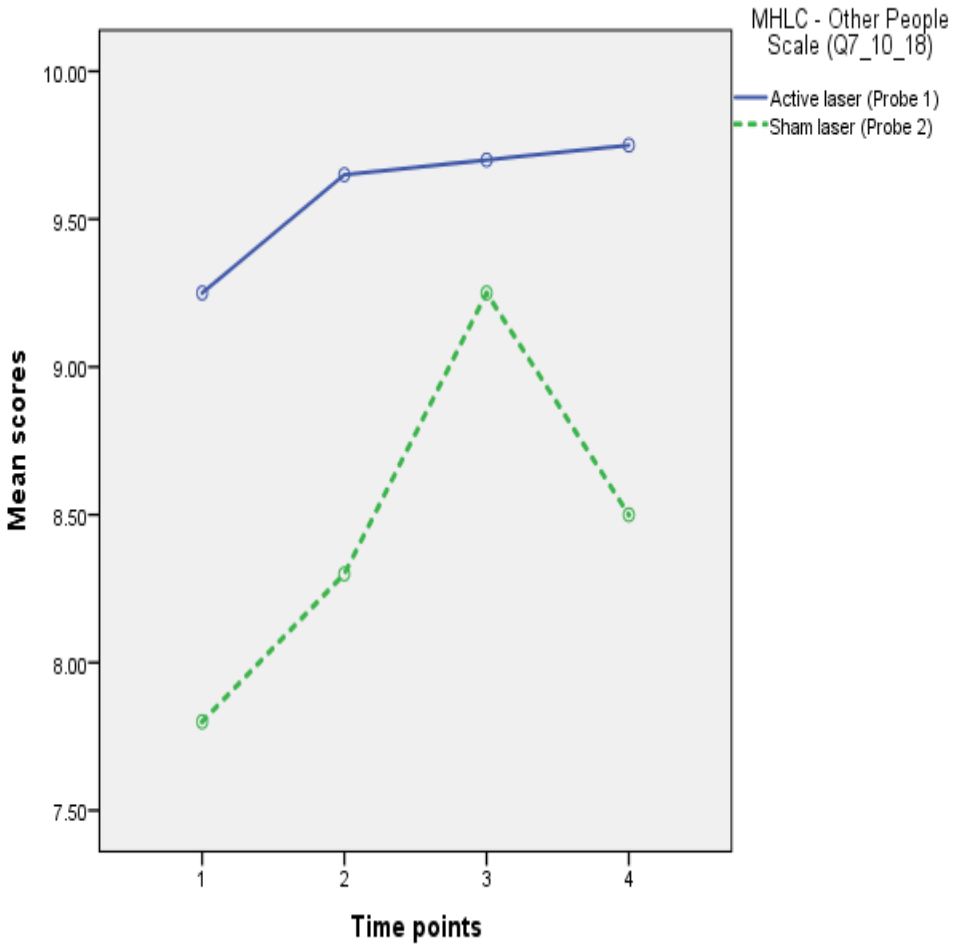

Figure 24 – MHLC-C – Other People Scale (Q7, 10, 18) Total Mean Scores for Active Laser & Sham Laser Groups at All 4 Time Points

5.23.2 Comparison Between Groups at Each Time Point

Table 129 (below) shows there was no statistically significant difference at baseline between two groups in the MHLC-C Other People Scale scores. When comparing between two groups (pairwise comparison), mean difference scores for the active laser were not statistically significantly different from sham laser at all successive time points. Mean differences for time points 2, 3 and 4 were 1.35 (p = 0.205), 0.45 (p = 0.719) and 1.25 (p = 0.300) respectively.

Table 129 – MHLC-C – Other People Scale (Q7, 10, 18) Mean Difference Scores Between 2 Groups at Each of 4 Time Points

Multi-dimensional Health Locus of Control (Form C) - Other People Scale (Q7, 10, 18) Pairwise Comparisons				
Between active laser & sham laser groups - Time point	Mean difference between active and sham laser	P-value	95% Confidence Interval for Difference	
			Lower Bound	Upper Bound
Baseline (week 0) (T1)	1.45	0.223	-0.92	3.82
4 weeks (T2)	1.35	0.205	-0.77	3.47
8 weeks (T3)	0.45	0.719	-2.06	2.96
12 weeks (T4)	1.25	0.300	-1.16	3.66

5.23.3 Between Group Mean Comparison at Time Point 1 (Baseline) Compared with Time Point 2 (4 Weeks), Time Point 3 (8 Weeks) & Time Point 4 (12 Weeks) & Overall Comparison Effect

Table 130 (below) shows that, when the mean differences between the two groups were compared to the baseline mean in the MHLC-C Other People Scale scores, active laser was not statistically significantly different from sham laser at all three time points. The mean difference for time point 2 was -1.00 ($p = 0.382$); for time point 3 it was -0.20 ($p = 0.867$); and for time point 4 it was -0.20 ($p = 0.867$). The overall comparison effect mean difference was 1.13 ($p = 0.269$).

Table 130 – MHLC-C – Other People Scale (Q7, 10, 18) Mean Difference Scores Between 2 Groups from Baseline Week 0 (Time Point 1) Over Time Point 2, 3 & 4 & Overall Comparison Effect

Multi-dimensional Health Locus of Control (Form C) - Other People Scale (Q7, 10, 18) Between groups comparison from baseline week 0 (Time point 1) over time point 2, 3, & 4 & overall comparison effect		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
	Mean Difference	P-value	Lower Bound	Upper Bound
Time point 1 Vs Time point 2	-0.10	0.922	-2.15	1.95
Time point 1 Vs Time point 3	-1.00	0.382	-3.29	1.29
Time point 1 Vs Time point 4	-0.20	0.867	-2.60	2.21
Overall comparison effect	1.13	0.269	-.90	3.15

Chapter 6: Discussion

This chapter begins with a summary of the results of the study and is followed by a discussion on the development of the clinical trial method and the findings of the outcome measures as compared with the previous studies under review. The discussion focuses on the key elements of the design method, including sample size; drop-out rate; randomisation; double-blinding; placebo; inclusion and exclusion criteria; diagnostic method and the TCM paradigm; laser acupuncture mechanism; treatment protocol (i.e. laser parameters, treatment program); the benefit of using acupuncture points; outcome measures; study results; commonalities of outcome measures; factors associated with the placebo effect; and a comparison of the trial results with similar studies. The unique features of this RCT and their impact on the study's findings are also discussed. The chapter concludes with observations about the study's limitations, opportunities for improving the trial design, and draws out implications for future research.

6.1 Study Objective

The objective of this RCT was to assess the effectiveness of laser acupuncture compared to sham laser in reducing pain and stiffness, and improving physical function in individuals suffering from OAK, as measured by the primary outcome measure: WOMAC. Another primary outcome measure, the Visual Analogue Scale (VAS), and a secondary outcome measure, Short Form McGill Pain Questionnaire (SF-MPQ), were used to validate multi-dimensional aspects of pain.

The null hypothesis stated that:

H_o: Laser acupuncture does not reduce pain and stiffness and improve physical function in individuals with OAK.

In the event that the null hypothesis is rejected, the alternative hypothesis would be accepted, i.e.

H_a: Laser acupuncture reduces pain and stiffness and improves physical function in individuals with OAK.

Results from WOMAC showed laser acupuncture was statistically significant in reducing pain and stiffness, and improving physical function while VAS reduced pain with overall comparison effect p values < 0.001. Furthermore, all sub-scales in SF-MPQ Q1-15 (Sensory and Affective Pain); Q16 (VAS Pain Scale); and Q17 (Present Pain Intensity) scored p values of 0.030; 0.000; and 0.000 < 0.05 respectively, correlating with the WOMAC pain sub-scales and the VAS scale. Therefore, the null hypothesis was rejected and the alternative hypothesis accepted.

As part of the study design, four specific research questions were postulated to investigate the influence of laser acupuncture on treatment outcomes. Those questions and findings were:

a) *Did the study establish a valid and effective trial design for replication in future laser acupuncture studies on OAK?*

Yes. The trial design established a clear and standardised protocol for a design method that complied with CONSORT, STRICTA and WALT guidelines and recommendations. The design used protocols for sample size calculation, randomisation, practitioner and participant double-blinding and a valid placebo arrangement. It also followed strict inclusion and exclusion criteria to achieve a homogeneous population sample for reliable statistical analyses. A unique feature of the design was the application of TCM diagnostic disease pattern differentiation, treatment principles and standardised acupuncture point formulae that targeted the specific underlying causes and symptoms of OAK. A clear rationale was provided for selecting laser parameters, the treatment program and outcome measures to assess treatment efficacy. As a result, this RCT reported explicitly on the standardisation and provision of a rationale for selecting TCM

protocols and laser parameters that would allow replication and validation of the findings.

b) *Did strict adherence to the TCM paradigm (i.e. using diagnostic pattern-differentiation, treatment rationale/principle and formulae-specific acupuncture points that treat the underlying causes and symptoms of OAK) influence laser acupuncture treatment outcomes?*

The positive findings of this RCT suggest a benefit in applying TCM principles to laser acupuncture treatments, specifically through the use of diagnostic pattern differentiation, treatment rationale and principle, and formulae-specific acupuncture points treating the underlying causes and symptoms of OAK. The overall results showed, for the first time, that low-intensity laser acupuncture achieved a significant improvement in all symptoms of OAK pain, stiffness and physical function – unlike Yurtkuran et al. 2007, Shen et al. 2009, Wang et al. 2013 and Hinman et al. 2014, who were unable to achieve positive results for all OAK symptoms, possibly due to the lack of diagnosing and treating the underlying causes and symptoms of degenerative OAK.

c) *Did the study help lead to more appropriate laser parameters for the treatment of OAK?*

The positive results achieved in this RCT provide a foundation for further exploration of using lasers with a higher output power and lower fluence for time-efficient and resource-efficient treatments. Additionally, the laser parameters selected for this RCT confirmed that high-range fluences recommended by WALT do not produce an inhibitory or adverse effect.

d) *Did the therapeutic alliance between the practitioner and participants impact on treatment outcomes?*

Yes. Results for factors related to the placebo effect – credibility, expectancy, practitioner-patient relationship, bonding, goal setting and task compliance – indicated differences that might have had some relationship with treatment outcomes. Further elaboration is provided later in this chapter.

6.2 Overall Study Findings for Pain, Stiffness & Physical Function

The two primary outcome measures, WOMAC used for pain, stiffness and physical function and VAS for pain, collectively indicated that laser acupuncture significantly decreased pain and improved stiffness and physical function. Both measures showed an overall effect that resulted in p values < 0.001. The secondary outcome measure, the Short Form McGill Pain Questionnaire (SF-MPQ) (Q1-15) recorded an overall p value of 0.030 < 0.05 while the SF-MPQ VAS sub-scale (Q16) and the SF-MPQ Presenting Pain Intensity sub-scale (Q17) both produced a p value < 0.001. All pain scales showed statistically significant differences between active and sham laser groups. It should be noted that although pain medications were not restricted, participants did not report any increased usage of such medications during this study.

6.3 Overall Findings on Placebo Factors

Two of the three secondary outcome measures assessing placebo effects – the Credibility/Expectancy Questionnaire (C/E) and the Working Alliance Inventory Short Form C (WAI-C) – showed statistically significant differences between groups in overall effect, scoring p values of 0.018 and 0.017 < 0.05 respectively. However, the third placebo measure, the Multi-dimensional Health Locus of Control – Form C (MHLC-C) overall effect scores on five sub-scales – internal belief, chance, powerful others, doctors, and other people – scored p values of 0.36, 0.413, 0.548, 0.548 and 0.269 > 0.05 respectively, indicating no statistically significant difference between the active and sham laser groups.

In short, the overall results indicated that five factors – credibility and expectancy from C/E, and task, bond and goals from WAI (C) – were more strongly associated with the

intervention. It appears that the active group's higher score in two placebo instruments – C/E and WAI (C) – were due to progressive improvement in their condition. Before intervention, there were no statistically significant differences between groups, but differences did occur after intervention. This indicates that those statistical differences could have been due to differences in treatment effects. It is therefore posited that as the active group's condition improved, so too did their belief, expectation, goals, bonds and task compliance over the four time points. However, placebo factors in MHLC-C, such as internal belief, chance and the influences of powerful others, did not show any statistical differences before and after intervention. The impact of placebo effects related to treatment outcomes is discussed later in this chapter.

6.4 Adverse Events/Safety

No adverse events or harms were experienced during this study, indicating that the parameters used were safe.

6.5 Design Methods

Of all the many study types available, randomised controlled studies (RCTs) provide the strongest empirical evidence of the effectiveness of a therapeutic procedure when properly executed (Western Sydney University 2010). In simple terms, RCTs are prospective, analytical treatment experiments in which participants are randomly allocated to two or more groups and comparisons made of outcome measurements recorded over appropriate follow-up periods.

A feature of RCTs is that participants are allocated to, say, active or sham treatments at random without their knowledge, thus eliminating potential unknown confounding factors and providing a more robust foundation for statistical analyses. Other study types are not as well regarded. For example, randomised cross-over clinical trials in

which different treatments are provided over different periods are susceptible to bias if carry-over effects occur from one treatment to the next.

As analysed earlier, 20 of the 27 laser clinical trials reviewed (74.07%) used a two-group parallel design method to compare results from active and sham treatment groups. These factors, coupled with CONSORT and STRICTA recommendations, led to the decision to use the two-group parallel RCT placebo-controlled design for this study. Unlike acupuncture-based RCT designs, laser acupuncture studies do not suffer the same design issues regarding study controls because laser acupuncture can be more easily controlled through the delivery of a credible placebo. However, other factors can affect placebo. Consequently, this study was among the first to incorporate outcome measures that specifically assess placebo effects.

The following sections discuss the specific design elements that contributed to a quality RCT design for laser acupuncture in the context of the reviewed literature.

6.5.1 Sample Size, Drop-outs, Randomisation, Blinding & Placebo Compliance & Study Rationale

Sample Size Calculation

Developing robust and reliable clinical research demands that an appropriate sample size be determined, including the effect size, standard deviation and the underlying event rate in the general population (Kadam 2010). Of the 27 studies reviewed in the literature, only 10.71% appeared to comply with CONSORT (2010) sample size criteria and other essential elements. Only three of the 27 studies – Ebneshahidi et al 2005, Brosseau et al. 2005, Chow et al. 2004 – considered these essential elements and complied with CONSORT criteria, thus avoiding potentially biased outcomes.

The sample size used in this RCT aligned with CONSORT/STRICTA requirements and the key sampling elements outlined by Kadam (2010). The population sample was estimated from the size of test groups used in previous acupuncture trials conducted

at UTS and a review of the literature. It was subsequently determined that 60 participants would provide sufficient statistical power to validate trial results.

The paucity of reliable studies using laser acupuncture for OAK made it difficult to estimate the effect size of the intervention. However, a conservative estimate was derived from similar studies that used WOMAC as the primary outcome measure. With an estimated effect size of 0.75, a standard deviation of 1, alpha of 0.05 for a two-tailed t-test, it was found 30 subjects per group resulted in a power of 0.81 (81%). Consequently, the total number of participants for the study was set at 60, comprising 30 for active laser intervention and 30 for sham laser.

Unfortunately, several factors hampered recruitment. Most prospective participants interviewed over a 12-month period were found to suffer co-morbidities, including diabetes and severe OA in other joints; were unable to meet other inclusion criteria; or had undergone knee surgery. These constraints resulted in the recruitment of 40 participants (20 females and 20 males with a mean age of 62 years). Of the 40 participants, 34 completed all treatments and outcome measures. As a result, data was analysed on an intention-to-treat basis. This limited bias because all data were carried forward for the six participants that dropped out. The positive results achieved in this RCT suggest that the reduction in the originally proposed sample size did not significantly undermine analyses of the results.

Drop-outs

Of the six participants who dropped out, four were in the sham treatment group and two in the active treatment group. Five of the drop-outs said they were too busy to continue, while one was involved in an accident unrelated to this study.

Randomisation, Blinding and Placebo

Only eight of the 27 reviewed studies (29.63%) clearly reported the randomisation method according to CONSORT criteria. Consequently, studies that did not describe randomisation methods might have reported results that were not reliable and valid.

Three of the 27 studies (Fukuda et al. 2010, Gur et al. 2002, Chow et al. 2004), representing 11.11 %, complied with CONSORT blinding requirements in reporting explicitly on the use of a credible placebo device. This low rate of compliance reflected poorly on the overall quality of the study designs because robust and reliable clinical research demands double blinding to minimise bias in trial outcomes.

Further assessment of the nine laser acupuncture and low-intensity laser therapy OAK studies found a number of shortcomings in terms of reporting on randomisation, blinding and placebo methods. For example, only three of the nine laser acupuncture and low-intensity laser therapy OAK studies (Gur et al. 2003, Yurtkuran et al. 2007, Shen et al. 2009) – or 33.33% – met CONSORT/STRICTA requirements by clearly reporting how randomisation was done. In terms of double blinding and the use of a credible placebo, only two of the nine studies (Fukuda et al. 2010, Gur et al. 2003) – or 22.22% – complied with CONSORT requirements by reporting explicitly on these factors.

Placebo Issues

Many of the studies appeared to lack an understanding of basic laser science when attempting to establish a credible laser placebo. In discussing this issue, it is necessary to consider established facts. There are seven laser classes in common use worldwide. The laser classes used in the reviewed studies were, in the main, non-thermal (i.e. Class 3B cold lasers. However, Shen et al (2009) used a combination laser incorporating a Class 3B laser and a high-intensity thermal Class 4 CO_2 laser.

The Class 3B laser is commonly used in laser acupuncture and low-intensity laser therapy because it produces photo-chemical and biomodulatory effects and interacts with cellular substrates within the body. Class 3B therapeutic lasers come in two different types – visible laser and invisible infrared laser. Class 4 CO_2 lasers are generally used for cutting, cauterising and ablating tissue because they produce heat. It is therefore obvious that turning off a CO_2 laser, as the Shen et al (2009) study did to provide a placebo treatment *sans* heat, would not enable the active and sham groups to experience the same sensation expected from any believable alternative to a moxa heat treatment. Consequently, the placebo group would be aware they were not

receiving anything that felt like a heat treatment when the CO_2 laser was turned off. Another issue that complicated the establishment of a credible placebo was the fact that many studies used laser probes fitted with red or blue light-emitting diodes (LEDs) that illuminated treatment sites. When an inactive infrared laser probe or a visible red laser was used to provide a so-called sham treatment, the red or blue guide light on the probe stayed on to give the impression that an active treatment was being given. However, this was not a real sham treatment because LEDs are known to produce photo-biomodulatory effects, resulting in physiological changes in the body. Experiments in space have shown that red LED wavelengths stem the loss of bone and muscle mass in astronauts (NASA 2005). As a result of these findings, tiny LEDs are now being used on earth for cancer treatments, and to improve cell growth for wound healing and to alleviate chronic pain. The NASA studies imply that the use of red or blue light as a placebo device in OAK studies could produce physiological effects that might impact on treatment targets and skew treatment outcomes. Further supporting this view is the fact that LEDs are often combined with laser diodes in Class 3B laser cluster probes designed for therapeutic treatments because both types of diode produce similar effects.

It might be argued that a red or blue guide light on both an active and a sham laser probe might of itself serve as a placebo in that any physiological effect would be the same for both the active and sham laser treatment groups. However, that argument only serves to further complicate matters since it would be difficult to separate with any degree of certainty the therapeutic effects resulting from a combination of an active laser and red or blue LED light. As noted by Shapiro et al. (1978), any credible placebo treatment should not produce any therapeutic effect on the targeted condition. Therefore, a red or blue light that could produce physiological changes during the treatment of OAK would not be a credible placebo.

Clearly, the six researchers out of 27 who used a red light or an LED as a placebo (Haker et al. 1990, Aigner et al. 2005, Yurtkuran et al. 2007, Gottschling et al. 2008, Hegedus et al., 2009, Glazov et al. 2009) did not account for the photo-biomodulation impacts that might result from physiological changes on treated areas, suggesting their knowledge of laser science may not have been comprehensive.

Double Blinding

Double-blinding of both the practitioner and the participants was an important aspect of the current laser acupuncture study design. Schultz (2002) rightly argued that there were greater benefits to blinding the practitioner than the assessor, demonstrating that studies with blinded practitioners produced less biased outcomes. For this RCT, the practitioner was supplied with two identical laser probes marked 1 and 2. One probe delivered real laser; the other was deactivated for sham laser. Blue LEDs on both probes were covered with Blue Tac and black insulation tape to eliminate the possibility of photo-physiological effects during treatments (see Appendix 8). Additionally, a third party used a computer to generate random numbers. These numbers were placed in separate sealed envelopes that were used to sequentially allocate participants to either probe 1 or probe 2 treatments. Consequently, neither the practitioner nor the participant was aware of allocations to active laser and sham laser groups. This arrangement was markedly different from the double-blinding method used by the Yurtkuran et al. (2007) study, which only blinded participants and the assessor.

6.6 Diagnostic Method, Inclusion & Exclusion Criteria

Western Biomedical Diagnosis

Five out of nine laser acupuncture and low-intensity laser therapy studies (Gur et al. 2003, Tascioglu et al. 2004, Shen et al. 2007, Yurtkuran et al, 2009, Fukuda et al, 2010) – or 55.56% – used the Kellgren-Lawrence (K&L) osteoarthritis grading scale to diagnose the degree of OAK in participants. The K&L scale is a well-regarded international standard commonly used for assessing the presence of osteophytes and the degree of joint space narrowing in the knee joint capsule. Grade 2-3 defines minimal to moderate change, characterised by multiple osteoarthritis and definite joint space narrowing. Other objective measures, such as thermography or physician examination, appear not to be able to standardise the condition of OAK to the same degree as K&L.

As a result, this RCT used K&L as an objective measure to standardise participant inclusion, thus helping to achieve study group homogeneity and reduce the possibility of statistical variance.

TCM Framework & the Importance of Disease Pattern Differentiation & Specific Acupuncture Point Formulae

Of the five laser acupuncture OAK RCTs, only two studies (Yurtkuran et al. 2007, Shen et al. 2009) acknowledged the TCM theory known as Bi Syndrome, which triggers the OAK syndrome. However, none of these studies applied TCM disease pattern differentiation, treatment principles and OAK-specific acupuncture point formulae to the treatment of Bi Syndrome. Nor did the studies strictly follow the essence of the TCM framework to treat the cause of chronic degenerative OAK – deficiency of Liver and Kidney. Furthermore, Yurtkuran et al. (2007) and Shen et al. (2009) only irradiated a single point, SP9 and ST35 respectively. Treating a single acupuncture point did not address the underlying causes, signs and symptoms of OAK.

6.7 Laser Mechanisms: Integrating Ancient & Modern Techniques

Unlike the reviewed studies, the current RCT attempted, for the first time, to fully integrate the ancient TCM framework into the design of a contemporary OAK laser acupuncture controlled trial in a vigorous way. A key feature was the differentiation of OAK into TCM disease patterns or symptom clusters (Bian Zheng) associated with this healing modality.

The two main categories of TCM differentiation for OA were based on a manualisation of the literature (see Appendix 10), which identified the two patterns of “Blood Stasis” (Xue Yu Zheng) or “Phlegm Retention Syndrome” (Tan Tin Zheng) as the primary patterns associated with OAK/Bi Syndrome. In strictly applying the TCM paradigm, this RCT utilised disease pattern differentiation and diagnostic concepts as a defining characteristic of the inclusion criteria and, hence, the study design.

This approach led to a treatment rationale/principle and specific acupuncture point formulae targeting the underlying causes and symptoms of OAK. This appeared to account for more effective treatment outcomes and the positive results obtained in the primary and secondary outcome measures tracking the signs and symptoms of OAK. A plausible explanation for the positive results might be that laser acupuncture applied within the TCM paradigm addresses the Blood Stasis that must be cleared from blocked channels to relieve pain. Irradiating points also would soothe the Liver (responsible for sinews and tendons) to ensure a free flow of Blood and Qi, relieving stiffness and tonifying the Kidney which, according to TCM theory, nourishes bone growth and helps avoid OAK degeneration.

How Acupuncture & Lasers Heal

Earlier researchers appeared not to be able to capture the essence of the mechanism of the two modalities – acupuncture and low-intensity laser therapy – in targeting the pathophysiological changes associated with OAK.

The following elaboration on the healing mechanisms in combining both modalities provides a background to the reasons that led to the selection of laser parameters employed in this RCT.

Acupuncture Effects

Studies of needle acupuncture analgesia have indicated that this modality releases neuro-transmitters and endogenous opioid-like substances within the central nervous system. Other biochemical changes stimulate the body's homeostatic mechanisms, promoting emotional well-being (Zhao 2008). Furthermore, acupuncture has been found to be effective in improving OA symptoms, including reductions in disease activity, joint tenderness, swollen joints and morning stiffness, and improving health-related quality of life (Lee, Shin & Ernst 2008).

Laser Acupuncture Effects

Since the invention of lasers more than 50 years ago, low levels of visible and near infrared light have been known to reduce pain, inflammation and oedema, heal

nerves, wounds and deeper tissues, and prevent cell death and tissue damage (Huang et al. 2009).

Many studies report that laser boosts production of the “feel good” neuro-transmitter, serotonin, and endorphins (peptides that activate the body's opioid receptors), causing analgesic effects (Laakso 1994). Laser light also blocks depolarisation of C-fibre afferents and the release of acetylcholine for pain relief (Vizi, Harsing Jr & Knoll 1977).

Laser acupuncture produces local and distant analgesic effects that may be mediated by different mechanisms. For example, laser stimulation of certain acupuncture points has been shown to affect areas of the brain known to reduce sensitivity to pain (Hui et al. 2010). One study that used functional magnetic resonance imaging (fMRI) to investigate the cerebral effects of laser acupuncture at both the left and right GB43 acupuncture points produced significant ipsilateral brain activation within the thalamus, nucleus subthalamus, nucleus ruber, brain stem and Brodmann areas 40 and 22 (Siedentopf et al. 2005). No significant brain activations were seen in the placebo group. The observed ipsilateral effects may support the assumption that laser acupuncture is mediated by meridians. Other fMRI evidence of laser acupuncture-mediated effects have demonstrated visual cortex activation in response to laser irradiation of BL67 (Whittaker 2004). Significantly, fMRI recorded no visual cortex activation when an inactive laser probe was applied to BL67, which is sometimes used to treat eye pain.

The role of endogenous opiate-like peptides and serotonin in laser acupuncture anaesthesia has been demonstrated. Other evidence suggests laser acupuncture produces anti-inflammatory and anti-nociceptive effects (Erthal et al. 2013). In the treatment of OAK, the application of laser acupuncture has been found to produce analgesic effects (Baxter 1989) and opiate-mediated pain relief (Bischko 1980). Surprisingly, pathology samples taken in studies indicate that laser and needle acupuncture produce similar profiles in urine (Bischko et al. 1980). In one study, 1mW He-Ne laser irradiation increased urinary secretion of 5-hydroxyindoleacetic acid (5-HIAA), a by-product of serotonin metabolism in patients experiencing pain relief (Walker 1983). Increased levels of urinary 17-hydroxy-corticosteriods also were noted

following laser stimulation (Choi, Srikantha & Wu 1986). Furthermore, laser acupuncture has also been shown to be effective in reducing swelling associated with OAK (Yurtkuran et al. 2007).

These findings have identified laser acupuncture effects, such as the release of endogenous opioids, serotonin and acetylcholine for pain relief and anti-inflammatory properties, all of which are good indicators for relieving pain and reducing inflammation/swelling and, in turn, improving physical function in OAK.

6.8 How Laser Acupuncture Benefits OAK

To understand how the integration of laser and TCM-based acupuncture are able to improve OAK, it is essential to first consider the pathophysiology of this chronic degenerative condition.

OAK is related to supra-physiological joint stress, which impairs the ability of chondrocytes to adapt and leads to osteophyte formation and development of OA (Chikanza & Fernandes 2000). Subsequently, low-grade inflammation and additional cartilage damage can occur in joints.

One study (Jones et al. 2001) concluded that low-intensity laser irradiation increases the formation of new cartilage – raising the prospect that lasers might help heal cartilage-lined joints affected by disease or injury. Another study (Renno et al. 2007) reported that an 830nm wavelength acts as proliferative stimulus on osteoblasts, suggesting that laser might aid bone regeneration.

TCM-based laser acupuncture therefore appears to provide healing that targets the cause of health imbalance through the manipulation of Qi or energy to maintain homeostasis. Moreover, stimulating or balancing this energy involves not only choosing appropriate acupuncture points, but also consideration of other important laser properties.

6.9 Treatment Protocol

There are two key aspects to effective treatment protocols – one involving the selection of acupuncture points that address a specific disease pattern; the other relating to laser parameters based on how the laser beam interacts with human tissue and cellular substrates at the targeted treatment site.

Acupuncture Protocol

Much thought – coupled with an understanding of the healing mechanisms of laser, TCM-based acupuncture and the pathophysiological changes occurring in OAK – went into framing the CONSORT/STRICTA-compliant treatment protocols used in this study.

As discussed in the Method Chapter, a manualisation process determined acupuncture points most commonly used for the two TCM disease patterns associated with OAK – Blood Stasis and Phlegm Retention. A total of 13 acupuncture points (see Table 40 in the Method Chapter) addressed the TCM treatment principle, which was aimed at removing Blood Stasis; clearing blockages in the channels; relieving pain; improving Qi and blood circulation; soothing the Liver; resolving phlegm and dampness; reducing swelling; improving stiffness; tonifying the Kidney; and nourishing bone growth.

Laser Parameters Used in this RCT

In view of the variable results produced by variable laser parameters in earlier studies, this RCT rationalised the use of a wavelength to target the anatomical region; selection of an optimal fluence, power density and output power; and the duration and number of treatments required for the degenerative OAK syndrome.

For this RCT, the following equipment and parameters were used: (1) a laser wavelength of 810nm; (2) a power density of 1.1W/cm^2; (3) a spot size of 2.8 mm x 1.1 mm (elliptical beam profile); (4) an output power of 100mW (continuous wave) applied perpendicularly to each acupuncture point in skin contact mode; and (5) a fluence of 18J/point applied for two minutes per point to 13 acupuncture points three times a week over four weeks, i.e. a total of 12 treatments. The duration of each treatment

session was 26 minutes, resulting in the delivery of 234J per treatment session and a total of 2,808J over 12 treatment sessions.

The 810nm wavelength is preferentially absorbed more easily by cellular substrates in comparison to wavelengths of 670nm or 904nm (Anders & Wu 2016). The 810nm also is able to penetrate the knee for about 3-4mm, a depth reported to be required for knee treatments (Bjordal et al. 2003).

The power density of 1.1W/cm^2 selected for the study was within the range of 10mW/cm^2 to 17.8W/cm^2 used in the 27 reviewed studies. It was therefore postulated that the power density was not too low and complemented other key laser parameters. These included an output power of 100mW and irradiating 13 acupuncture points for 2min/point in continuous wave mode to stimulate or tonify degenerative OAK.

The 100mw output power was considered strong enough to deliver sufficient energy within a reasonable treatment time. This was an important consideration because the lower the output power, the longer the treatment time required for a specified laser fluence. A low output power also is not time efficient or practical in a clinical environment. It should be noted that the highest output power of 500mW, used by Stump et al. (2006), also produced a positive outcome with the advantage of completing the treatment in much less time.

Yurtkuran et al. (2007) used 4mW, the lowest output power in all of the 27 studies reviewed. However, the Yurtkuran study reported a positive outcome only for swelling – not pain – indicating that a low output power and a low fluence of 0.48J/point may not be able to reduce pain or improve physical function.

Furthermore, a systematic review found that trials with negative outcomes for pain reduction used daily dosages below 5J (Bjordal et al. 2006) whereas another study (Trelles et al 1991) reported positive results with 18J/cm^2. The Bjordal study further recommended that 810nm to 820nm lasers targeting anti-inflammatory mechanisms should use 6J for small acute injuries and more than 10J for larger injuries, implying that higher joules are better for chronic conditions like OAK. The 2008-2010 literature

review confirmed that most dosages in the nine reviewed laser acupuncture and LILT studies for OAK ranged from 0.4J-18J/point.

WALT (2010) suggests the use of 12J/point for knee arthritis with a therapeutic dose window typically ranging from +/- 50% of given values. This appears to indicate that the maximum dosage for knee arthritis would be 18J/point, if indeed 12J/point is the given value. The 18J/point this RCT used is in the high range of parameters recommended by WALT (2010), but matches the laser dose employed successfully by Trelles et al. (1991). Notably, the 18J/point did not produce any adverse effects.

To ensure a maximum effect for the treatment of chronic OAK, this study postulated that a higher dose of 18J/point would help stimulate collagen formation and reduce inflammation (Jones 2001) in the knee joint capsule, activate fibroblasts (Belletti et al. 2015) and increase osteoblastic proliferation, collagen deposition and bone reformation (Pinheiro & M.M. Gerbi 2006).

Using recommended WALT (2010) guidelines, it was concluded that 12 laser acupuncture treatments programmed three times a week over four weeks would allow energy to be absorbed regularly and accumulatively to accelerate the healing process and improve biological and physiological metabolism. Another indicator was the literature review, which found that most studies programmed 10-12 treatments (see Tables 27, 28 & 29).

The overall results indicated that the high energy dosage and parameters this RCT used contributed to its positive outcomes. Equally important, the treatment sites and acupuncture points selected also appeared to be crucial factors in the results.

6.10 Treatment Sites: Benefit of Using Formulae-specific Acupuncture points for OAK

As mentioned earlier, a manualisation process was used to identify, from the TCM literature, acupuncture points most commonly used to treat OAK. Consequently, 11

acupuncture points were identified as a standard treatment protocol and two extra acupuncture points were added to establish a treatment-specific formulae for each of the identified OAK disease patterns – Blood Stasis and Phlegm Retention.

Treating acupuncture points appears to be more effective than treating symptomatic tender points or trigger points. Laboratory studies using computerised tomography (CT) scans confirm that acupuncture points in the human body have a higher density of micro-vessels and contain a large amount of involuted microvascular structures (Liu et al. 2014). Acupuncture points are described as containing a high density of vascularised blood vessels exhibiting special oxygen characteristics, which apparently are not found in non-acupuncture points.

The functions of the acupuncture points used to address Blood Stasis and Phlegm Retention were explained in the Method Chapter (see Tables 37, 38 and 39). To elaborate further, acupuncture points that target the cause of degenerative OAK are ST36 (Zushanli), BL40 (Weizhong) and GB34 (Yanglingquan), which are called “3 Leg Yin”. These three acupuncture points serve to nourish Yin energy and Essence in the body. SP6 (Sanyinjiao), meaning “3 Yin Interaction” (the meeting point of the Liver, Kidney and Spleen channels), nourishes these three organs and Yin/Essence in the body. Additionally, GB34 (Yanglingquan) soothes the Liver while KD3 (Taixi) nourishes Kidney Yin and bone growth. ST36 (Zushanli) is an important acupuncture point that tonifies Qi (Nutritious and Defensive Qi) and Blood, and strengthens the legs and body (Maciocia 1990). Therefore, the acupuncture points used in this study tonify the Yin, Essence, Liver and Kidney, and target the cause of OAK.

It should be noted that other researchers (Yurtkuran et al. 2007, Shen et al. 2009) used a single acupuncture point to treat OAK – and both did not address the cause of the Bi Syndrome disease pattern. Consequently, the Yurtkuran study was only able to achieve a positive outcome in swelling, but not pain. The Shen result was inconclusive. Furthermore, the low-intensity laser therapy OAK clinical trials reviewed did not recognise the benefit of using TCM-based acupuncture points, concentrating instead on irradiating tender points or areas around OA-affected knees.

Consequently, all of the OAK studies reviewed did not produce robust, reliable and conclusive outcomes for all symptoms of OAK. This suggests the positive effects obtained in this well-designed and robust RCT might be due to the special characteristics of acupuncture points and the specificity of its acupuncture formulae which, according to TCM theory, hypothetically connect channels to internal organs, skin, tissue and brain that target the underlying causes and symptoms of OAK. The specific acupuncture points were aimed at clearing Blood Stasis and resolving Phlegm, soothing the Liver and tonifying the Kidney, which appear to be the key to the success of this RCT.

It is very likely that even if optimum laser parameters were to be devised for treating OAK, the ultimate outcome might not be as beneficial as using the TCM-based paradigm with specific acupuncture point formulae. However, the positive outcomes this study achieved for all OAK symptoms (i.e. reducing pain and improving stiffness and physical function) requires further investigation to confirm this assumption.

6.11 Outcome Measures Used

As previously mentioned, the review of earlier studies led to the selection of six outcome measures for the current RCT. WOMAC and VAS were chosen as the two primary measures because they are both widely used in research and clinical studies. WOMAC is the disease-specific gold standard for measuring the effects of OA in the human body and VAS is the most frequently used method for assessing pain. The Short Form McGill Pain Questionnaire (SF-MPQ) – one of four secondary measures – was added to give the study a three-dimensional view of pain in the active laser and sham laser groups throughout the trial.

In manualising the use of outcome measures in previous laser acupuncture and low-intensity laser therapy studies for OAK, four out of nine studies (Gur et al. 2003, Tascioglu et al. 2004, Yurtkuran et al. 2007, Shen et al. 2009) – representing 44.44% – were found to have used WOMAC. VAS was used in five out of nine studies,

representing 55.56% (Trelles et al. 1991, Gur et al. 2003, Tascioglu et al. 2004, Yurtkuran et al. 2007, Hegedus et al. 2009).

The remaining three secondary measures – Credibility/Expectancy Questionnaire (C/E), Working Alliance Inventory Short Form C (WAI-C) and the Multi-dimensional Health Locus of Control – Form C (MHLC-C) – were used to assess, for the first time, the placebo effects of laser acupuncture. C/E provided an insight into the way participants perceive and react to a new therapy; WAI (C) monitored aspects of the participant-practitioner relationship; and MHLC-C identified treatment variables related to internal belief as well as influences by other people, chance and doctors.

6.12 Study Results

The statistical software, SPSS Ver. 23, was used to analyse treatment outcomes while a General Linear Model with repeated measures tested the null hypothesis of the RCT, which was subsequently rejected. A univariate variance of analysis and t-test comparison assessed differences between each time point. A p value of less than 0.05 was considered statistically significant for all comparisons.

Data for the 40 participants enrolled in the RCT were analysed on an intention-to-treat basis. This allowed data for the six participants who dropped out (15% of the sample size) to be carried forward from their last visit, thus limiting statistical bias.

At baseline (time point 1), there were no statistically significant differences between groups in all primary and secondary outcome measures, showing that the homogeneity of the study sample made for reliable statistical analyses.

The following section discusses the study results. Each outcome measure is presented with comparisons made against other low-intensity laser acupuncture and laser therapy studies to provide contextual background and draw out the implications for future studies. The first part of the discussion analyses the two primary measures, WOMAC and VAS. SF-MPQ, while being a secondary measure for pain, is examined to

assist in the validation of the results. The second part of this section deals with the placebo instrument analyses.

6.12.1 WOMAC

Overall Results & Significant Findings

WOMAC, one of the primary outcome measures used in this RCT to assess pain, stiffness and physical function, indicated a positive effect for the overall scale (Q1-24), scoring a p value < 0.001 – a statistically significant difference between groups. The overall effect of the pain sub-scale scored p = 0.002 < 0.05; the stiffness sub-scale p = 0.008 < 0.05 and the physical function sub-scale p < 0.001 – indicating statistically significant difference in all sub-scales between groups.

Comparisons between groups at each of the time points 2, 3 and 4 also showed statistically significant differences with respective p values of 0.000, 0.000 and 0.002 < 0.05. When time point 1 was compared with time points 2, 3 and 4, the overall effect scored p values < 0.05, again showing statistically significant differences.

In short, the WOMAC overall scales indicated that TCM-based laser acupuncture reduces pain, stiffness and improves physical function.

Table 131 – WOMAC Result Comparisons with Other Low-Intensity Laser Acupuncture & Laser Therapy Studies Treating OAK (2008-2010)

Studies between 2008 & 2010	WOMAC Overall Scale	Significant	Insignificant	Interpretation	Comment
Yurtkuran et al. 2007	0.606 > 0.05		✔	No significant difference	Negative outcome
Gur et al. 2003	P < 0.05	✔		No meaningful details/data provided Between groups comparison data not provided, but abstract stated that the p < 0.05 was statistically significantly different between groups	Positive outcome, but not supported with statistical analyses. May not be reliable
Tascioglu et al. 2004	P value not provided		✔	No significant difference	Negative outcome, but not reliable because no statistical data analysis provided

Comment

When compared to results from other studies as noted in Table 131 (see above), the only positive finding in that table (Gur et al. 2003) might not be reliable. Although Gur indicated in the study abstract that the p value of the between groups comparison was $p < 0.05$, no specific statistical data was reported. In contrast, this RCT has provided substantial statistical analyses relating to within groups and between groups data comparisons that produced a p-value < 0.05 (see Results Chapter).

WOMAC – Significance of Pain, Stiffness & Physical Function Sub-scales

Although the WOMAC pain and stiffness sub-scales showed no differences between two groups when time point 1 was compared with time point 2 and 4, significant differences occurred at time point 3 (see Tables 48 & 54 in Results Chapter). This suggests the positive effect of laser acupuncture might have resulted from gradual biological changes that did not manifest themselves until time point 3 and might have reduced over time once active treatment ceased. Another possible explanation for the insignificant changes at time point 4 might have been due to the ebb and flow of the degenerative condition or that laser effects wear off over time. Intriguingly, the physical function sub-scale maintained a statistically significant difference at time points 2, 3 and 4. This might suggest that the effects of laser on pain and stiffness are different to its effect on physical function.

It is not clear why statistically significant differences were recorded in overall effects for the pain, stiffness and physical function sub-scales but not in the individual sub-scales. It is very likely that the overall effect findings related to the analysis showing an overall statistically significant difference over the four time points.

Further studies will need to be undertaken with larger sample sizes to better understand anomalies in these data.

6.12.2 VAS Findings

Overall findings from VAS correlated with the WOMAC pain sub-scales, scoring a p value < 0.001, indicating statistically significant difference between active and sham

laser groups. Between group comparisons at each of time points 2, 3 and 4 showed statistically significant differences with respective p values of 0.000, 0.000 and 0.013 < 0.05. When time point 1 was compared with time points 2, 3 and 4, the overall effect scored a p value < 0.05, again showing statistically significant differences.

In short, the VAS overall scales indicated that laser acupuncture significantly reduced pain at all time points, correlating with the WOMAC pain sub-scale result and demonstrating consistency and reliability.

Table 132 – VAS Comparisons with OAK Studies Using Low-intensity Laser Acupuncture & Low-intensity Laser Therapy

Research Study	P Value	Significant Differences	Not Significant	Interpretation	Conclusion	Comment
Yurtkuran et al. 2007	P = 0.502 > 0.05		✔	No statistically significant difference	Not positive for all symptoms	Not strictly TCM paradigm
Fukuda et al. 2010	(P >0.10) in post-laser evaluation		✔	Claimed statistically significant difference No statistical data showing p value	Report contradicted conclusion	Not significant & not reliable
Hegedus et al. 2009	P < 0.05	✔ (Only before & after comparison for treatment) group)		Claimed treatment group had significant changes from initial value compared with follow-up period, but no comparison analysis made between groups	inconclusive	Not reliable
Montes-Molina et al. 2009	P > 0.05		No significant difference between interferential laser & conventional laser groups	Conclusion could not be reached because no placebo group to compare	No placebo group	Not robust
Tascioglu et al.2004	p value not reported		No significant difference			Not robust
Trelles et al. 2004	p value not reported	Positive result (only 1 group used)			No placebo group for comparison	Not robust

Table 132 (above) indicates only two studies out of six (Hegedus et al. 2009 & Trelles et al. 2004) produced positive findings. However, those results appeared not to be

reliable and robust. The Hegedus study only reported a positive result for the active laser treatment group since no comparison was made between groups. Hence, the results appear to be inconclusive. The Trelles study did not use a placebo control. Its findings were therefore not as robust as this RCT, which provided a credible placebo-controlled arrangement that enabled a clear analysis between active treatment and placebo treatment groups.

Contemporary Literature Findings

The review of four recent laser acupuncture and low-intensity laser therapy OAK studies conducted between 2011 and mid-2016 was undertaken following the conclusion of the trial period. A comparison of the reported results for WOMAC and VAS are provided below in Tables 133 and 134:

Table 133 – WOMAC Outcomes from Recent Laser OAK Studies

Research Study	P Value	Significant Differences	Not Significant	Interpretation	Conclusion	Comment
LOW-INTENSITY LASER ACUPUNCTURE						
Hinman et al. 2014	0.71 (1 year follow-up)		✔	Active laser Vs. Sham laser	Negative	Not robust
LOW-INTENSITY LASER THERAPY						
Alfredo et al. 2011	0.003	✔		Positive outcome	Significantly different in WOMAC, but not VAS	No correlation with VAS Result appears to be inconclusive
Alghadir et al. 2014	P < 0.008 (pain) P = 0.001 (function) P = 0.08 (stiffness)		✔	Inconclusive (no overall data reported)		Not correlation with VAS Result appears inconclusive

Table 134 – VAS Outcomes From Recent Laser OAK Studies

Research Study	P Value (VAS)	Significant Differences	Not Significant	Interpretation	Conclusion	Comment
LOW-INTENSITY LASER ACUPUNCTURE						
Al Rashoud et al. 2014	0.003	✔			Positive	
Hinman et al. 2014	0.94 VAS		✔	Active laser vs. sham laser	Negative	Not robust
LOW-INTENSITY LASER THERAPY						
Alfredo et al. 2011	0.120		✔	Negative outcome	Significantly different in WOMAC, but not VAS	No correlation with WOMAC Result appears to be inconclusive
Alghadir et al. 2013	P < 0.05	✔		Positive outcome	Significantly different in VAS, but not WOMAC	No correlation with WOMAC Result appears to be inconclusive

Low-intensity Laser Acupuncture

The Hinman et al (2014) study produced a negative outcome, which might have been due to the use of non-standardised acupuncture points for specific chronic knee pain, the use of a low fluence and a red light sham laser device that might have generated physiological changes in OAK. The Al Rashoud et al. (2014) study obtained a positive outcome in VAS, but did not use WOMAC, the gold standard for validating the effectiveness of OAK treatments. Instead the Saudi Knee Function Scale (SKFS), which contains activity items that relate to Arabic and Muslim societies, was employed.

Low-intensity Laser Therapy

Findings from two studies (Alfredo et al. 2011, Alghadir et al. 2013) appeared to be inconclusive because results generated from the two primary measures both used (WOMAC and VAS) did not correlate with each other (see Tables 126 and 127, above).

Comment

Unlike Yurtkuran at al (2007) and Shen et al (2009), who each irradiated only one acupuncture point, Al Rashoud et al. (2014) used five acupuncture points. However, the Al Rashoud study did not adhere to the essence of the TCM paradigm with disease pattern differentiation and formulae-specific acupuncture points that addressed the diagnosed OAK disease pattern. Al Rashoud et al (2014) was the only study that produced a positive outcome in VAS. It is perhaps unfortunate that the Al Rashoud study did not use WOMAC because a positive outcome with that internationally recognised measure would have given the outcome greater credibility.

Overall, the four studies listed above did not reflect robust and reliable outcomes due to a number of factors. Some studies did not use a credible placebo device or arrangement, lacked a placebo control or were not able to validate results with a range of appropriate outcome measures. This indicates that there has been little progress in the design of quality studies investigating laser acupuncture for OAK. This study represents a significant improvement in RCT design and the positive findings achieved correlate with a range of outcome measures that recorded statistically significant differences, confirming consistency and reliability of the results.

6.12.3 McGill Pain Questionnaire – Short Form (SF-MPQ)

Sensory and Affective Pain Sub-scales

The overall findings from the SF-MPQ sub-scale for Sensory and Affective Pain (Q1-15) correlated with the WOMAC pain sub-scales and the VAS scale, scoring a p value of $0.030 < 0.05$ – indicating statistically significant differences between active and sham laser groups. Between group comparisons at each of time points 2, 3 and 4 also showed statistically significant differences with respective p values of 0.037, 0.011 and $0.042 < 0.05$ (see Table 135, below).

However, when time point 1 was compared with time points 2, 3 and 4, the p values scored 0.206, 0.105 and 0.201 > 0.05 respectively, showing no statistically significant differences. It is unclear how these fluctuations came about. They might have resulted from statistical aberrations or some other causes. Whatever the reason, further studies are needed to find out why no significant differences occurred when time point 1 was compared with time points 2, 3 and 4. Nevertheless, the overall results from the SF-MPQ Sensory and Affective sub-scales indicated statistically significant differences in pain reduction.

Table 135 – Overall Pain Effects Measured by WOMAC, VAS & SF-MPQ in This RCT

Outcome Measure	Overall Effect P-Value	Statistically Significant Difference
WOMAC Overall Scales (Q1-24)	0.000*	Positive
WOMAC Pain Sub-scale (Q1-5)	0.002*	Positive
WOMAC Stiffness Sub-scale (Q6-7)	0.008*	Positive
WOMAC Physical Function Sub-scale (Q8-24)	0.000*	Positive
VAS	0.000*	Positive
McGill Pain Scale (Sensory) Q1-11	0.037*	Positive
McGill Pain Scale (Affective) Q12-15	0.070	Negative
McGill Pain Scale (Q1-15)	0.030*	Positive
McGill Pain VAS Scale (Q16)	0.000*	Positive
McGill Pain VAS Scale (Q17)	0.000*	Positive

*p-value < 0.05 significant

VAS Pain Sub-Scale (Q16)

SF-MPQ Q16 is a VAS pain sub-scale similar to the VAS scale primary outcome measure used in this study. Overall findings from the SF-MPQ VAS Pain sub-scale (Q16) also correlated with the WOMAC pain sub-scales and VAS scale, scoring a p value < 0.001, indicating statistically significant differences between active and sham laser groups. Between group comparisons at each of time points 2, 3 and 4 also showed statistically significant differences with all p values < 0.001 (see Table 78, above). When time point 1 was compared with time points 2, 3 and 4, the p values scored 0.001, 0.000 and 0.003 < 0.05 respectively, showing statistically significant differences.

In summary, all results for the SF-MPQ VAS Pain sub-scale indicate that laser acupuncture statistically significantly reduces pain, again validating with the primary outcome measures – WOMAC pain sub-scale and VAS – and demonstrating consistency and reliability.

Present Pain Intensity (PPI) Sub-scale Q17

The overall findings from the SF-MPQ PPI sub-scale (Q17) correlated with the WOMAC pain sub-scale, scoring a p value < 0.001, indicating statistically significant differences between active and sham laser groups. Between-group comparisons at each of time points 2, 3 and 4 scored respective p values of 0.000, 0.000 and 0.001 < 0.05, showing statistically significant differences. When time point 1 was compared with time points 2, 3 and 4, the p values scored 0.000, 0.001 and 0.003 < 0.05 respectively, again showing statistically significant differences.

Overall, the SF-MPQ VAS PPI sub-scale results indicated that laser acupuncture statistically significantly reduces pain.

6.12.4 Commonalities of Outcome Measures

Measuring Pain, Stiffness & Physical Function

The positive outcomes observed for WOMAC were supported by the VAS scores. Scores for the active laser group in VAS dropped significantly over time from 4.88 to 0.28 at week 2; 0.44 and 0.98 at weeks 3 and 4 respectively. In comparison, the sham laser scores started at 4.88, dropped to 2.67 at time point 2 and to 3.39 for time point 3, finally stopping at 2.85 at time point 4 (p = 0.001; 0.0001 and 0.013 respectively).

In terms of SF-MPQ, two-group comparisons were made on different sections, namely the Sensory Sub-scale (Q1-11), Affective Sub-scale (Q12-15), Sensory and Affective Sub-scale (Q1-15), Pain VAS Sub-scale (Q16) and Presenting Pain Intensity Sub-scale (PPI) (Q17). Overall effect scores produced respective p values of 0.037, 0.070, 0.030,

0.000 and 0.000. It was noted that the active laser group significantly improved in the sub-scales for Sensory Pain, Sensory and Affective Pain, VAS Pain and PPI while Affective Pain recorded no difference.

The SF-MPQ sub-scale results demonstrated that all pain measurements except the Affective Pain Sub-scale produced a positive outcome. The insignificant response in the Affective Pain sub-scale (see Table 70 in the Results Chapter) might have been connected to the way the affective scale measures pain as tiring-exhausting, sickening, fearful and punishing-cruel. Given that OAK measured at Kellgren-Lawrence Grade 2-3 is a chronic degenerative condition rather than an acute painful condition that is punishing and cruel, etc, it is reasonable to assume that the Affective sub-scale might be a more appropriate measure for acute pain rather than chronic OAK pain. This might explain why there were no differences between the two groups in the SF-MPQ Affective Pain Sub-scale.

However, other pain measurements from VAS, WOMAC, SF-MPQ Sensory and Affective sub-scale, SF-MPQ VAS sub-scale and SF-MPQ PPI all showed statistically significant difference between two groups. This indicates that the positive treatment outcomes for pain in this study were consistent and reliable, and, furthermore, were validated by VAS, WOMAC and SF-MPQ. This implies that the treatment effects on the different elements of pain were highly successful as demonstrated across the different types of measures, i.e. pain sensations subjectively measured by (VAS) or physical pain measured by (WOMAC) or pain in different situations and contexts (WOMAC) or sensory and affective types of pain (SF-MPQ).

Comparisons with Other Studies Using Low-Intensity Laser Acupuncture for OAK

The positive results of this study exceeded the findings of Yurtkuran et al. (2007) and Hinman et. al (2014), both of which reported no positive outcome for pain. Possible reasons for negative findings in other studies might relate to the misuse of a red light as a placebo, coupled with a low laser dose not based on WALT recommendations. However, other differences might have accounted for anomalies in results. For example, Yurtkuran et al. (2007) irradiated a single acupuncture point with very low energy (0.4J) while Hinman et al. (2014) did not standardise the acupuncture points

used, leaving it to eight different laser operators to choose from a list of more than 30 acupuncture points.

Additionally, both studies did not rationalise TCM disease pattern differentiation; nor did they use a formula-specific treatment principle. Despite this, the Yurtkuran study did achieve a reduction in swelling. However, the Hinman study concluded that neither laser nor needle acupuncture conferred benefit over sham for pain or function, with the WOMAC and VAS sub-scales indicating no statistically significant difference between groups. The use of a low laser dosage and a non-credible sham laser device appear to have contributed to the Hinman study's negative outcomes.

6.13 Assessing Factors Associated with Placebo Effect

As noted earlier, the placebo effect can have a significant impact on study outcomes. Many studies in this field fail to adequately account for or measure the placebo effect. Consequently, this study undertook a vigorous examination of the placebo effect by adapting a number of standardised instruments that measure various elements of the placebo effect. The Credibility Expectancy Questionnaire (C/E), Working Alliance Inventory - Short Form C (WAI-C) and Multi-dimensional Health Locus of Control – Form C (MHLC-C) were used to assess potential factors associated with placebo. These are examined below (see also copies of placebo instruments provided in Appendices 15, 16 & 17).

6.13.1 Credibility/Expectancy Questionnaire

The Credibility Expectancy Questionnaire (C/E), which measures the psychometric properties of treatment expectancy and rationale credibility in participants, yielded some interesting differences. Findings from the Credibility sub-scale (Q1-3) showed there was no significant difference ($p = 0.838$) between the two groups at baseline prior to treatment (see Table 84 in the Results Chapter). However, over time, the

scores for the two groups diverged to become statistically different at time point 4 (12 weeks; p = 0.035). This suggests that participants in the sham laser group may have become aware over time that they had received sham treatments. This is very evident when the timelines are observed. While the active laser scores were maintained or even increased, the sham laser scores dropped and continued to drop over time (see Table 82 in Results Chapter). On the other hand, this could imply that the credibility and expectancy score increased because the active laser group improved while the sham laser group worsened. This meant that those receiving the active treatment perceived a greater sense of credibility and expected better outcomes as they noticed an improvement in their symptoms and this may have compounded the positive therapeutic effect. Conversely, the credibility and expectancy score decreased in the control group because they did not perceive any improvement in their condition.

The Expectancy sub-scale (Q4-6) evaluated whether participants believed they would get better. Other than the baselines, the follow-up scores at time points 2, 3 and 4 (p = 0.034, 0.007 and 0.003 respectively) were significantly different (see Table 88 in Results Chapter). This suggests that, like the credibility questions, participants in the sham group may have believed they were not receiving a real laser intervention. Furthermore, the progress of treatment might have impacted on the expectations of the sham laser group, where improvement was not significant.

However, the fact that the expectancy scale differed between the two groups might also be due to the participants' beliefs, personal traits (optimism, pessimism, anxiety) and attitudes towards treatment. The patient's expectation of what a treatment might achieve is an important determinant of the placebo response (Abhishek et al. 2013). This is the reason why optimists have been found to experience greater and more reproducible sham analgesia (Morton et al. 2009). In any event, it is very likely the differences in the expectancy score in this RCT were due to the positive treatment effect experienced by the active group, as borne out by WOMAC and VAS results and the Credibility Expectancy (Q1-6). Many of the indicators for therapeutic treatments described by Abhishek et al. (2013) and Morton et al. (2009) appear to correlate with the findings C/E generated in this RCT. Those findings indicated that belief in and expectancy of a treatment can influence treatment outcomes due to psychological

influences and confirmed the effect of expectancy on the reward system of the brain if patients undergoing therapy are conditioned about expectancy (Pariente et al. 2005). Such psychological influences may also suggest benefit in the practitioner conditioning credibility and expectancy in patients to maximise treatment outcomes.

6.13.2 Working Alliance Inventory Short Form C– WAI (C)

The Working Alliance Inventory Short Form C (WAI-C) was a unique measure introduced to the study to evaluate the relationship between the practitioner and the participant. This instrument has three separate sub-scales that measure agreement on (1) the therapy task; (2) development of an affective bond between the practitioner and participant; and (3) therapy goals. As noted earlier, there was no significant difference between the two groups at baseline, signifying that the working alliance was similar for the two groups. Over time, the total WAI (C) scores (Q1-12) dropped for the sham laser group while the active laser group scores increased at all three time points, p = 0.028; 0.012 and 0.008 respectively (see Table 108 in the Results Chapter).

Again, this might reflect the failure of the sham group to improve in their primary outcome (pain and function as measured by WOMAC and VAS), translating to a poorer working relationship. This supposition was supported by findings from the sub-scale that evaluated the "affective bond" occurring in a therapeutic relationship. At time point 3 and 4, it was found that scores were significantly different between the two groups (p = 0.008 and 0.011 respectively), with the scores increasing for those in the real laser group and the sham laser group scores decreasing slightly (see Table 94 in Results Chapter).

These findings showing the between group differences in three factors – task, bond and goals – illustrate the importance of establishing a co-operative practitioner-patient working relationship to achieve an optimum therapeutic outcome. This is in line with observations noted by Webb, DeRubeis & Barber (2010), who claimed that variations in symptom change were significantly related to the WAI (C) factor that assesses practitioner-patient agreement on the goals and tasks of therapy.

6.13.3 Multi-dimensional Health Locus of Control – Form C (MHLC-C)

No significant differences were found in all scales of the Multi-dimensional Health Locus of Control – Form C (MHLC-C), which measured the participant's belief in their health being controlled by their own internal beliefs ($p = 0.840 > 0.05$) or influenced by external factors – chance ($p = 0.413 > 0.05$), powerful others ($p = 0.548 > 0.05$), doctor ($p = 0.548 > 0.05$) and other people ($p = 0.269 < 0.05$), indicating that the psychological element of belief between the two groups was homogeneous. This implies that the positive treatment result was not due to placebo or psychological influences, but more likely to the treatment effect. It also suggests that changes in the C/E and WAI (C) for the active treatment group might have resulted from the positive effects of treatment, which then translated into changes in their beliefs and expectations of treatment.

It appears that the MHLC–C scales for internal belief, chance, powerful others, doctor and other people might have less impact on the treatment outcome than the credibility, expectancy, task, bond and goal factors.

6.14 Importance of the Patient-Practitioner Relationship

It is interesting to observe the link between the sub-scales of "Doctor" in MHLC-C with the "Bond" in WAI (C). Both "Doctor" and "Bond" scales referred to the relationship with doctor or practitioner. The mean score p value score in "Doctor" was significantly different at time point 3 ($p = 0.041$), but no significant difference occurred in results for factors covering "Internal Belief", "Chance", "Powerful Others" and "Other People" (see Results Chapter). This suggests that the "Doctor" relationship is more important than other factors for this population sample.

In the WAI (C) "Bond" scale, there was significant difference between groups in the overall effect with a p value of 0.032. This highlighted the importance and significance of the patient-practitioner/doctor relationship for any therapeutic treatment because the treatment group had a better relationship or bonding with the practitioner, which could have helped improve the OAK condition.

The relationship with “Doctor” in MHLC-C and “Bond” in WAI (C) appears to share some similarities in faith, belief and trust, but WAI (C) seems to focus more on personal and mutual bonding between patient and practitioner. This suggests that WAI (C) is a more sensitive scale than MHLC-C in measuring the patient-practitioner relationship, reflecting in the significant differences that WAI (C) showed between groups and impacted on the treatment outcome, where MHLC-C did not. In summary, this implies that mutual bonding between patient and practitioner is an important influence on the success of a therapeutic treatment.

6.15 Unique & Significant Features of this RCT

Conclusions

The positive outcomes this RCT achieved for OAK pain, stiffness and physical function stemmed from a number of unique design features. These included strict adherence to the TCM paradigm, and using a diagnostic and pattern differentiation strategy that addressed the cause and symptoms of OAK with standardised treatment-specific acupuncture points.

Other design features were a valid and credible placebo and the use of optimum laser parameters and protocols based on a sound understanding of laser-tissue reactions, cellular substrates, the relationship between laser wavelengths, laser penetration depths at targeted anatomical sites and the optical properties of tissue.

Strictly following CONSORT/STRICTA/WALT guidelines also contributed to the achievement of robust and reliable findings, as did calculation of the estimated sample size, randomisation process, double-blinding of the practitioner and participants, use of a credible placebo device/arrangement and a homogeneous sampling. Furthermore, participants indicated they were not sure they were in an active or sham laser group. For all outcome measures, baseline scores were found to be similar between the two groups, demonstrating that homogeneity was achieved for both groups.

Another aspect of the design was the intention-to-treat approach to data analysis. This feature has been shown to limit bias because all data is carried forward for those participants that dropped out of the study (N=6). Interestingly, the number of participants who dropped out were greater in the sham laser group (N=4) than in the active laser group (N=2).

Additionally, three different outcome measures were selected to validate the reliability and consistency of pain factors (WOMAC, VAS, SF-MPQ) and three instruments to assess factors associated with the placebo effect (C/E, WAI (C) and MHLC-C).

Another unique feature was the use of instruments to specifically assess the credibility and expectancy of individual participants at each time point throughout the study. The results demonstrated that the random allocation to either group at baseline was successful in that both groups were similar in the belief of laser to treat their condition and the expectancy that they would improve over the course of the treatment.

WAI (C), which assessed the relationship between the practitioner and participant, was a design feature not used in previous laser studies. MHLC-C assessed factors relating to the placebo effect, such as whether the condition being treated would get better by chance; whether the practitioner would contribute to the treatment outcome; the influence of powerful others, such as doctors; as well as the participants' internal beliefs.

In all, these design features resulted in a vigorous and well-designed study that overcame many of the issues and design limitations found in previous studies. It is suggested that future studies should consider including such features to ensure research veracity.

6.16 Study Limitations

With the benefit of hindsight, a number of observations have been made about this study's limitations.

Observational Group

Study limitations precluded an opportunity to turn this RCT into a three-armed study with the addition of an observation group. Comparing the placebo group with an observational group would help to clearly identify differences in factors relating to the placebo effect. Subject to any ethical considerations, future researchers may wish to consider this option.

Recruitment

One possible criticism of the study is whether the study was sufficiently powered to identify statistical differences between groups. As mentioned previously, recruitment difficulties allowed only 40 participants to be enrolled rather than the 60 participants originally planned. Despite this limitation, positive outcomes were achieved. Nevertheless, the study would have benefited from a larger sample size and an efficient way of measuring swelling objectively. A larger sample size is therefore warranted to confirm the outcome of this RCT.

Scope for More Objective Measures

Lack of resources also limited the use of additional outcome measures that would have improved analysis of any improvements flowing from the application of TCM-based laser acupuncture on OAK pain. The use of post-intervention x-rays, for example, would have been beneficial because initial diagnosis was made under the Kellgren & Lawrence osteoarthritis grading system. Post-treatment x-rays would have shown whether changes in the severity of OAK did indeed produce a progressive effect after 12 laser acupuncture treatments and at six months' follow-up.

Thermography, a non-invasive, non-contact and radiation-free tool that uses body heat to help diagnose a host of health conditions, also might have benefited the study. Thermographic systems measure temperatures ranging from 10°-55° C to an accuracy of 0.1° C and can focus down to 75 x 75mm. Thermography appears to be ideal for tracking reductions in inflammation associated with OAK and improvements in microcirculation.

Magnetic resonance imaging (MRI) is another measure worthy of consideration because of its ability to show changes in cartilage, tissue and bone resulting from laser acupuncture. Again, the limited resources available to this PhD study precluded these measures.

6.17 Possible Inferences & Implications

The positive outcomes of this study should encourage further research into the effectiveness of TCM-based laser acupuncture and the establishment of optimum scientifically-based parameters for the treatment of a range of health disorders.

With more evidence-based studies, it is reasonable to assume that the healing mechanisms of this dual energy laser acupuncture system could lead to further development of a unique healthcare modality built around TCM principles.

Western-trained scientists have already established, through clinical research and laboratory studies, that low-intensity laser therapy is beneficial for health conditions as diverse as traumatic brain injury, stroke, spinal cord injury and degenerative central nervous system disease, wound and scar healing (Chung et al. 2012).

However, results from this study raise a number of important questions for future research. For example, is it possible to apply integrative laser acupuncture to other forms of degenerative conditions? This appears to be likely so. Chung et al. (2012) has reported that low-intensity laser therapy is a viable treatment for degenerative brain disorders, such as familial amyotropic lateral sclerosis, dementia, Alzheimer's disease and Parkinson's disease. Furthermore, experiments have found low-intensity laser therapy increases respiration and ATP production, promoting neurogenesis and the migration of neurons (Chung et al. 2012). It is therefore suggested that laser acupuncture may be beneficial for the treatment of other forms of degenerative conditions because of its dual-energy system.

Although this RCT's findings complement the outcomes of other clinical studies showing low-intensity laser therapy reduces other pain conditions, including migraine

and musculo-skeletal disorders affecting the neck, back and extremities, more research is needed to compare the effects of irradiating acupuncture points and trigger points/tender points with a view to establishing more precise treatment protocols.

Exploring how different acupuncture points might react to different laser energy doses and treatment times presents another research opportunity. For example, it is not known whether acupuncture points with a higher density of vascular structures are more responsive to laser energy than other points or whether vascularised acupuncture points need to be irradiated with smaller doses of laser energy than less vascularised points.

Answers to these questions are important because they may lead to establishing an appropriate laser fluence or dosage to achieve an optimum therapeutic benefit – something that has so far eluded low-intensity laser therapy researchers trying to master the Arndt-Schultz Law.

Of special interest is establishing whether differentiating OAK disease patterns into disease stages (e.g. onset, acute or chronic) and varying laser acupuncture energy doses or acupuncture points might more precisely address particular stages of the presenting condition.

Other possible areas of study include determining whether treating underlying causes of OAK would remain unchanged if laser acupuncture interventions used fewer acupuncture points to treat a health condition or whether it is possible to reduce treatment times by using a laser with a higher output power or slightly less energy, thus making treatments more efficient and saving resources.

In advocating further research, this study points to the need for acupuncture practitioners wishing to practice laser acupuncture to first develop a sound understanding of laser science, tissue interaction and its healing mechanisms. Conversely, laser therapists wishing to use Chinese medicine-based principles need to master the essence of the TCM paradigm so that they might capture the best of a unique dual-energy system that has the potential to provide treatments with maximum effect.

Essentially, this study provides a robust design methodology to aid replication based on the following key factors: (1) the need to establish a credible blinding and placebo arrangement; (2) utilising science-based laser protocols; (3) employing treatments powered by the TCM paradigm, including diagnostic disease pattern differentiation, treatment principle and the use of a standardised treatment-specific acupuncture formulae that addresses the cause and symptoms of OAK; and (4) differentiating placebo factors that may impact on treatment outcomes. This study also demonstrates the benefits of following CONSORT, STRICTA and WALT guidelines and recommendations.

Significantly, the outcomes of this study indicate, for the first time, that laser acupuncture applied in strict accordance with TCM principles enhances laser OAK treatment outcomes. However, further research is required to substantiate its benefit.

Chapter 7 Conclusion

This RCT achieved its objective of testing the effectiveness of laser acupuncture for the treatment of degenerative OAK. The results rejected the null hypothesis and confirmed that laser acupuncture, when applied in strict accordance with Traditional Chinese Medicine (TCM) principles, reduces pain and stiffness and improves physical function in OAK.

The primary outcome measures, WOMAC and VAS, scored an overall positive effect with p values < 0.001, showing statistically significant differences between active laser and sham laser groups. This was further validated by the secondary measure of pain – the Short Form McGill Pain Questionnaire (SF-MPQ) and its three sub-scales, Q1-15 (Sensory & Affectory), Q16 (Pain VAS) and Q17 (Present Pain Intensity), which scored respective p values of 0.030, 0.000 and 0.000 < 0.05.

Significantly, the study infers the benefit of integrating photo-biomodulation with 2,500-year-old TCM theory to treat what TCM identifies as Bi Syndrome using acupuncture points that specifically target OAK. It is therefore interesting to contemplate whether other forms of laser acupuncture, based for example on the Japanese or Korean systems, might yield similar results.

Nevertheless, the vascular density of acupuncture points appears to amplify two energy transporting systems – one based on the Channel Theory that forms the basis of TCM; the other cellular and peripheral nerve transduction signaling believed to occur in photo-biomodulation. The study results therefore suggest that integrating these two energy transport systems – low-intensity laser with acupuncture – may benefit OAK by magnifying and accelerating the human body's healing and metabolic processes.

Notably, the level of OAK pain and related symptoms in the active intervention group did not return to the original baseline, even at three months' follow-up. This may

relate to a treatment protocol that strictly followed the TCM paradigm, which is believed to treat the cause and the symptoms of health imbalances, and embraced physical and psychological factors involved in healing, coupled with appropriate laser parameters selected for the treatment of OAK (i.e. 18J/point three times a week over four weeks for a total of 12 treatments). This suggests that acupuncture point formulae developed specifically to address the two main causes of Bi Syndrome – Blood Stasis and Phlegm Retention – contributed to the finding that OAK pain levels and related symptoms did not rebound to baseline.

Placebo Impacts

In response to claims that laser acupuncture treatment is no better than placebo, this RCT assessed, for the first time, how factors associated with the placebo effect relate to treatment outcomes. Three Instruments – C/E, WAI (C) and MHLC-C – evaluated the effect of the practitioner-patient relationship; the benefit of rationalising client expectancy and beliefs; and building a caring practitioner-patient bond as both parties work towards the same treatment goal. The three outcome measures also acted as a proxy measure of task compliance and its effects related to treatment outcomes. While some practitioners may view these factors as a placebo-analgesia effect, they are in fact part of "psychological medicine" validated in two significant studies investigating neural influences of acupuncture on pain response (Pariente et al. 2005) and placebo response mechanisms in osteoarthritis pain (Abhishek el al. 2013). Pariente et al. (2005) demonstrated that expectation of – and belief in – a treatment has a physiological effect on the brain that appears to mediate a potentially powerful non-specific clinical response to acupuncture. Abhishek et al. (2013) reported that most parts of the brain involved in pain processing are influenced by placebo-induced analgesia, postulating that factors enhancing treatment response should be used to manage chronic pain conditions like OAK. These conclusions suggest that incorporating placebo-psychological medicine in TCM treatments might serve as a valid adjunct to the modality's mind, body and spirit philosophy and maximise treatment effects.

Significance of Study Design

Many elements contributed to the robust and reliable design developed for the current study. This was enabled by reviewing the strengths, weaknesses and flaws found in previous clinical trials and consideration of research guidelines and recommendations made by CONSORT, STRICTA and WALT.

Attention was given to ensuring the veracity of this study's sample size; randomisation; recruitment; and inclusion and exclusion criteria to ensure a homogeneous population.

Robust protocols for double blinding with a credible placebo; standardisation of the intervention; use of validated, relevant and highly regarded objective measures; and appropriate assessment periods were employed to allow for reliable statistical analyses of data and ensured the study was replicable.

STRICTA guidelines for conducting needle acupuncture trials were adapted to permit the integration of TCM-based acupuncture treatment principles and practices with laser acupuncture protocols. A key part of this process was the development of OAK-specific point formulae to address the symptoms and causes of OAK and designing complementary laser parameters.

Significantly, the laser dosage employed for this study – 18J/point – appears to confirm that this comparatively high fluence is effective for OAK and does not produce adverse effects. Until now, most laser studies have tended to use low joules to avoid the inhibitory effects high fluences sometimes produce in photo-biomodulation. The 18J/point used here thus provides a foundation for further research.

Need for Further Research

This study suggests that laser acupuncture may also benefit other health conditions similar to OAK. Unlike conventional needle acupuncture, laser acupuncture applied with a Class 3B low-intensity laser is non-invasive and its non-thermal properties produce little or no sensation. Consequently, adults and children who are needle-phobic towards traditional needle acupuncture can be treated with a dynamic dual-energy healing system that produces health gains without pain.

Moreover, there is a very real need for laser acupuncture researchers and practitioners to work towards establishing TCM-based acupuncture rationale/principles with specific point formulae and more precise laser parameters for a range of common health disorders. Ideally, such protocols and parameters should include allowance for the way laser acupuncture parameters apply to different types of disease or injury; stages of pathophysiological disease (acute, chronic and remission); optical properties of anatomical regions and treatment sites; ethnicity; as well as the participants' age and gender differences.

More guidance is also needed on wavelengths, power density, output power, fluence/dosage, mode of frequency and application, and treatment program duration, particularly as these parameters may vary according to the condition being treated as well as patient characteristics.

In this regard, it would be beneficial for organisations like the Society for Acupuncture Research or WALT to recommend that clinicians attain essential laser science knowledge before starting a clinical trial. Improved understanding of laser science and the way it can be used to advance heath care would help make trial designs more robust and accelerate evidence-based research to substantiate the expanding benefits of laser acupuncture.

Furthermore, this study indicates that the full potential of TCM-based laser acupuncture remains largely untouched. More evidence-based research into the benefit of integrating laser acupuncture with the TCM paradigm is needed for it to develop into a cogent modality that merges ancient Eastern philosophies and healing systems with science-based technologies from the West.

Wider application of TCM-based laser acupuncture has the potential to alleviate the financial burden placed on OAK sufferers and health care systems because it may alleviate the current over-reliance on symptomatic NSAIDs and other pain-killing medications that can lead to undesirable side-effects. Similarly, more robust laser acupuncture studies are needed to confirm its potential for improving many perplexing health conditions and determining cost–benefits, including potential reductions in pharmacotherapy or surgery.

However, any future research must be scientifically sound, explicit and clearly state the type of laser acupuncture used, i.e. TCM-based laser acupuncture, medical laser acupuncture, trigger point laser acupuncture or tender point laser acupuncture. If this is not done, the current confusion about intervention efficacy will continue, making it impossible to validate the effectiveness of laser acupuncture as a treatment modality.

Recommendations for Future Studies

In the interests of developing a better understanding of the way TCM-based laser acupuncture works and encouraging its wider use, clinicians and researchers undertaking studies are encouraged to:

- Replicate this RCT to validate its treatment outcomes;

- Set appropriate laser wavelengths and parameters for the condition being treated, bearing in mind the effectiveness and safety of higher fluences noted in this study;

- Where possible, use a larger sample size with a longer treatment program and longer follow up assessment, such as six months or one year;

- Subject to ethical considerations, add an observational group as a third arm to track treatment differences in the active laser and sham laser treatment groups or incorporate a fourth arm for an acupuncture treatment group to compare against laser acupuncture, sham laser and observational groups to identify which group has a better treatment outcome;

- Explore the possibility of shortening treatment times and minimising clinic resources by using lasers with a higher output power to deliver the same fluences/dosage;

- Strictly follow the TCM paradigm by applying pattern differentiation to diagnosis, providing a treatment rationale/principle, treating the cause and

the symptoms of the imbalance and developing a point-specific treatment strategy; and

- Further explore factors that may influence placebo effects on mind, body and spirit elements in TCM-based laser acupuncture, and how they affect treatment outcomes.

In keeping with the Chinese philosophy of the Tao, it is hoped these recommendations, together with the design methodology, TCM treatment principles and laser parameters used in this study, help point *The Way* for further research into the untapped benefits of using laser acupuncture as a safe, effective and painless treatment for OAK and other chronic health conditions.

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Appendix 1 – Glossary

GLOSSARY OF LASER TERMS

Absorb To transform radiant energy into a different form, with a resultant rise in temperature.

Absorption Transformation of radiant energy to a different form of energy by the interaction of matter, depending on temperature and wavelength.

Accessible Emission Level The magnitude of accessible laser (or collateral) radiation of a specific wavelength or emission duration at a particular point as measured by appropriate methods and devices. Also means radiation to which human access is possible in accordance with the definitions of the laser's hazard classification.

Accessible Emission Limit (AEL) The maximum accessible emission level permitted within a particular class. In ANSI Z 136.1, AEL is determined as the product of accessible emission

Maximum Permissible Exposure limit (MPE) and the area of the limiting aperture (7 mm for visible and near-infrared lasers).

Aperture An opening through which radiation can pass.

Argon A gas used as a laser medium. It emits blue-green light primarily at 448 and 515 nm.

Attenuation The decrease in energy (or power) as a beam passes through an absorbing or scattering medium.

Aversion Response Movement of the eyelid or the head to avoid an exposure to a noxious stimulant, bright light. It can occur within 0.25 seconds, and it includes the blink reflex time.

Beam A collection of rays that may be parallel, convergent, or divergent.

Beam Diameter The distance between diametrically opposed points in the cross section of a circular beam where the intensity is reduced by a factor of e^{-1} (0.368) of the peak level (for safety standards). The value is normally chosen at e^{-2} (0.135) of the peak level for manufacturing specifications.

Beam Divergence Angle of beam spread measured in radians or milliradians (1

milliradian = 3.4 minutes of arc or approximately 1 mil). For small angles where the cord is approximately equal to the arc, the beam divergence can be closely approximated by the ratio of the cord length (beam diameter) divided by the distance (range) from the laser aperture.

Blink Reflex See aversion response.

Brightness The visual sensation of the luminous intensity of a light source. The brightness of a laser beam is most closely associated with the radio-metric concept of radiance.

Carbon Dioxide Molecule used as a laser medium. Emits far energy at 10,600 nm (10.6 μm).

Closed Installation Any location where lasers are used which will be closed to unprotected personnel during laser operation.

CO_2 Laser A widely used laser in which the primary lasing medium is carbon dioxide gas. The output wavelength is 10.6 μm (10600 nm) in the far infrared spectrum. It can be operated in either CW or pulsed mode.

Coherence A term describing light as waves which are in phase in both time and space. Monochromaticity and low divergence are two properties of coherent light.

Collimated Light Light rays that are parallel. Collimated light is emitted by many lasers. Diverging light may be collimated by a lens or other device.

Collimation Ability of the laser beam to not spread significantly (low divergence) with distance.

Continuous Mode The duration of laser exposure is controlled by the user (by foot or hand switch).

Continuous Wave (CW) Constant, steady-state delivery of laser power.

Controlled Area Any locale where the activity of those within are subject to control and supervision for the purpose of laser radiation hazard protection.

Diffuse Reflection Takes place when different parts of a beam incident on a surface are reflected over a wide range of angles in accordance with Lambert's Law. The intensity will fall off as the inverse of the square of the distance away from the surface and also obey a Cosine Law of reflection.

Divergence The increase in the diameter of the laser beam with distance from the exit aperture. The value gives the full angle at the point where the laser radiant exposure or irradiance is e-1 or e-2 of the maximum value, depending upon which criteria is used.

Embedded Laser A laser with an assigned class number higher than the inherent capability of the laser system in which it is incorporated, where the system's lower classification is appropriate to the engineering features limiting accessible emission.

Emission Act of giving off radiant energy by an atom or molecule.

Enclosed Laser Device Any laser or laser system located within an enclosure which does not permit hazardous optical radiation emission from the enclosure. The laser inside is termed an "embedded laser."

Energy (Q) The capacity for doing work. Energy is commonly used to express the output from pulsed lasers and it is generally measured in Joules (J). The product of power (watts) and duration (seconds). One watt second = one Joule.

Excimer "Excited Dimer" A gas mixture used as the active medium in a family of lasers emitting ultraviolet light.

Fail-safe Interlock An interlock where the failure of a single mechanical or electrical component of the interlock will cause the system to go into, or remain in, a safe mode.

Gas Discharge Laser A laser containing a gaseous lasing medium in a glass tube in which a constant flow of gas replenishes the molecules depleted by the electricity or chemicals used for excitation.

Gas Laser A type of laser in which the laser action takes place in a gas medium.

Helium-Neon (HeNe) Laser A laser in which the active medium is a mixture of helium and neon. Its wavelength is usually in the visible range. Used widely for alignment, recording, printing, and measuring.

Infrared Radiation (IR) Invisible electromagnetic radiation with wavelengths which lie within the range of 0.70 to 1000 μm. These wavelengths are often broken up into regions: IR-A (0.7-1.4 μm), IR-B (1.4-3.0 μm) and IR-C (3.0-1000 μm).

Intrabeam Viewing The viewing condition whereby the eye is exposed to all or part of a direct laser beam or a specular reflection.

Irradiance (E) Radiant flux (radiant power) per unit area incident upon a given surface. Units: Watts per square centimeter. (Sometimes referred to as power density, although not exactly correct).

Laser An acronym for light amplification by stimulated emission of radiation. A laser is a cavity with mirrors at the ends, filled with material such as crystal, glass, liquid, gas or dye. It produces an intense beam of light with the unique properties of coherency, collimation, and monochromaticity.

Laser Accessories The hardware and options available for lasers, such as secondary gases, Brewster windows, Q-switches and electronic shutters.

Laser Controlled Area See Controlled Area.

Laser Device Either a laser or a laser system.

Laser Medium (Active Medium) Material used to emit the laser light and for which the laser is named.

Laser Rod A solid-state, rod-shaped lasing medium in which ion excitation is caused by a source of intense light, such as a flash lamp. Various materials are used for the rod, the earliest of which was synthetic ruby crystal.

Laser Safety Officer (LSO) One who has authority to monitor and enforce measures to control laser hazards and effect the knowledgeable evaluation and control of laser hazards.

Laser System An assembly of electrical, mechanical and optical components which includes a laser. Under the Federal Standard, a laser in combination with its power supply (energy source).

Lens A curved piece of optically transparent material which, depending on its shape, is used to either converge or diverge light.

Light The range of electromagnetic radiation frequencies detected by the eye, or the wavelength range from about 400 to 760 nm. The term is sometimes used loosely to include radiation beyond visible limits.

Limiting Aperture The maximum circular area over which radiance and radiant exposure can be averaged when determining safety hazards.

Maintenance Performance of those adjustments or procedures specified in user information provided by the manufacturer with the laser or laser system, which are to

be performed by the user to ensure the intended performance of the product. It does not include operation or service as defined in this glossary.

Maximum Permissible Exposure (MPE) The level of laser radiation to which a person may be exposed without hazardous effect or adverse biological changes in the eye or skin.

Nd:Glass Laser A solid-state laser of neodymium:glass offering high power in short pulses. A Nd-doped glass rod used as a laser medium to produce 1064 nm light.

Nd:YAG Laser Neodymium:Yttrium Aluminium Garnet. A synthetic crystal used as a laser medium to produce 1064 nm light.

Neodymium (Nd) The rare earth element that is the active element in Nd:YAG laser and Nd:Glass lasers.

Nominal Ocular Hazard Area (NOHA) The Nominal Ocular Hazard Area describes the space within which the level of the direct, reflected or scattered radiation during normal operation exceeds the applicable MPE. Exposure levels beyond the boundary of the NOHA are below the appropriate MPE level.

Optical Cavity (Resonator) Space between the laser mirrors where lasing action occurs.

Optical Density A logarithmic expression for the attenuation produced by an attenuating medium, such as an eye protection filter.

Optical Fibre A filament of quartz or other optical material capable of transmitting light along its length by multiple internal reflection and emitting it at the end.

Optical Pumping The excitation of the lasing medium by the application of light rather than electrical discharge.

Optical Radiation Ultraviolet, visible, and infrared radiation (0.35-1.4 μm) that falls in the region of transmittance of the human eye.

Output Power The energy per second measured in watts emitted from the laser in the form of coherent light.

Power The rate of energy delivery expressed in watts (Joules per second). Thus: 1 Watt = 1 Joule x 1 sec.

Protective Housing A protective housing is a device designed to prevent access to radiant power or energy.

Pulse A discontinuous burst of laser, light or energy, as opposed to a continuous beam. A true pulse achieves higher peak powers than that attainable in a CW output.

Pulse Duration The "on" time of a pulsed laser, it may be measured in terms of milliseconds, microseconds, or nanoseconds as defined by half-peak-power points on the leading and trailing edges of the pulse.

Pulsed Laser Laser which delivers energy in the form of a single or train of pulses.

Pump To excite the lasing medium. See Optical Pumping or Pumping.

Pumped Medium Energized laser medium.

Pumping Addition of energy (thermal, electrical, or optical) into the atomic population of the laser medium, necessary to produce a state of population inversion.

Radiant Energy (Q) Energy in the form of electromagnetic waves usually expressed in units of Joules (watt-seconds).

Radiant Exposure (H) The total energy per unit area incident upon a given surface. It is used to express exposure to pulsed laser radiation in units of J/cm2.

Reflection The return of radiant energy (incident light) by a surface, with no change in wavelength.

Refraction The change of direction of propagation of any wave, such as an electromagnetic wave, when it passes from one medium to another in which the wave velocity is different. The bending of incident rays as they pass from one medium to another (e.g., air to glass).

Resonator The mirrors (or reflectors) making up the laser cavity including the laser rod or tube. The mirrors reflect light back and forth to build up amplification.

Ruby The first laser type; a crystal of sapphire (aluminum oxide) containing trace amounts of chromium oxide.

Scanning Laser A laser having a time-varying direction, origin or pattern of propagation with respect to a stationary frame of reference.

Secured Enclosure An enclosure to which casual access is impeded by an

appropriate means (e.g., door secured by lock, magnetically or electrically operated latch, or by screws).

Semiconductor Laser A type of laser which produces its output from semiconductor materials such as GaAs.

Service Performance of adjustments, repair or procedures on a non-routine basis, required to return the equipment to its intended state.

Solid Angle The ratio of the area on the surface of a sphere to the square of the radius of that sphere. It is expressed in steradians (sr).

Source The term source means either laser or laser-illuminated reflecting surface, i.e., source of light.

Tunable Laser A laser system that can be "tuned" to emit laser light over a continuous range of wavelengths or frequencies.

Tunable Dye Laser A laser whose active medium is a liquid dye, pumped by another laser or flash lamps, to produce various colors of light. The color of light may be tuned by adjusting optical tuning elements and/or changing the dye used.

Ultraviolet (UV) Radiation Electromagnetic radiation with wavelengths between soft X-rays and visible violet light, often broken down into UV-A (315-400 nm), UV-B (280-315 nm), and UV-C (100-280 nm).

Visible Radiation (light) Electromagnetic radiation which can be detected by the human eye. It is commonly used to describe wavelengths in the range between 400 nm and 700-780 nm.

Wavelength The length of the light wave, usually measured from crest to crest, which determines its color. Common units of measurement are the micrometer (micron), the nanometer, and (earlier) the Angstrom unit.

YAG Yttrium Aluminium Garnet, a widely used solid-state crystal composed of yttrium and aluminum oxides and a small amount of the rare earth neodymium.

- o -

Appendix 2 – Consolidated Standards of Reporting of Trials (CONSORT)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	(v - vi)
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	43-55
	2b	Specific objectives or hypotheses	37-38
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	176-177
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	177-178
Participants	4a	Eligibility criteria for participants	178
	4b	Settings and locations where the data were collected	187
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	180
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	187-193
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N.A.
Sample size	7a	How sample size was determined	290
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N. A.

Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	178-179
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	178-179
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	178-179
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	178-179
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	187
	11b	If relevant, description of the similarity of interventions	187
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	193
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	193
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	194
	13b	For each group, losses and exclusions after randomisation, together with reasons	194
Recruitment	14a	Dates defining the periods of recruitment and follow-up	184-187
	14b	Why the trial ended or was stopped	195
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	195-197
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	194
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	194
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	197-285
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N.A.

Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	290
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	321-323
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	323
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	306-320
Other information			
Registration	23	Registration number and name of trial registry	ACTRN 12813000499788
Protocol	24	Where the full trial protocol can be accessed, if available	UTS library
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	N.A.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Appendix 3: STandards for Reporting Interventions in Clinical Trials of Acupuncture

TABLE X (b)

HOW LASER ACUPUNCTURE FOR OAK RCT MET STRICTA 2010 GUIDELINES FOR REPORTING LASER ACUPUNCTURE TRIALS*

(*Adapted from STRICTA Extension for Reporting Acupuncture Trials – replaces Item 5 in 2010 CONSORT)

Item	Detail	Page number
1. Acupuncture rationale	1a) Laser acupuncture applied according to Traditional Chinese Medicine principles.	43-56
	1b) Reasoning for treatment provided based on historical context, literature sources, and/or consensus methods.	151-152
	1c) Nil variations in treatment.	181
2. Details of laser acupuncture treatments	2a) Number of laser acupuncture treatments per participant per treatment program	185
	2b) Acupuncture points used	1182-183
	2c) Duration of laser acupuncture irradiation and energy level expressed in Joules.	185
	2d) Response sought – reduction in pain and/or swelling.	307-317
	2e) Laser beam applied directly to selected acu-points	182-187
	2f) Irradiation time for each acupuncture point	185 & 187
	2g) Type of laser (Metron Class 3B – 100 mW 810nm, single GaAs diode) applied in CW mode	187
3. Treatment regimen	3a) Number of treatment sessions	185-187
	3b) Frequency and duration of treatment sessions	185 & 187
4. Other components of treatment	4a) Details of other interventions administered to the acupuncture group - nil (although participants were allowed to continue taking any prescribed OA medication	187
	4b) Setting and context of treatment – provided at two private TCM clinics. Each participant was told they would be assigned to either a treatment group or non-treatment group. Participants also were given written information and explanations about the nature of the treatments	187
5. Practitioner background	5) Description of participating laser acupuncturist (AHPRA-registered acupuncturist and TCM practitioner with more than 20 years' experience in the clinical application of Class 3B lasers)	188
6. Control or comparator interventions	6a) Inactive probe provided by laser supplier further adapted to eliminate possible confounding issues caused by pilot light on laser probe	181
	6b) Inactive probe used for sham laser acupuncture treatments.	181

Note: This checklist should be read in conjunction with the explanations of the STRICTA items. It is designed to replace CONSORT 2010's item 5 when reporting an acupuncture trial.

Appendix 4: World Association for Laser Therapy Dosage Recommendations

Recommended treatment doses for Low Level Laser Therapy

Laser class 3 B, 780 - 860nm GaAlAs Lasers. Continuous or pulsed, mean output: 5 - 500mW Irradiation times should range between 20 and 300 seconds

Diagnoses

Tendinopathies	**Points or cm2**	**Joules 780 - 820nm**	**Notes**
Carpal-tunnel	2-3	8	Minimum 4 Joules per point
Lateral epicondylitis	1-2	4	Maximum 100mW/cm2
Biceps humeri c.l.	1-2	6	
Supraspinatus	2-3	8	Minimum 4 Joules per point
Infraspinatus	2-3	8	Minimum 4 Joules per point
Trochanter major	2-4	8	
Patellartendon	2-3	8	
Tract. Iliotibialis	1-2	4	Maximum 100mW/cm2
Achilles tendon	2-3	8	Maximum 100mW/cm2
Plantar fasciitis	2-3	8	Minimum 4 Joules per point
Arthritis	**Points or cm2**	**Joules**	
Finger PIP or MCP	1-2	4	
Wrist	2-4	8	
Humeroradial joint	1-2	4	
Elbow	2.4	8	
Glenohumeral joint	2-4	8	Minimum 4 Joules per point
Acromioclavicular	1-2	4	
Temporomandibular	1-2	4	
Cervical spine	4-12	16	Minimum 4 Joules per point
Lumbar spine	4-8	16	Minimum 4 Joules per point
Hip	2-4	12	Minimum 6 Joules per point
Knee medial	3-6	12	Minimum 4 Joules per point
Ankle	2-4	8	

Daily treatment for 2 weeks or treatment every other day for 3-4 weeks is recommended
Irradiation should cover most of the pathological tissue in the tendon/synovia.
Start with energy dose in table, then reduce by 30% when inflammation is under control
Therapeutic dose windows typically range from +/- 50% of given values, and doses outside these windows are inappropriate and should not be considered as Low Level Laser Therapy. Recommended doses are for white/caucasian skin types based on results from clinical trials or extrapolation of study results with similar pathology and ultrasonographic tissue measurements.

Disclaimer

The list may be subject to change at any time when more research trials are being published. World Association of Laser Therapy is not responsible for the application of laser therapy in patients, which should be performed at the sole discretion and responsibility of the therapist.

Revised¦April¦2010

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Appendix 5: UTS Ethics Committee Approval

9 December 2010

Dr Peter Meier
Medical and Molecular Biosciences
Faculty of Science
CB01.11.25
UNIVERSITY OF TECHNOLOGY, SYDNEY

Dear Peter,

UTS HREC 2010-340 – MEIER, Dr Peter, SMITH, Dr Narelle (for REES, Ms Mei-kin Li, PhD student) – "Evaluation of the Effectiveness of LASER Acupuncture on Osteo Arthritic Knee Pain: A Randomised, Double Blind, Placebo-controlled Clinical Trial"

Thank you for your response to my email dated 21/09/2010. Your response satisfactorily addresses the concerns and questions raised by the Committee, and I am pleased to inform you that ethics clearance is now granted.

Your clearance number is UTS HREC REF NO. 2010-340A

Please note that the ethical conduct of research is an on-going process. The *National Statement on Ethical Conduct in Research Involving Humans* requires us to obtain a report about the progress of the research, and in particular about any changes to the research which may have ethical implications. This report form must be completed at least annually, and at the end of the project (if it takes more than a year). The Ethics Secretariat will contact you when it is time to complete your first report.

I also refer you to the AVCC guidelines relating to the storage of data, which require that data be kept for a minimum of 5 years after publication of research. However, in NSW, longer retention requirements are required for research on human subjects with potential long-term effects, research with long-term environmental effects, or research considered of national or international significance, importance, or controversy. If the data from this research project falls into one of these categories, contact University Records for advice on long-term retention.

If you have any queries about your ethics clearance, or require any amendments to your research in the future, please do not hesitate to contact the Ethics Secretariat at the Research and Innovation Office, on 02 9514 9772.

Yours sincerely,

Associate Professor Marion Haas
Chairperson
UTS Human Research Ethics Committee

Appendix 6 - Information for Recruitment

UNIVERSITY OF TECHNOLOGY SYDNEY

INFORMATION SHEET

Research Project to Test the Effectiveness of LASER Acupuncture on Osteo Arthritis Knee Pain

My name is Meikin Li Rees. I am undertaking post-graduate research studies at the University of Technology, Sydney.

I am conducting research to test the effectiveness of LASER acupuncture on osteo arthritic knee pain and would welcome your assistance.

The research would involve your receiving LASER acupuncture or placebo treatments three times a week for four weeks – a total of 12 treatments with a follow-up assessment at two months. Participants receiving placebo treatments will be offered active treatments on completion of the clinical trial and analysis if the treatment outcomes are proven to be beneficial.

LASER acupuncture is painless. Treatment involves the stimulation of acupuncture points with a beam of low level laser light instead of traditional needles.

LASER acupuncture is safe, provided some simple precautions are followed. For example, you would be required to wear safety goggles during the treatment to protect your eyes.

You may also experience some increase in pain temporarily after treatment. This may be due to the LASER stimulating the flow of blood in the knee, promoting healing.

You would also be required to complete some simple questionnaires about the effects of the treatments on such things as pain, stiffness, walking, general wellbeing, lifestyle and your personal beliefs and attitudes to illness, life, etc.

Each treatment would take about 45-60 minutes and you would be given A$50 at the end of the clinical trial to cover travelling expenses.

Prospective participants will be assessed according to the inclusion criteria to determine their eligibility. Medication intake will not be restricted, although you will be required to track any increase/reduction of dosage.

Inclusion criteria for the 60 subjects will be:

- Adult males or females aged between 35 and 80 years
- Meet TCM and Western diagnostic criteria.
- Have no cognitive disorder and/or other serious health condition.
- Have suffered OAK for less than 10 years.
- Have no history of receiving LASER acupuncture treatment for OAK.
- No restriction on medication intake including anti-inflammatory or analgesics medication.

Exclusion criteria:

- Participants who do not fit the above criteria.
- Participants suffering from other medical conditions, e.g. multiple sclerosis, diabetes, asthma, dementia, cognitive disorders, kidney disease, etc.
- Participants that received hydrocotisones injection directly into knee joints.
- Participants that are photo (light) sensitive or on medication that increases photosensitivity
- Participants who have extensive impaired mobility that that would make participation difficult.

Note: Participants taking arthritis medication will be asked to record whether the LASER acupuncture treatment they receive in the study impacts on their regular intake of medication or reduces OAK pain. Information provided by medication users will allow the amount of medication taken to reduce pain to be measured. Questionnaires and interviews will be used to screen subjects.

If you are interested in taking part in this unfunded research, I would be pleased if you would contact me on (02) 9630 6388 or my supervisor, Associate Professor Peter Meier, on (02) 9514 7858.

You are under no obligation to participate in this research and you have the right to withdraw at any time.

Yours faithfully,

Meikin Li Rees

PhD Candidate

C/-

UTS telephone number 02-9514 78 58/02-9630 6388

E-mail Mei-kin.L.Rees@student.uts.edu.au

Appendix 7: Participants Consent Form

UNIVERSITY OF TECHNOLOGY SYDNEY

PARTICIPANT CONSENT FORM

I, _____, agree to take part in the research project to test the effectiveness of LASER acupuncture on osteo arthritis knee pain being conducted by Meikin Li Rees (telephone number (02) 9630 6388/UTS Tel No. 02-9514 7858), of the University of Technology, Sydney for her PhD degree.

I understand the research is unfunded and its purpose is to find out whether LASER acupuncture can reduce pain and dependency on drug treatments for osteo arthritis and alleviate drug side effects.

I understand that participation in this research will involve:

- Receiving three LASER acupuncture or placebo treatments a week for four weeks – a total of 12 treatments with a follow-up assessment at two months – and each treatment will take about 45-60 minutes.

- The requirement to wear safety goggles to prevent any eye injury during treatments.

- Possible treatment reactions such as light-headedness and slight but temporary increase in pain.

- Completing some simple questionnaires about the effects of those treatments on such things as pain, stiffness, walking, general wellbeing, lifestyle and your personal beliefs and attitudes to illness, life, etc.

I am aware that I can contact Meikin Li Rees or her supervisors, Associate Professor Peter Meier or Dr Narell Smith, if I have any concerns about the

research. I also understand that I am free to withdraw from this research project at any time I wish without consequences and without giving a reason.

I agree that Meikin Li Rees has answered all of my questions fully and clearly.

I agree that the research data gathered from this project may be published in a form that does not identify me in any way.

_____ Date: _____

(Signature participant)

_____ Date: _____

(Signature research or delegate)

Note: This study has been approved by the University of Technology, Sydney Human Research Ethics Committee. If you have any complaints or reservations about any aspect of your participation in this research which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: 61-2-9514 9772 or e-mail Research.Ethics@uts.edu.au and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

Appendix 8: Photograph of laser probes & laser unit

Appendix 9: TCM Diagnostic History Sheet

Client History Sheet

Name: _____ **Male/Female:** _____ **Date (1st Consultation**):_____
Tel No: _____ **Email Address:** _____
Address: _____ **Suburb:** _____ **Postcode:** ____
Date of Birth: _____ **Age:** _____ **Ethnic Background:**
_____
Health Fund: _____ **Marital Status (Children):** _____ **Occupation:** _____
Doctor: _____**Solicitor:** _____ **Workers Compensation:** _____ **Third Party:**_____

Presenting condition (signs and symptom)/chief complaints:
_____
_____
_____

Medical condition/history (circle & mark yes or no):
_____
Haemophilia/HIV+/Aids/Hepatitis/Asthmatic/Epileptic/Allergy**:** _____
Diabetes/sugar level**:** _____ Other: _____
Heart condition:_____ High/low blood pressure: _____ Cholesterol level: _____
Pregnant: Yes/No. Trying to conceive: Yes/No. Other medical conditions: _____
Medication: _____ Supplements: _____
Notes:_____

Spirit/Emotional State (circle for yes):

Frustrated/Angry/Anxiety/Depressed/Upset/Sad/Weepy/Emotional/Low spirit/Flat.

Stress (0-10 being highest & caused by):
_____

Sleep: Good/quality/less than 4/5/6/7 hours/insomnia/wake up frequently __ times/night.

Energy: Low/medium/high/sluggish.

Exercise – Type: _____ Frequency/week: _____ Duration: _____
Current weight: _____ Height: _____ Optimum weight: _____ Preferred weight: ____

Diet – No. meals/day _____ AM: _____Lunch: _____ Evening: _____

Female reproductive system – Age at first menses**:**_____ Duration/Period (days): _____
Regular/irregular: _____ Frequency: ____ Period Pain Level (0-10 being highest): _____
When: _____Where: _____ Duration: _____
Irregular/amenorrhea/dysmenorrhoea: _____
Notes: _____

Type & nature of menses – Flow (heavy/light). Clots (size): _____ Discharge: _____ **Colour –**
Light/bright red/dark red/light brown/other _____
Changes in body/psyche prior to menstruation: _____

Sore breast/bloated/water retention/Mood/Others _____
No. of pregnancies: _____ **No. of miscarriages**: _____ **Contraception**: _____
Notes: _____

Body Temperature: Cold (hands & feet)/Warm/Hot/Sweaty/Night sweat/clammy/Hot Flush/
Other:_____

Concurrent therapies: _____

Tongue diagnosis – Cracks/ulcerations/teeth marks:
_____
Shaped: _____
Coat::_____
Body colour: _____
Notes: _____

Pulses – Excess/deficient/fast/slow
Left/right: Balance or imbalance Rate: _____ Depth: _____ Qualities: _____
Notes: _____

Differentiation of syndrome/diagnosis:
_____
_____
_____

Treatment principle:
_____
_____

Treatment plan:
_____
_____
_____

Treatment methods used – Acup/herbs/moxa/cupping/electro/laser/ear acup/
massage/other: _____

Acupuncture points used:
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Herbs used:_____

Evaluation /review of treatment/prognosis:

Recommendations:

Name of practitioner:

Appendix 10: Signs & Symptoms Checklist (2 Disease Patterns)

Phlegm Retention Signs & Symptoms Checklist

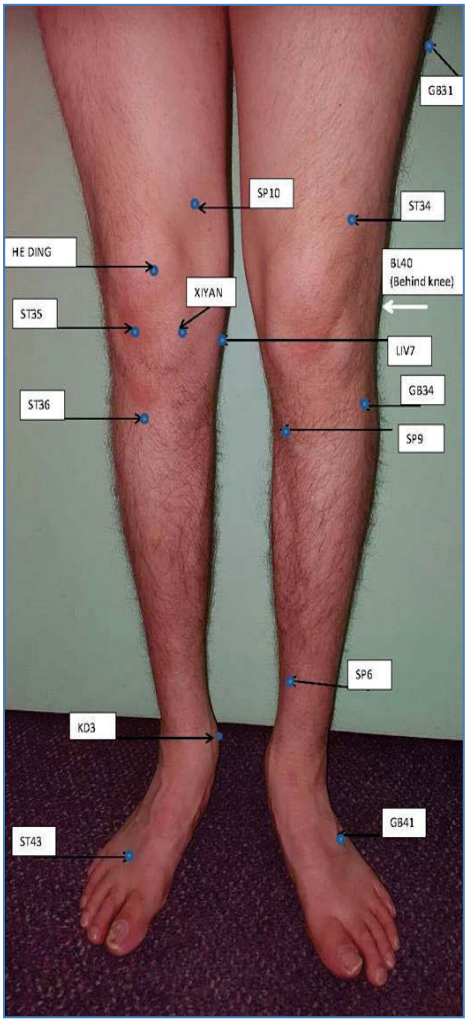
	Signs and Symptoms	**Yes/No**
1	Heaviness/obstruct circulation	
2	Tongue - white greasy coat	
3	Swelling	
4	Pain & Soreness	
5	Pulse slippery	
6	Deformity in joints	
7	Numbness of limb	
8	Muscular atrophy	
9	Aggravated by damp weather	
10	No sweating	
11	No desire to drink	

Blood Stasis Signs & Symptoms Checklist

	Signs and Symptoms	Yes/No
1	Pain usually fixed in one place & boring or stabbing in character	
2	Tongue - purple with dark spots	
3	Swelling	
4	Restricted movement	
5	Pulse choppy and wiry	
6	Stiffness due to Stagnant blood	
7	Pain worse on pressure	
8	Pain worsens during the night	

Appendix 11: Acupuncture point Locations

BLOOD STASIS ACUPOINTS	PHLEGM RETENTION ACUPOINTS
1. SP6	1. SP6
2. SP9	2. SP9
3. ST36	3. ST36
4. GB34	4. GB34
5. LIV7	5. LIV7
6. SP10	6. SP10
7. ST34	7. ST34
8. He ding	8. He ding
9 . Xi Yan	9. Xi Yan
10. ST35	10. ST35
11. GB31	11. KD3
12. GB41	12. ST43
13. BL40	13. BL40



Appendix 12: Western Ontario-MacMasters University Arthritis Index (WOMAC)

WOMAC OSTEOARTHRITIS INDEX VERSION VA3.1

INSTRUCTIONS TO PATIENTS

In Sections A, B, and C questions will be asked in the following format. You should give your answers by putting an " ✗ " on the horizontal line.

EXAMPLES:

1. If you put your " ✗ " at the left of the line as shown below, then you are indicating that you have **no** pain.

2. If you put your " ✗ " at the right end of the line as shown below, then you are indicating that your pain is **extreme**.

3. Please note:
   a) that the further to the right you place your " ✗ " the **more** pain you are experiencing.
   b) that the further to the left you place your " ✗ " the **less** pain you are experiencing.
   c) **please do not** place your " ✗ " **past the end of the line.**

You will be asked to indicate on this type of scale the amount of pain, stiffness or disability you have experienced in the last 48 hours.

Think about your _____ (study joint) when answering the questionnaire. Indicate the severity of your pain, stiffness and physical disability that you feel is caused by arthritis in your _____ (study joint).

Your study joint has been identified for you by your health care professional. If you are unsure which joint is your study joint, please ask before completing the questionnaire.

Australia - V4

WOMAC VA3.1 QUESTIONNAIRE **WOMA**

Section A

PAIN

Think about the pain you felt in your _____ (study joint) due to your arthritis during the last 48 hours.

(Please mark your answers with an " ✗ " on the horizontal line.)

QUESTION: **How much pain do you have?**

1. Walking on a flat, even surface.

No Pain ——— Extreme Pain

2. Going up or down stairs.

No Pain ——— Extreme Pain

3. At night while in bed, i.e., pain that disturbs your sleep.

No Pain ——— Extreme Pain

4. Sitting or lying awake in bed.

No Pain ——— Extreme Pain

5. Standing upright (but not moving).

No Pain ——— Extreme Pain

Study Coordinator Use Only

PAIN1 ____

PAIN2 ____

PAIN3 ____

PAIN4 ____

PAIN5 ____

Australia - V4

WOMAC VA3.1 QUESTIONNAIRE **WOMB**

Section B

STIFFNESS

Think about the stiffness (not pain) you felt in your_____ (study joint) due to your arthritis during the last 48 hours.

Stiffness is a sensation of **decreased** ease in moving your joint.

(Please mark your answers with an " ✗ " on the horizontal line.)

	Study Coordinator Use Only
6. How **severe** is your stiffness **after first awakening** in the morning? No Stiffness ——— Extreme Stiffness	STIFF6 ____
7. How **severe** is your stiffness immediately after sitting, lying or resting **later in the day**? No Stiffness ——— Extreme Stiffness	STIFF7 ____

Australia - V4

WOMAC VA3.1 QUESTIONNAIRE **WOM**C1-3

Section C

DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities due to arthritis in your _____ (study joint) during the last 48 hours. By this we mean **your ability to move around and to look after yourself.** (Please mark your answers with an " ✗ " on the horizontal line.)

QUESTION: **What degree of difficulty do you have?**	Study Coordinator Use Only
8. Going down stairs. No Difficulty ——— Extreme Difficulty	PFTN8 _____
9. Going up stairs. No Difficulty ——— Extreme Difficulty	PFTN9 _____
10. Standing up after sitting. No Difficulty ——— Extreme Difficulty	PFTN10 _____
11. Standing (in one position). No Difficulty ——— Extreme Difficulty	PFTN11 _____
12. Bending to the floor, i.e., to pick something up. No Difficulty ——— Extreme Difficulty	PFTN12 _____
13. Walking on a flat, even surface. No Difficulty ——— Extreme Difficulty	PFTN13 _____

Australia - V4

WOMAC VA3.1 QUESTIONNAIRE **WOM**C2-3

DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities due to arthritis in your _____ (study joint) during the last 48 hours. By this we mean **your ability to move around and to look after yourself.** (Please mark your answers with an "✗" on the horizontal line.)

QUESTION: **What degree of difficulty do you have?**	Study Coordinator Use Only
14. Getting in or out of a car, or getting on or off a bus. No Difficulty — Extreme Difficulty	PFTN14 _____
15. Going shopping. No Difficulty — Extreme Difficulty	PFTN15 _____
16. Putting on your socks or stockings. No Difficulty — Extreme Difficulty	PFTN16 _____
17. Getting out of bed. No Difficulty — Extreme Difficulty	PFTN17 _____
18. Taking off your socks or stockings. No Difficulty — Extreme Difficulty	PFTN18 _____
19. Lying and turning in bed. No Difficulty — Extreme Difficulty	PFTN19 _____

Australia - V4

WOMAC VA3.1 QUESTIONNAIRE **WOMc3-3**

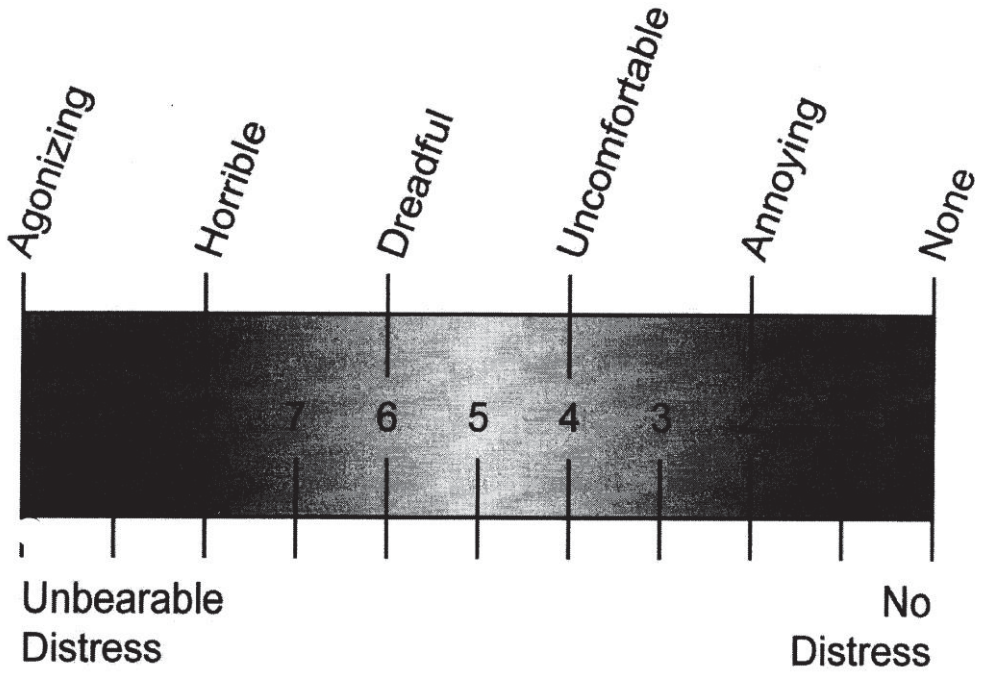
DIFFICULTY PERFORMING DAILY ACTIVITIES

Think about the difficulty you had in doing the following daily physical activities due to arthritis in your _____ (study joint) during the last 48 hours. By this we mean **your ability to move around and to look after yourself.** (Please mark your answers with an " ✗ " on the horizontal line.)

QUESTION: **What degree of difficulty do you have?**	Study Coordinator Use Only
20. Getting in or out of the bath. No Difficulty ——— Extreme Difficulty	PFTN20 ____
21. Sitting. No Difficulty ——— Extreme Difficulty	PFTN21 ____
22. Getting on or off the toilet. No Difficulty ——— Extreme Difficulty	PFTN22 ____
23. Performing heavy domestic duties. No Difficulty ——— Extreme Difficulty	PFTN23 ____
24. Performing light domestic duties. No Difficulty ——— Extreme Difficulty	PFTN24 ____

Australia - V4

Appendix 13: Visual Analoge Scale



Task _____

Date _____ *Start* _____ *End* _____

Appendix 14: Short-Form McGill Pain Questionnaire (SF-MPQ)

SHORT-FORM McGILL PAIN QUESTIONNAIRE

RONALD MELZACK

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0)	1)	2)	3)
SHOOTING	0)	1)	2)	3)
STABBING	0)	1)	2)	3)
SHARP	0)	1)	2)	3)
CRAMPING	0)	1)	2)	3)
GNAWING	0)	1)	2)	3)
HOT-BURNING	0)	1)	2)	3)
ACHING	0)	1)	2)	3)
HEAVY	0)	1)	2)	3)
TENDER	0)	1)	2)	3)
SPLITTING	0)	1)	2)	3)
TIRING-EXHAUSTING	0)	1)	2)	3)
SICKENING	0)	1)	2)	3)
FEARFUL	0)	1)	2)	3)
PUNISHING-CRUEL	0)	1)	2)	3)

NO PAIN ——— WORST POSSIBLE PAIN

PPI

0 NO PAIN _____
1 MILD _____
2 DISCOMFORTING _____
3 DISTRESSING _____
4 HORRIBLE _____
5 EXCRUCIATING _____

Fig. 1. The short-form McGill Pain Questionnaire (SF-MPQ). Descriptors 1–11 represent the sensory dimension of pain experience and 12–15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe. The Present Pain Intensity (PPI) of the standard long-form McGill Pain Questionnaire (LF-MPQ) and the visual analogue (VAS) are also included to provide overall intensity scores.

Appendix 15: Credibility & Expectancy Questionnaire (C/E)

Credibility Expectancy Questionnaire – Version II

We would like you to indicate below how much you believe, **right now**, that the treatment you are receiving will help you to reduce your stress and trauma symptoms. Belief usually has two aspects to it: (1) what one **thinks** will happen and (2) what one **feels** will happen. Sometimes these are similar, sometimes they are different. Please answer the questions below. In the first set, answer in terms of what you **think.** In the second set answer in terms of what really and truly **feel.**

SET I

1. At this point, how logical does the treatment offered you seem?

1	2	3	4	5	6	7	8	9
Not at all				Somewhat logical				Very logical

2. At this point, how useful do you **think** the treatment will be in reducing your trauma symptoms?

1	2	3	4	5	6	7	8	9
Not at all useful				Somewhat useful				Very useful

3. How confident would you be in recommending this treatment to a friend who experiences similar problems?

1	2	3	4	5	6	7	8	9
Not at all				Somewhat				Very much

4. By the end of the therapy period, how much improvement in your trauma symptoms do you think will occur?

1	2	3	4	5	6	7	8	9
None at all								Total Improvement

SET II

For this set, close your eyes for a few moments and try to identify what you really feel about the treatment and its likely success. Then answer the following questions.

4. At this point, how much do you really *feel* that therapy will help you to reduce your trauma symptoms?

1	2	3	4	5	6	7	8	9
Not at all useful				Somewhat useful				Very useful

5. By the end of the therapy period, how much improvement in your trauma symptoms do you really *feel* will occur?

1	2	3	4	5	6	7	8	9
Not at all				Somewhat				Very much

Appendix 16: Working Alliance Inventory Short Form C

Working Alliance Inventory

Short Form (C)

Instructions

On the following pages there are sentences that describe some of the different ways a person might think or feel about his or her therapist (counsellor). As you read the sentences mentally insert the name of your therapist (counsellor) in place of _____ in the text.

Below each statement inside there is a seven point scale:

1	2	3	4	5	6	7
Never	Rarely	Occasionally	Sometimes	Often	Very Often	Always

If the statement describes the way you always feel (or think) circle the number 7; if it never applies to you circle the number 1. Use the numbers in between to describe the variations between these extremes.

This questionnaire is CONFIDENTIAL: neither your therapist nor the agency will see your answers.

Work fast, your first impressions are the ones we would like to see. (PLEASE DON'T FORGET TO RESPOND TO EVERY ITEM.)

Thank you for your cooperation.

WAI(S)

1. _____ and I agree about the things I will need to do in therapy to help improve my situation.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
2. What I am doing in therapy gives me new ways of looking at my problem.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
3. I believe _____ likes me.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
4. _____ does not understand what I am trying to accomplish in therapy.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
5. I am confident in _____'s ability to help me.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
6. _____ and I are working towards mutually agreed upon goals.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
7. I feel that _____ appreciates me.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
8. We agree on what is important for me to work on.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
9. _____ and I trust one another.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
10. _____ and I have different ideas on what my problems are.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
11. We have established a good understanding of the kind of changes that would be good for me.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always
12. I believe the way we are working with my problem is correct.						
1 Never	2 Rarely	3 Occasionally	4 Sometimes	5 Often	6 Very Often	7 Always

WAI(S)

Appendix 17: Multi-dimensional Health Locus of Control –Form C

Multidimensional Health Locus of Control (Form C) Page 1 of 1

Form C

Instructions: Each item below is a belief statement about your medical condition with which you may agree or disagree. Beside each statement is a scale which ranges from strongly disagree (1) to strongly agree (6). For each item we would like you to circle the number that represents the extent to which you agree or disagree with that statement. The more you agree with a statement, the higher will be the number you circle. The more you disagree with a statement, the lower will be the number you circle. Please make sure that you answer **EVERY ITEM** and that you circle **ONLY ONE** number per item. This is a measure of your personal beliefs; obviously, there are no right or wrong answers.

1=STRONGLY DISAGREE (SD) 2=MODERATELY DISAGREE (MD) 3=SLIGHTLY DISAGREE (D)	4=SLIGHTLY AGREE (A) 5=MODERATELY AGREE (MA) 6=STRONGLY AGREE (SA)

		SD	MD	D	A	MA	SA
1	If my condition worsens, it is my own behavior which determines how soon I will feel better again.	1	2	3	4	5	6
2	As to my condition, what will be will be.	1	2	3	4	5	6
3	If I see my doctor regularly, I am less likely to have problems with my condition.	1	2	3	4	5	6
4	Most things that affect my condition happen to me by chance.	1	2	3	4	5	6
5	Whenever my condition worsens, I should consult a medically trained professional.	1	2	3	4	5	6
6	I am directly responsible for my condition getting better or worse.	1	2	3	4	5	6
7	Other people play a big role in whether my condition improves, stays the same, or gets worse.	1	2	3	4	5	6
8	Whatever goes wrong with my condition is my own fault.	1	2	3	4	5	6
9	Luck plays a big part in determining how my condition improves.	1	2	3	4	5	6
10	In order for my condition to improve, it is up to other people to see that the right things happen.	1	2	3	4	5	6
11	Whatever improvement occurs with my condition is largely a matter of good fortune.	1	2	3	4	5	6
12	The main thing which affects my condition is what I myself do.	1	2	3	4	5	6
13	I deserve the credit when my condition improves and the blame when it gets worse.	1	2	3	4	5	6
14	Following doctor's orders to the letter is the best way to keep my condition from getting any worse.	1	2	3	4	5	6
15	If my condition worsens, it's a matter of fate.	1	2	3	4	5	6
16	If I am lucky, my condition will get better.	1	2	3	4	5	6
17	If my condition takes a turn for the worse, it is because I have not been taking proper care of myself.	1	2	3	4	5	6
18	The type of help I receive from other people determines how soon my condition improves.	1	2	3	4	5	6

 *HOME PAGE*

Form A
Form B
Scoring Instructions
Bibliography
FAQs