Investigation of the effects of needling the acupuncture point Houxi (SI 3) on pressure pain threshold, needling sensation and needling pain in healthy participants

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

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CERTIFICATE OF ORIGINAL AUTHORSHIP

I, Xiaoqin Wu declare that this thesis, is submitted in fulfilment of the requirements for the award of the Doctor of Philosophy, in the School of Life Sciences in the Faculty of Sciences at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

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Remember tonight... for it is the beginning of always.

Abstract

Background: During the past decades, there has been a surge in prescribing opioids for pain related conditions, the "opioid epidemic". It is critical for researchers and clinicians to explore other non-pharmacological approaches to manage pain instead of relying on opioid analgesics. Acupuncture could be an effective tool to modulate pain.

Since 1999, studies on the effect of acupuncture on pressure pain threshold (PPT), at the University of Technology Sydney (UTS), have been conducted. The effects of the acupuncture to the acupoint LI 4 (*Hegu*) on PPT, the strength and quality of needling sensation (*deqi*) and the intensity of needling pain have been investigated by researchers from the UTS acupuncture group. However, the effects of another acupoint, Small Intestine 3 (SI 3 -*Houxi*) a commonly used acupoint for the treatment of various pain-related conditions has not been explored for its effect on PPT and *deqi*.

Aim: The primary aim of this study was to investigate the effects of needling the acupoint SI 3 in healthy people on:
1. Regional PPT at ten sites (SI 11^{R}, SI 11^{L}, GV 4, GV 14, HT 7^{R}, HT 7^{L}, BL 60^{R}, BL 60^{L}, GB 21^{R}, GB 21^{L}) following three different interventions - $SI3m^{+}$, $SI3m^{-}$ and SL;
2. The strength and quality of needling sensation (*deqi*) reported by subjects; and
3. The intensity of pain associated with the intervention.

Methods: Prior to commencing the study a systematic review was undertaken on the clinical use of acupoint SI 3 and PPT in acupuncture clinical studies. Following the reviews, this prospective study was designed as a randomised, double-blind, three-arm, and cross-over experimental study to investigate the effects of needling SI 3 on regional PPT, *deqi* and needling pain.

Results: For $SI3m^{+}$ and $SI3m^{-}$ interventions, the post intervention mean % PPT scores were significantly elevated compared with SL ($p < 0.001$). $SI3m^{+}$ statistically significantly elevated PPT% comparing to $SI3m^{-}$ ($p < 0.001$). The mean needle sensation and pain scores were similar for the two needling interventions, but both increased when comparing to SL. The subjects' anxiety and tension levels were not significantly different across the interventions.

Conclusions: Both intervention and site of needling were found to be important contributors to the effects on regional PPT in healthy participants. This study has provided

findings that support the belief that obtaining *deqi* during acupuncture is necessary for eliciting a pain modulating effect. Needling pain had no correlation with PPT.

Abbreviation List

ACR	American College of Rheumatology criteria
ADHD	Attention Deficit Hyperactivity Disorder
AIS	Adolescent Idiopathic Scoliosis
AMED	Allied and Complementary Medicine Database
AMT	Abbreviated Mental Test
ANDS	Australian National Data Service
ANOVA	Analysis of Variance
AT	Acupuncture Treatment
BCE	Before Common Era
BDI	Beck Depression Inventory
BI	Barthel Index
BIS	Baseline Index Score
BL	Bladder Meridian
BMed	Bachelor of Medicine
BMI	Body Mass Index
BFI	Brief Fatigue Inventory
BPI-SF	Brief Pain Inventory-Short Form
BUCM	Beijing University of Chinese Medicine
C	Cervical Vertebra
CA	Combined acupuncture which consists of traditional acupuncture and ear acupuncture
Ca^{2+}	Calcium
CDT	Cold Detection Threshold
CES-D	Centre for Epidemiologic Studies–Depression Scale

CG	Control Group
CI	Confidence Intervals
cm	centimetre
CM	Chinese Medicine
CMD	Craniomandibular Disorders
CMI	Cornell Medical Index
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus disease 2019
COX-2	Cyclooxygenase-2
CPT	Cold Pain Threshold
CPGS	Chronic Pain Grade Scale
CRF	Cancer-Related Fatigue
CS	Cervical Myofascial Syndrome
CSQ	Coping Strategies Questionnaire
CT	Connecticut
CV	Conception Vessel
CZ	Christopher Zaslawski
DLQI	Dermatology Life Quality Index
DN	Dry Needling
DNIC	Diffuse Noxious Inhibitory Control
DOMS	Delayed-Onset Muscle Soreness
EA	Electro acupuncture
EA	Ear Acupuncture
EASI	Eczema Area and Severity Index

ECG	Electrocardiography
EEG	Electro-encephalography
EIF	Education Investment Fund
EPT	Electrical Pain threshold
et al	and others
FACT-G	Functional Assessment of Cancer Therapy-General
FIM	Functional Independence Measure
FIQ	Fibromyalgia Impact Questionnaire
EMBASE	Excerpta Medica Database
FMA	Fugl-Meyer Assessment of Physical Performance
FMAM	Fugl-Meyer Assessment of Physical Performance—Motor subsection
fMRI	functional Magnetic Resonance Imaging
Ex	Extraordinary point
F	Female
FMS	Fibromyalgia Syndrome
FSS	Fatigue Severity Scale
f-TCD	functional Transcranial Doppler Sonography
fVAS	final Visual Analog Scales
GB	Gigabyte(s)
GB	Gallbladder Meridian
GLM	General Linear Model
GON	Gonarthrosis
GV	Governor Vessel
HF	Acupuncture with high-frequency electrical stimulation

HPT	Heat Pain Threshold
HREC	Human Research Ethics Committee
HT	Heart Meridian
IASP	International Association for the Study of Pain
IBM	International Business Machines Corporation
ICD-11	International Statistical Classification of Diseases and Related Health Problems 11th Revision
ICOAP	Intermittent and Constant Osteoarthritis Pain
ID	Identification
IL	Interleukin
iVAS	initial Visual Analog Scales
K^+	Potassium
kg	Kilogram(s)
KI	Kidney Meridian
kPa	Kilopascal
KWOMAC	Korean translation of Western Ontario and McMaster Universities Osteoarthritis Index
L	Lumbar Vertebra
LBP	Lower Back Pain
LF	Acupuncture with low-frequency electrical stimulation
LI	Large Intestine Meridian
LR	Liver Meridian
LSS	Lumbar Spinal Stenosis
LTF	Lateral Trunk Flexibility
LU	Lung Meridian

M	Male
m	Metre(s)
MA	Manual Acupuncture
MASS	Massachusetts General Hospital Acupuncture Sensation Scale
MDI	Massachusetts General Hospital Acupuncture Sensation Scale *Deqi* index
MEDLINE	on-line Medical Literature Analysis and Retrieval System
MGH	Massachusetts General Hospital
MGPQ	McGill Pain Questionnaire
MIG	Migraine
MIVF	Maximum Isometric Voluntary Force
mm	Millimetre
MMedSc	Master of Medical Sciences
MNS-PC6	Median Nerve Stimulation through Acupuncture Needles at the PC 6 (*Neiguan*) Acupoint
MPS	Myofascial Pain Syndrome
MPT	Mechanical Pain Threshold
MRI	Magnetic Resonance Imaging
MYMOP-2	Measure Yourself Medical Outcome Profile
NAP	Nonacupoint
NDI	Neck Disability Index
NG	NICE guideline
NHMRC	National Health and Medical Research Council
NHP	Nottingham Health Profile
NICE	National Institute for Health and Care Excellence

NIHSS	National Institutes of Health Stroke Scale
NM	Naturopathic Medicine
NPQ	Northwick Park Questionnaire
NPSA	Nonpenetrating Sham Acupuncture
NRS	Numeric Rating Scale
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
OIRD	Opioid-induced Respiratory Depression
PA	Placebo Acupuncture
PC	Pericardium Meridian
PEDro	Physiotherapy Evidence Database
PET	Positron Emission Tomography
Ph. D	Doctor of Philosophy
POEM	Patient Oriented Eczema Measure
PPT	Pressure Pain Threshold
PS	Pain Scores
qEEG	Quantitative Electroencephalography
QOL	Quality of Life
QST	Quantitative Sensory Testing
RA	Rheumatoid Arthritis
RA	Real Acupuncture
RCT	Randomised Controlled Trial
RMDQ	Roland-Morris Disability Questionnaire
ROM	Range of Motion
s	Second

SA	Sham Acupuncture
SASS	Subjective Acupuncture Sensation Scale
SC	State-of-the-art Specialty Care
SCI	Spinal Cord Injury
SCORAD	SCORing Atopic Dermatitis
SDS	Self-Rating Depression Scale
SF-36	Short Form-36
SF-36 BPS	Short Form-36 Bodily Pain Scale
SF-36v2 MCS	Short Form 36 version 2 health survey, mental component
SF-36v2 PCS	Short Form-36 version 2 health survey, physical component
SF-MPQ	Short-Form McGill Pain Questionnaire
SI	Small Intestine Meridian
$SI3m^{+}$	Manual acupuncture to SI 3 with manipulation
$SI3m^{-}$	Manual acupuncture to SI 3 without manipulation
Sig.	Significance level
SIS	Shoulder Impingement Syndrome
SL	Sham Laser
SMT	Spinal Manipulative Therapy
SP	Spleen Meridian
SPADI	Shoulder Pain and Disability Index
SPECT	Single Photon Emission Computed Tomography
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
SPSS	Statistical Package for the Social Sciences
STAXI	State-Trait Anger Expression Inventory

STRICTA	Standards for Reporting Interventions in Clinical Trials of Acupuncture
T	Thoracic Vertebra
TA	True Acupuncture
TCA	Traditional Chinese Acupuncture
TCM	Traditional Chinese Medicine
TE	Triple Energizer Meridian
TENS	Transcutaneous Electric Nerve Stimulation
TG	Test Group
TMDs	Temporomandibular Joint Disorders
TTH	Tension-Type Headache
TTM	Thai Traditional Massage
TUG	Timed Up and Go Test
UCLA	University of California, Los Angeles
UE	Upper-Extremity
UK	United Kingdom
USA	United States of America
USB	Universal Serial Bus
UTS	University of Technology Sydney
VA	Verum Acupuncture
VAS	Visual Analog Scales
WAD	Whiplash-Associated Disorders
WDT	Warm Detection Threshold
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
XQW	Xiaoqin Wu

YNSA	Yamamoto New Scalp Acupuncture

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Public Speech and media interview:

Taking Science to your local library for Sydney Science Festival, "From Empirical Medicine to Experimental Medicine", 15 August 2018.
SBS interview: https://www.sbs.com.au/language/english/audio/sydney-science-festival-wuxiaoqin-interview

Contents

Tables

Figures

Chapter 1: Introduction

Pain is defined as an unpleasant physiological and emotional sensation that is associated with actual or potential tissue damage (Merskey & Bogduk 1994, p 210). By any measure, pain is an enormous global health problem. Worldwide, it has been estimated that 20% of adults suffer from pain and 10% are newly diagnosed with chronic pain each year (Goldberg & McGee, 2011). Numerous modulatory systems have been identified that control pain through a complex process. In the recent decade, it has been reported that many countries are facing a surge in the prescribing of opioids, which has prompted the term "opioid epidemic" (Alam, 2016). Approximately 1 in 20 people taking opioid painkillers may become addicted (Carmichael et al. 2016). Therefore, it is vital for researchers and clinicians to explore whether non-pharmacological approaches to manage pain can be effective instead of relying on opioid analgesics. Acupuncture is one of the most popular modalities of complementary and alternative medicine (CAM) and is now a widely accepted modality for the treatment of a variety of pain conditions (Ernst 2006). Acupuncture it has been argued, can be an effective tool to modulate pain. In the United States, acupuncturists have now been included in the Veterans Health Administration in USA to address the opioid crisis (Bauer et al. 2017). However, there is currently limited evidence concerning the ability of acupuncture to modulate pain.

Acupuncture is the insertion of fine needles into acupuncture points in human body, which has a long history dating back to ancient times in China. In the years before the Common Era – Neolithic Period - stone needles were employed to treat ailments. For more than two thousand years Chinese people have been applying acupuncture to diseases including pain symptoms. Chinese medicine believes a life-force energy – *qi* - permeates the human body through channels punctuated by acupuncture points. Think of the channels as a pipeline through which life-force energy flows and the points as periodically placed, flow-controlling valves. Treatment by acupuncture was first introduced and described by Dr. Davis in the Bristol Medico-Chirurgical Journal in June 1915, and since then acupuncture has been administered in cases of sciatica and other forms of neuritis for many years (Goulden, 1921). In recent decades, the study of acupuncture in fundamental research as well as clinical trials has led to a new pathway of development and demonstrated the scientific basis for the mechanism underlying effective pain relief.

In regard to the study of acupuncture, we need not only clinical trial research but also investigations of different single acupoints to assess their individual effects as clinical trials use a prescription of needling sites across the body. Several Chinese medicine researchers at University of Technology Sydney (UTS) conducted a series of studies on the acupoint sites LI 4 (*Hegu*) and LI 11(*Quchi*) (Yuan 2002, Zaslawski et al. 2003, Szabo 2007, Li et al. 2008) and will continue to explore single acupuncture points to contribute further evidence to the understanding of acupuncture.

The anatomical features of acupuncture sites, the effects and mechanism underlying acupuncture, especially its analgesic effects have been explored worldwide by medical scientists from several different aspects. The scientific research of acupuncture in neurophysiology, neurochemistry and neuropharmacology have been developed to some extent. Some studies explored the acupuncture points, channels and collaterals via anatomical and histological study (Lou & Jiang 2012; Lou et al. 2013). However, the structure and function of acupuncture points, channels and the *qi* flowing must reside in a living body. Furthermore, the human body is an organic whole, which should not be dissevered during the study. Thereby, more effective parameters need to be introduced to human acupuncture study.

In regard to the parameters in the pain research, pain threshold is an important pain measurement. The experimental study of pain on healthy participants can be induced by several methods (e.g., pressure, heat/cold, chemical, electrical stimuli) and there are several aspects of pain which can be studied (e.g. pain thresholds, tolerance, ratings of unpleasantness and intensity) (Stanke & Ivanec 2016). Pain can be recorded directly using indirect measures such as questionnaires in humans as well as in the animal experiments using heat stimuli. PPT algometry on the other hand causes minimal trauma and harm to the subject during human experimental studies compared to heat/cold, chemical and electrical stimuli. Moreover, humans can express any slight change or uncomfortable sensation promptly during the increase of pressure.

Pressure algometry is a commonly employed technique in the assessment of both regional and widespread musculoskeletal pain (Linde et al. 2018). Pain threshold is more dependent on physiological factors, while pain tolerance is more dependent on psychological factors (Merskey and Spear 1967). In addition, a significant, positive linear relationship exists between the rate of algometer application and PPT outcome which has

been verified (Linde et al. 2018). Therefore, PPT has been widely used in physiotherapy researches. However, in acupuncture human experimental studies, the application of PPT is still not widely used.

Fortunately, some useful attempts at using PPT in acupuncture studies have been made by healthcare researchers. The effects of needling the acupuncture point LI 4 and LI 11 on regional PPT, has been investigated by researchers from the UTS during the past two decades (Coyle et al. 2000; Aird et al. 2002; Zaslawski et al. 2003; Aird 2005; Zaslawski 2006; Li et al. 2008; Loyeung et al. 2013). PPT has become an accepted pain challenger employed in the acupuncture human experimental studies.

However, the effects of needling another commonly used acupuncture point, that of Small Intestine 3 (SI 3 *Houxi*) and its effect on PPT and *deqi* sensations have not been explored. SI 3, is the third acupuncture point on the Small Intestine channel, and is a commonly used acupuncture point for the treatment of various pain-related conditions including headache, arm and finger pain (Porkert & Hempen 1995). In the following chapters, the author will explore the published literature and human experiments on the needling of SI 3 as well as a review on PPT – an important parameter in acupuncture treatment.

According to traditional Chinese acupuncture theory, *deqi* is a psychophysical response to needling an acupoint site and believed to be a parameter of a successful therapeutic acupuncture response in treating pain syndromes (Chen et al 2013). Hence, it is essential to probe intensities and the characteristics of *deqi* in the acupuncture research so that acupuncturist can acquire valuable instruction when they apply treatment to deal with pain.

This research project compared the effect of two different acupuncture techniques as well as a sham laser control to the acupuncture point SI 3 in healthy participants. The observation focused on the ten regional PPT recording sites both within and between the three interventions as well as needling pain and *deqi* sensation as experienced by the participants during each intervention.

Study aims

Even though traditional and modern textbooks mentioned the use of the acupoint SI 3 for pain related conditions, no studies have been conducted to date to investigate the effects

of SI 3 on PPT. This project used a similar research design to the clinical studies investigating the effects of LI 4 of PPT previously conducted at UTS.

The primary aim of this study was to investigate the effects of needling the acupuncture point SI 3 on:

- Regional PPT at ten sites (SI 11^{R}, SI 11^{L}, GV 4, GV 14, BL 60^{R}, BL 60^{L}, HT 7^{R}, HT 7^{L}, GB 21^{R}, GB 21^{L}) under three different interventions;
- The strength and quality of needling sensation (*deqi*) reported; and
- The strength of pain associated with the intervention at the needling site (both needling and sham laser).

The secondary aims of this study were to determine:

- Whether effects on PPT were localised or generalized across the body;
- Whether CM channel theory may contribute to the modulation of pain in specific areas of the body following acupuncture;
- Whether needling of SI 3 affects PPT when comparing unilateral or bilateral, ipsilateral or contralateral measurement sites across the body.

The specific research questions addressed were:

- Are there any significantly different effects on PPT measured at ten regional sites produced by the following three different interventions?
  - SI 3 needling with manipulation - $SI3m^{+}$
  - SI 3 needling without manipulation - $SI3m^{-}$
  - SI 3 Sham laser (control) - SL
- Are there any statistically significantly different effects on *deqi* measures when comparing the three different interventions?
- Are there any significantly different effects on needling pain measures produced by the three different interventions?
- Are there any correlations amongst PPT, *deqi* and needling pain measures?

A further aim was to evaluate and compare the subjects' perceptions of the various interventions such as did the subjects' perceptions of the acupuncture experience differ amongst the three interventions?

Significance of the project

Nowadays, it is vital for researchers to explore potential complementary and alternative approaches to pain management instead of relying on opioid analgesics. Acupuncture could be an effective management strategy for pain relief according to present studies (Johnston 2013). However, there is currently limited evidence supporting its use.

This study evaluates the effects of needling the acupuncture point SI 3 on PPT, needling sensation and needling pain. It will provide human experimental evidence to examine Chinese medicine channel theory and explore the pain relief indications for the needling of SI 3. This study will provide evidence concerning the pain modulating affects following acupuncture, which include measuring the pain threshold changes at acupoints on the traditional acupuncture channels that have a theoretical relationship with the Small Intestine channel such as the Governor Vessel (GV 14, GV 4), Bladder Channel (BL 60), Heart Channel (HT 7) and the Small Intestine Channel (SI 11). For example, the SI 3 point is the confluence point (*ba mai jiao hui xue*) for the Governing Vessel, the Bladder Channel is the partner channel from a six channel (*liu jing*) perspective, the Heart Channel is its partner channel from a five phase perspective (*zang fu- biao li*), the Small Intestine 11 is on the same channel as SI 3 while the Gall Bladder Channel (GB 21) has no specific relationship to the Small Intestine Channel.

Thesis structure

Chapter 1: Introduction

This chapter contains a brief introduction to the current situation of pain syndromes and pain control, the aims and significance of this study and the thesis format.

Chapter 2: Background

This chapter will address the following areas: the definition and epidemiology of pain, approaches to treating pain, and the efficacy of acupuncture in pain management, records of SI 3 in both classical and modern textbooks.

Chapter 3: Systematic literature review

This chapter includes two systematic reviews of published randomised clinical trials: the application of SI 3 for pain and the application of pressure pain threshold in acupuncture clinical studies.

Chapter 4: Methods

This chapter documents the study protocol for the randomised controlled study and the ethics approval details.

Chapter 5: Results

This chapter will present the results including PPT regional measurements, *deqi* and needling pain scores and subsequent analyses.

Chapter 6: Discussion and implications

The key findings of the whole research project related to all the investigated parameters will be summarized and discussed in this chapter.

Chapter 7: Conclusion

This final chapter will summarise the main study outcomes and detail the shortcomings of the current research of the effects on needling SI 3 together with suggestions for future research.

Chapter 2: Background

This chapter presents the background of this research project and reviews several important concepts and theories.

2.1 Pain

2.1.1 Pain definition and physiology

Pain is a part of our life which is necessary to warn us about a potential risk to body tissues and is often an unpleasant experience. The definition of pain by the International Association for the Study of Pain (IASP) is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' (Merskey & Bogduk 1994, p 210).

According to neurobiological principles, pain is a subjective torturous sensation. Mechanic, thermal or chemical noxious stimuli are coded into electric impulses by pain receptors. The transduction and transmission of impulses are then transmitted to the spinal cord, which codes the signal and information, then further transmits the electrical impulse to the brain via particular pathways in the higher centres (Eshkevari 2017). Pain is not only a physical concept but also a combination of physiological, pathological, emotional, psychological, cognitive, environmental, and social factors (Holdcroft & Power 2003).

2.1.2 Pain classifications

Pain can be classified according to the pathophysiological mechanism, duration, anatomic location and the presence of malignancy. It can be broadly classified as acute or chronic, episodic or recurrent pain and end of dose pain, based on the duration. Acute pain is connected with cuts, incisions, ischemia, broken bones, and burns, while chronic pain is related with conditions such as arthritis and nerve injury such as pain experienced with neuropathies (e.g., diabetes; chemotherapy) or mechanical injury (e.g., amputations, spinal cord injury). Improperly treated acute pain may further develop into chronic pain. Based on the pathophysiological mechanism, pain can also be classified as nociceptive or neuropathic pain. Finally pain can be categorized on etiology, whether it is associated with a malignancy (malignant and nonmalignant) and also by the anatomic location of pain (Abd-Elsayed & Deer, p 15).

2.1.3 Pain epidemiology

Pain is a universal health care issue. Further, chronic pain is a prevalent problem with significant costs to individuals, their families and society. A study that involved 42,249 adult cases collected from 18 countries using a questionnaire showed that one year age-standardized prevalence of chronic pain conditions was 37.3% in developed countries and 41.1% in developing countries (Tsang et al. 2008).

In Australia, 3.24 million people were living with chronic pain in 2018, with 53.8% female (1.74 million) and 46.2% male (1.50 million). Furthermore 68.3% (2.21 million) were at working age while 56% of Australians living with chronic pain had restricted their activities. It has been estimated that chronic pain for Australians would increase from 3.24 million in 2018 to 5.23 million by 2050. An audit in 2018 has reported that $139.3 billion was estimated as spent on chronic pain in Australia. Moreover, 44.6% of chronic pain patients had depression or anxiety disorder, while the statistical figures are two to three times than that of the general population (Pain Australia n.d.).

Due to the critical morbidity, the management of pain deserves serious concern and research.

2.1.4 Conventional pain treatment

The most widely used pain therapies are shown in Table 2.1 (B cker & Hammes 2010, p. 31). Following are the major accepted approaches used in the Western world to modulate and treat pain.

Table 2.1: Range of pain treatments

Pharmacological methods	• Conventional analgesics • Co-analgesics
	• European phytotherapy
	• Chinese phytotherapy
	• Local anaesthesia/neural therepy, anaesthetic techniques
Physical methods	• Neuro-surgery (seldom indicated)
	• Hydrotherapy • Balneotherapy • Thermotherspy • Climatetherapy • Exercise therapy
	• Physiotherapy • Manual therapy • *Tuina* • Draining techniques
	• Acupuncure and related methods • TENS
Psychological methods	• Nutrition • Fasting
	• Relaxation techniques • *Qigong* • Imaginative techniques • Hypnosis
	• Patient education • Teaching • Providing self-help strategies
	• Psychotherapy

2.1.4.1 Current pharmacological approaches

Although various and diverse medications have been developed by pharmaceutical companies, the relative number of novel pharmacological treatments that have been successfully developed and made available to patients remains relatively low.

Inflammatory pain is usually treated by Non-Steroidal Anti-inflammatory Drugs (NSAIDs) (such as aspirin, diclofenac, ibuprofen, piroxicam, rofecoxib, and celecoxib), selective cyclooxygenase-2 (COX-2) inhibitors or nonselective cyclooxygenase inhibitors, which all produce injury to the gastrointestinal tract (e.g., bleeding). Furthermore, COX-2 inhibitors drugs induce an increase in the incidence of cardiovascular events (Bannon 2012), toxicity, platelet dysfunction, and nephrotoxicity. Since the non-opioids for inflammatory associated pain have adverse effects, they are unsuitable for long-term therapy (Eshkevari 2017). Obviously, nonprescription forms of many NSAIDs are available to patients to treat minor aches and pains.

The treatment of moderate to severe pain, not controlled by other analgesics, involves the use of opioids such as tilidine, tramadol, fentanyl, morphine, buprenorphine, hydromorphone, oxycodone, and oxymorphone. Opioids activate endogenous opioid receptors, mu, delta, and kappa to exert their effects. Opioid receptors are located peripherally and centrally along the pain pathways. The locking of opioid substances at the receptor site lead to the obstruction of presynaptic calcium (Ca^{2+}) release, which further inhibits the release of pronociceptive neurotransmitters such as substance P. Hyperpolarization and suppression of nociceptive neurotransmitters are induced by increasing potassium (K^{+}) released, which is caused by postsynaptic activity. The release of potassium (K^{+}) also prevents the potential propagation of the pain signal. Withstanding organ toxicity, opioids possess numerous side-effects, including addiction, overdose, apnea, and depression, particularly addiction as well as fatal opioid-induced respiratory depression (OIRD) (Eshkevari 2017). Worldwide, two-thirds of drug-related deaths were a result of opioids (Lindsay & Scherrer 2019).

For less severe pain, less potent opioids such as codeine may be prescribed, often in combination with NSAIDs such as ibuprofen or acetaminophen (Bannon 2012).

Co-analgesics including antidepressants and anticonvulsants are appropriate for neuropathic pain. Drugs employed to treat neuropathic pain fall into diverse categories of

pharmacological mechanisms and include tricyclic antidepressants, anti-epileptics, and anesthetics (B cker & Hammes 2010, p. 33).

Additionally, there are some pharmacological agents used to treat special forms of pain including centrally-acting muscle relaxants/benzodiazepines, corticosteroids, calcitonin and bisphosphonate. Muscle relaxing drugs are usually limited to acute pain syndromes due to the potential for drug dependency (B cker & Hammes 2010, p. 33).

2.1.4.2 Physical medicine

The physical medicine options include physiotherapy, ergotherapy, exercise therapy, massage, thermotherapy, electrotherapy, hydrotherapy/balneotherapy and climate therapy. The physical stimulation can assist recovery from the pain possibly through self-awareness (B cker & Hammes 2010, p. 35).

Acupuncture can be considered as a physical medicine treatment to some extent because of the stimuli effect. Acupuncture is also an interventional therapy but much less traumatic compared to the following methods.

2.1.4.3 Interventional approaches

The implantation of a morphine pump can be employed, provided that an oral opiate method has been a failure. Only qualified anaesthetists can conduct anesthetic methods such as therapeutic local anaesthesia, peripheral nerve blockade, sympathetic nerve blockade and spinal anaesthesia. However, 'the more chronic the pain the less indicated is an invasive approach'. Clinicians should always consider this dictate before any invasive treatment decisions (B cker & Hammes 2010, p. 38).

Despite anaesthetic methods, neurosurgical methods, including invasive approaches such as neuro-stimulation and decompression methods can be applied for pain relief as well. Nevertheless, neurodestructive techniques can lead to greater therapeutic trauma. Thus, it is regarded as the last resort (B cker & Hammes 2010, p. 39).

2.1.4.4 Psychological pain therapy

Since pain is an unpleasant physiological and emotional sensation, psychological approaches can be essential in clinical practice. The following therapies could be applied in the treatment of pain: patient education, relaxation techniques, imaginative techniques,

hypnosis, biofeedback techniques, cognitive-behavioural therapy techniques and deep psychology techniques (B cker & Hammes 2010, p. 40).

2.1.5 Other naturopathic approaches for pain modulation

Other naturopathic approaches to relieve the pain include elimination or purging techniques including leech therapy, cantharidin plaster and cupping; as well as fasting, homeopathy, yoga, Qigong, meditation, mindfulness-based stress reduction or mind-body medicine and western phytotherapy (B cker & Hammes 2010, p. 43).

All naturopathic approaches for pain relief are well tolerated and side-effects are rarely reported. The disadvantage of naturopathic therapy is that they are rarely covered by government public health insurance systems. While it has been previously noted that in 2017-18,823 Australians are believed to have lost their lives as a consequence of unintentional prescription opioid overdose (Pain Australia n.d.) the need to battle opioid addiction and overdose, and successful methods in reducing overdose deaths should be investigated including naturopathic approaches. Thus, billions of dollars could be saved, and, more importantly, save the lives of thousands of Australians. Acupuncture could be a better way for pain management based on recent scientific studies (Appleyard 2018).

2.2 Acupuncture to pain treatment

2.2.1 Definition

Acupuncture is a complex intervention which originated in China and in traditional practice, is not simply the insertion of needles. The *Huang-Di-Nei-Jing* (The Yellow Emperor's Classic of Internal Medicine) is the earliest existing medical book in acupuncture which was proposed to have been written approximately 500-300 BCE (Ni 1995). The Mawangdui tombs, which were sealed in 168 BCE and recently discovered and reopened, contained writings and images related to acupuncture. Although the images found showed the channels, there were no references or indications of the acupuncture points (Li & Zhao 2016; Shaw et al. 2020).

Acupuncture is a system of healing in which fine stainless steel needles are inserted into the skin at specific acupuncture points along what are considered to be lines of *qi* in the channels, and used in the treatment of various physical and mental disorders including pain (Tai 1997, p. 1).

2.2.2 Traditional Chinese acupuncture theory

According to Chinese medicine theory, human health is maintained through a harmony or balance of two opposing but inseparable elements: *Yin* and *Yang*. *Yin* represents cold, slow and passive elements, whereas *Yang* represents hot, stimulating and active elements. *Qi* (or life energy) a central concept in Traditional Chinese acupuncture is the life force or vital energy that affects health. *Qi* is believed to travel in a human body through specific pathways called channels connecting to each energetic internal organ. A human body is considered to consist of 12 main channels and 8 secondary channels. Acupuncture involves the insertion of fine sterile needles through the skin at specific points namely the acupoints, which are mostly located along the channels. There are also acupoints located outside the channels termed extra-points. Health can be achieved by maintaining the human body in a balanced state of *Yin* and *Yang qi*. This harmony of the opposing forces of *Yin* and *Yang* is considered to be the basis for a healthy flow of *qi*. Any imbalance would cause a disruption or blockage of the flow of *qi* and result in a state of disease or pain (Eshkevari 2017).

Acupuncture heals a disease or pain state through removal of the blockage from the flow of *qi*, strengthening the weak *qi*, or releasing the excess *qi* enabling the restoration of the normal balance of the *Yin* and *Yang* system. The first record of *qi* and *deqi* was in the *Huang-Di-Nei-Jing*. "The acupuncturist must obtain the *qi* (*deqi*). If the *qi* has arrived, fastidiously hold it and do not lose it (*Ling Shu*-Chapter 3)" (Kong et al., 2007). As a basic acupuncture technique rule, the fine needle is manipulated either by twisting or insertion and lifting until a so-called *deqi* sensation is evoked. The patient's sensation could be ache, pressure, tension, warm, radiation or sensation of flow, cramping or electrical feeling. The acupuncturist would feel like the needle is tight within the connective tissue-'like having a fish on the hook' （Yuan et al. 2005）. Some researchers' acupuncture study findings showed that the hypothalamus activation was significantly associated with the *deqi* sensation (Liu et al. 2007). Some reported that elicitation of the *deqi* sensation improves the immediate analgesic effect of acupuncture at SP 6 in patients with primary dysmenorrhoea associated with the Chinese disease pattern known as cold and dampness stagnation (Zhao et al. 2017). In contrast, a prospective observational ultrasound imaging study during the needling of the acupoint PC 6, demonstrated no correlation between the number of nerve contacts by the needle and *deqi* (Streitberger et al., 2007). Thus, it is not clear if the *deqi* sensation is an assessment parameter of a

successful treatment. Further acupuncture study on the correlation between the *deqi* sensation and pain relief effects following acupuncture should be a subject worthy of further research.

While the theory of *qi* and channels from a Chinese medicine perspective gives an understanding of how acupuncture may moderate pain, one may also use principles of modern medicine to explain pain management following acupuncture.

2.2.3 Neurobiological mechanisms of action

2.2.3.1 Local and peripheral mechanisms

Regarding the local and peripheral mechanisms on pain, acupuncture stimulation possesses anti-inflammatory effects within human and animal tissues. Peripheral inflammatory cells and the released opioids are involved in the acupuncture inhibition of inflammatory pain. For instance, stimuli at local acupuncture point BL 23 had positive effects on the third lumbar vertebrae transverse process syndrome in rats through promotion of local muscle tissue repair, increased thermal pain threshold and reduced expression of inflammatory cytokines (Li et al. 2015). The underlying mechanism of acupuncture regarding musculoskeletal pain thought to be a type of micro-injury, which increases peripheral perfusion, facilitates healing, and induces analgesia. Acupuncture stimulation induces release of endogenous opioids from lymphocytes, monocytes/macrophages, and granulocytes into the inflamed local area of the body. The opioids in turn activate receptors on peripheral nerve terminals to suppress nociception. Acupuncture stimuli can activate sympathetic nerve fibres to increase endogenous opioid at inflammatory site as well (Zhang et al. 2014). In addition, acupuncture may release muscular trigger points, which are usually called *Ashi* points in traditional Chinese acupuncture, to induce a therapeutic local anaesthesia (B cker & Hammes 2010).

2.2.3.2 Segmental/spinal mechanisms

Despite the local/regional effects of acupuncture on pain management, there are also some non-regional, systemic effects revealed by some studies, such as studies on segmental/spinal mechanisms. Inhibition of nociceptive afferent fibres in the dorsal horn of the spinal cord is another mechanism of acupuncture on pain relief (Yu et al. 2019). Acupuncture stimuli induce the production of spinal cord opioids, serotonin,

norepinephrine, glutamate, glial cell/cytokines, and signal molecules to alleviate pain (Zhang et al. 2014).

Activation of the descending inhibition pathway is one of the most important mechanism of acupuncture analgesia. It inhabits the nociceptive afferents at the spinal level of pain and hence represent a main function in the body's own pain control. According to some authors, the analgesic effect of acupuncture was mediated in part by inhibiting Jun-N-terminal kinase activation in astrocytes after spinal cord injury (Lee et al. 2013).

2.2.3.3 Supraspinal mechanisms

The study of cerebral activation modulation response to acupuncture stimuli is an interesting area of research. During recent decades, an increasing number of studies have applied central imaging techniques to investigate the brain's response to acupuncture stimulation, using imaging techniques such as positron emission tomography (PET), and single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), electro-encephalography (EEG) and functional MRI (fMRI). Most studies suggest that acupuncture can modulate the brain activity within specific brain areas, and the evidence based on meta-analyses have partially confirmed these results (Huang et al. 2012).

2.2.3.4 Systemic mechanisms

Acupuncture can relieve headache by affecting other pain-modulating neurotransmitters such as met-enkephalin and substance P in addition to the nociceptive pathway (Cheng 2014).

Another area of descending inhibition is called stress-induced analgesia which transmitted by the endorphins. An animal model of electrically stimulating the acupoint PC 6 (*Neiguan*) in mice (MNS-PC6) was found to release an endogenous neuropeptide (orexin) from the hypothalamus to inhibit pain responses in mice through an endocannabinoid that reduces the inhibitory control in a midbrain pain-control region. The mechanism of the MNS-PC6-induced pain relief is independent of endogenous opioid system. Therefore, acupuncture on PC 6 may provide an alternative approach for pain management in opioid-tolerant patients (Chen et al. 2018). Additionally, diffuse noxious inhibitory control (DNIC) may play a minor role in inhibiting pain during acupuncture treatment as acupuncture insertion and manipulation are potentially painful.

Conditioned pain modulation was previously referred to as DNIC. A randomised cross-over trial' (Tobbackx et al., 2012) examined the influence of the DNIC system. It was found that one session of acupuncture treatment led to improvements in pressure pain sensitivity in chronic whiplash-associated disorders (WAD) patients while acupuncture had no effect on conditioned pain modulation or temporal summation of pressure pain. Both acupuncture and relaxation appear to be well-tolerated treatments for people with chronic WAD. These findings suggest that acupuncture treatment activates endogenous analgesia in patients with chronic WAD. The DNIC could explain the long-term treatment effects of acupuncture.

Acupuncture can also affect the emotional state and craving behaviour because pain is also an emotional response which can induce psychological factors (Cheng 2014).

Modulation of the vegetative tone is another field of research for pain management effects of acupuncture. A somatic autonomic reflex induced by acupuncture can change the levels of neurotransmitters such as serotonin and dopamine leading to the reduction of pain. However, further research is required regarding the effects of acupuncture on the autonomic nervous system (Bäcker et al. 2003).

2.2.4 Safe

Acupuncture is a safe treatment for pain management compared with other interventional approaches, as it has a significantly lower complication rate. Different from the archaic acupuncture techniques utilised in ancient China, the reputation of modern acupuncture has become popular and is classed low risk therapy since anatomy and infection control has been stringently taught in many acupuncture training programs.

An investigation (He et al. 2012) that examined whether there were "any unfavourable and unintended sign, symptom, or disease that presents during or after treatment with acupuncture regardless of causal relationship" found that the incidence of adverse events ranged from 6.71% to 8.6% with most of them mild and transient. The rate of serious adverse events (death, organ trauma, or hospital admission) was about 0.001%.

Acupuncture-related adverse events were mainly induced by mental tension of the patient, or caused by the improper operation by the doctor. Disposal single use needles have successfully affected infection risks. Most acupuncture-related adverse events can be avoided by standardizing teaching and clinical practices. Making the corresponding

safety standards can greatly lower the risk of adverse events and protect patient safety to the greatest extent.

2.2.5 Indications

Research studies have demonstrated the efficacy of acupuncture actions on pain conditions, both in animal or human pain models as well as in clinical trials. Acupuncture has been considered an effective therapy for headache, migraine, back pain and musculoskeletal pain, such as fibromyalgia and arthritis (Eshkevari 2017). Figure 2.1 shows rat and human maps of the most commonly used acupoints used in pain studies. It demonstrates that LI 4 and SI 3 are acupoints commonly used in pain research.

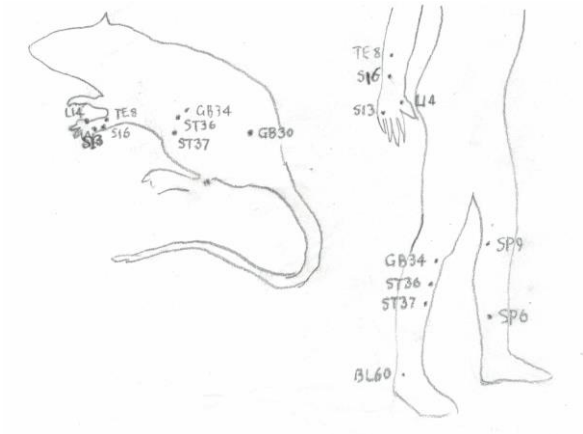


Figure 2.1: Rat and human maps of acupoints used in pain studies

As previously mentioned UTS researchers have conducted a series of human experimental study on LI 4 during the last twenty years (Coyle et al. 2000; Aird et al. 2002; Zaslawski et al. 2003; Aird 2005; Zaslawski 2006; Li et al. 2008; Loyeung et al. 2013). In the next section of this chapter, the author will explore the anatomical location and indications of SI 3 according to both classical and modern textbooks.

2.3 Location of SI 3 according to classical textbooks

The acupuncture point SI 3 was first mentioned in Chapter 2 of the *Ling Shu* (also known as Divine Pivot, Spiritual Axis, or Numinous Pivot), an ancient Chinese medical text whose earliest version was probably compiled in the first century BCE (Sivin 1993; Unschuld 2016). It is one of two parts of a larger medical manuscript known as the *Huangdi Neijing*, often translated to English as the "Inner Canon of Huangdi" or "Yellow Emperor's Inner Canon" (Ni 1995).

The anatomical location of SI 3 according to three Chinese medicine classic textbooks is described in Table 2.1. The operational definition of the SI 3 location according to the Ling Shu is not very clear. The definitions from the other two classical textbooks are better defined and are consistent with each other.

Table 2.2 Descriptions of SI 3 anatomical location according to three classical textbooks

Description	Book name	Author Publication year	Dynasty	Approximate year of publication
'*Houxi* is located on the exterior side of the hand behind the basic joint.' (p 67)	Ling shu (*Ling shu jing*)	Unschuld 2016	Zhou	722-221 BCE
'It is located on the outside of the small finger in a depression proximal to the base joint of the phalanx.' (p 182）	Systematic classic of acupuncture and moxibustion (*Zhenjiu Jia Yi Jing*)	Huang-fu 1994	Jin	282 CE
'(The point of) the tai yang (to be needled) is located in a depression of the base joint on the ulnar side of the little finger [i.e., the point Back Ravine, *Houxi*, SI3]' (p 32)	Classic of the pulse (*Mai Jing*)	Wang 1997	Jin	210-259 CE

2.4 Location of SI 3 according to modern textbooks

The anatomical location of SI 3 according to ten modern Chinese medicine textbooks is described in table 2.2. It can be seen that the locations of SI 3 are defined according to various anatomical landmarks such as 'hand is half clenched' (Li 1976), 'semi-closed position' (Chu et al 1979), 'hand is half closed' (Rogers and Rogers 1989), or 'hand is

slightly flexed' (WHO 2009). In conclusion, the descriptions of the location of SI3 in classical and modern textbooks are quite consistent to the World Health Organisation (WHO) definition as seen in Figure 2.4 and described in Table 2.2.

Table 2.3: A cross-text comparison of the operational definitions of the location of the acupoint SI 3

Source	Location
Li (1976)	'At the end of the transverse palm crease, when hand is half clenched. Bilateral.' (p 421)
Chu et al. (1979)	'Located at the end of the transverse crease and proximal to the fifth metacarpophalangeal joint in abductor digiti quinti muscle when hand is in a semi-closed position' (p 51)
Rogers & Rogers (1989)	'On the medial edge of the hand in the depression superior (proximal) to the 5th metacarpo-phalangeal joint. At the extremity of the transverse crease which is proximal to the metacarpo-phalangeal joint when the hand is half closed.' (p 67)
Lu (1992)	'With fist slightly clenched, it may be located on the palmar side behind the head of 5th metacarpal bone.' (p 115, 135); ' With the fist clenched, locate this point on the end if distal transverse crease on palm of hand, behind the 5th metacarpophalangeal joint.' (p 263)
O'Connor & Bensky (1992)	'When the hand is clenched in a fist, this point can be found behind and lateral to the head of the 5th metacarpus, at the top of the transverse crease formed by the clenched fist' (p 240)
Porkert & Hempen (1995)	'At the transverse plica of the hand, proximally of the 5th joint of the small finger, between metacarpus and phalanx, on a half clenched fist at the border between white and red flesh.' (p 246)
Tai (1997)	'Proximal to head of fifth metacarpal bone on ulnar side when fist is formed.' (p 135)
World Health Organisation (WHO, 2009)	'On the dorsum of the hand, in the depression proximal to the ulnar side of the fifth metacarpophalangeal joint, at the border between the red and white flesh. Note: When the hand is slightly flexed, the point is located at the ulnar end of the distal transverse skin crease of the palm, at the border between the red and white flesh.' (p 89)
Shi & Zhou (2007)	'It is located on the ulnar side of the palm, on the dorso-ventral boundary of the hand, on the distal palmar end of the transverse crease, behind the metacarpal phalangeal joint when a loose fist is made.' (p 156)
Liu & Liu et al. (2010)	'On the ulnar side of the hand, proximal to the fifth metacarpophalangeal joint, at the end of the transverse crease and the border between the darker and lighter skin, with the hand in a loose fist.' (p 53)

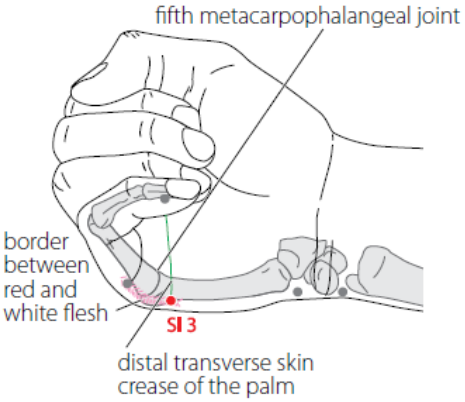


Figure 2.2: Location of SI 3 (WHO 2009), p 89

2.5 Neuroanatomical and stratified anatomical catalog of SI 3

The following anatomical structures underlying SI 3 have been categorized by Chapple (2013): additional specifications for point location, the stratified anatomy, motor innervation, cutaneous nerve and sensory innervation, dermatomes, Langer's lines, and somatotopic organization in the primary sensory and motor cortices. The location for SI 3 regarding the muscle, dermatome and myotome are shown in Table 2.3.

2.6 Explanation of the name

The name of *Houxi* in Chinese has been translated variously as 'Posterior Stream' (Porkert & Hempen 1995), 'Posterior Rivulet' (Tai 1997, p. 135), 'creek at rear' (Lu 1992), or 'back stream' (Shi 2007). This acupoint is located behind the 5th metacarpophalangeal joint of little finger which is why the expression, "at rear" is used to name the site; and also, this point is located behind the 5th metacarpal bone which makes it look like a creek (Lu 1992) or 'Back Creek' (O'Connor et al 1992), which is a topological designation of the acupoint foramen.

Acupuncture Point	Additional specification on location	Anatomical path of the needle	Motor innervation	Sensory innervation and dermatome	Langer's line	Somatotopic organization in the primary sensory and motor cortex
Houxi SI 3	This point lies just anterior to the metacarpal bone where the shaft meets the head. This location and hand positioning is important because it provides access to the lumbrical muscles beyond the 5th digit. It is deep to the abductor digiti minimi muscle, flexor digiti minimi brevis muscle, and flexor tendons. Deep to the palmar digital nerve and artery.	Intermediate insertion: Distal end of opponens digiti minimi muscle Deep insertion: Epimysium 4th lumbrical muscle Epimysium 3rd lumbrical muscle	Somatomotor: C8,T1 via the deep branch of the ulnar nerve for all muscles	To epidermis, dermis, and subcutaneous tissue: C8 via dorsal branch of the ulnar nerve	Vertical	Motor: 1/4 the distance of the precentral gyrus lateral to the falx cerebri Sensory: 1/3 the distance of the postcentral gyrus lateral to the falx cerebri

Table 2.4: Neuroanatomical and stratified anatomical substrate of SI 3

2.7 Applications of SI 3 according to classical textbooks

Only two of the three ancient Chinese Medicine classical textbooks documented the applications of SI 3 (refer to Table 2.4).

The most common indications were various pains, such as pain in the shoulder, upper arm, elbow, and forearm, painful eyes, stiff neck, spinning and ache of the head. As seen in table 1.3, all clinical applications of SI 3 as described in these two ancient books are related to the pathways of both the Small Intestine channel and Governor Vessel.

Table 2.5: Application of SI 3 according to classical textbooks

Source	Acupuncture Indication
Trans. Unschuld (2016) *Huang Di Nei Jing Ling Shu: The Ancient Classic on Needle Therapy*	• Did not mention the application of SI 3
Huang-fu (1994) *Systematic classic of acupuncture and moxibustion (Zhenjiu Jiayi Jing)*	• 'For shivering with cold, chills and fever, pain in the shoulders, upper arms, elbows, and forearms, spinning and ache of the head with inability to look back, vexation and fullness, generalized fever with aversion to cold, red, painful eyes, ulceration of the canthi, nebular screen generated (in the eye), acute pain, runny snivel nosebleeding, loss of hearing acuity, heavy, painful arms, hypertonicity of the elbows, scarred scabies, fullness of the chest sending a dragging (discomfort) to the upper arms, tearing with susceptibility to fright, stiffness of the neck, and generalized cold, Back Ravine (*Houxi*, SI3) is the ruling point.'(p. 431). • 'For cold and heat with swelling in the neck and the submandibular region, Back Ravine (*Houxi*, SI3) is the ruling point. (p 491). 'For mania with tugging (at the limbs) and frequent attack of madness, Back Ravine (*Houxi*, SI3) is the ruling point' (p. 633). • 'For ringing in the ear . . . Back Ravine (*Houxi*, SI3) are the ruling points' (p. 695).
Wang (1997) *The pulse classic (Mai jing*)	• 'Yang repletion in the *cun* distal to the guan on the left hand points to repletion of the small intestine. The bitterness includes urgent bi [acute pain in another version] below the heart, heat in the small intestine, and yellow or dark-coloured urine.' (p. 31-32).

2.8 Applications of SI 3 according to modern textbooks

Modern textbooks describe the use of SI 3 to treat painful disorders along the Small Intestine channel, (cervical spondylosis, cervical torticollis, stiff neck), lumbago (low back pain), diseases of inner- canthus, epicondylitis, periarthritis of the shoulder, rheumatic pain in the shoulder and back, convulsion and pain of the finger, toothache, trigeminal neuralgia, ears disorders, nebula, malaria, seizures (epilepsy), psychosis,

hysteria, madness, tetanus, facial spasm, intercostal neuralgia, night sweats, deafness (deaf-mutism, tinnitus), febrile diseases caused by exterior heat, dark and difficulty urine, jaundice, drowning, heat exhaustion or sunstroke, non-febrile convulsions, fainting, sequelae of infantile paralysis (poliomyelitis), multiple neuritis, conjunctivitis red eyes, acute tonsillitis throat blockage and attention deficit hyperactivity disorder (ADHD) (Chu et al. 1979; Stux et al. 1988; O'Connor & Bensky 1992; Porkert & Hempen 1995; Maciocia 2008; Wang & Robertson 2008; Shi & Zhou 2007). According to these textbooks, SI 3 can be used alone or combined with other acupuncture points for clinical application (refer to Table 2.5).

Table 2.6: SI 3 combined with additional acupoints

Combinations with SI 3	Indications	Source
Sanjian (LI 3)	'Redness and swelling of dorsum of hand with poor flexion and extension of the fingers' (p. 94)	Shi (2007)
Lieque (LU 7)	'Headache' (p. 89)	Shi (2007)
	'headache in the back of head and neck' (p. 795)	Lu (1992)
Fengfu (GV 16)	'for headache in the back of head and neck' (p. 795)	Lu (1992)
	'pain of the head and neck' (p. 156)	Shi (2007)
Dazhui (GV 14)	'malaria' (p. 156)	
Quepen (ST 12)	'pain of the shoulder" (p. 113)	
Shaohai (HT 3)	Tremor of hand (p. 149)	
Hegu (LI 4)	Spasmodic pain of the finger (p. 156)	
	Alternate chill and fever and Malaria (p. 156)	
Shenmai (BL 62)	'Both chronic and acute lumber pain' (p. 573)	Wang & Robertson (2008)
	'headache, stiff neck, red, swelling and pain of eye, pain in the lumber and back' (p. 156)	Shi (2007)

Combinations with SI 3	Indications	Source
Yinxi (HT 6)	'Spontaneous sweating' (p. 572)	Wang & Robertson (2008)
	'Night sweating' (p. 151)	Shi (2007)
Tianyou (TE 16)	'for stiffness of neck unable to look back' [from Classic 1220 A.D.] (p. 795)	Lu (1992)
Kunlun (BL 60)	'Occiput headache' (p. 13)	Shi (2007)
Liangmen (ST 21), Youmen (KI 21)	Spitting blood(p. 118)	
Quyuan (SI 13), Tianzong (SI 11)	'for spasmodic pain and fullness in the shoulder and back' (p. 162)	
Jianzhongshu (SI 15), Dazhui (GV 14), Weizhong (BL 40)	'for pain of the shoulder and back' (p. 163)	
Chongyang (ST 42), Shenmen (HT 7)	Mania (p. 130)	
Jiuwei (CV 15), Shenmen (HT 7)	'for epilepsy [from Jade Dragon Verses]' (p. 795)	Lu (1992)

2.9 SI 3 for pain relief from a Chinese Medicine perspective

There are two plausible explanations on how SI 3 modulates pain according to the classical and modern Chinese Medicine textbooks.

Firstly, SI 3 is the transporting point (Shu point) of the Small Intestine channel. Shu points mainly treat physical fatigue and joint pain. Being the Shu point of the Small Intestine channel, major indications of SI3 are pain relief along the SI channel such as shoulder, elbow and arm pain, as well as painful red eyes and upper and lower jaw toothache (Rogers and Rogers 1989, p 67).

Secondly, SI 3 is the meeting point of the Governor Vessel (GV), one of the eight extraordinary channels and is also connected to the Bladder channel. Therefore, according to Chinese medicine theory the stimulation of SI 3 can treat interior-exteriorly related Bladder channel areas of pain and pain on the Governing channel, such as headache, back pain, leg pain and heel pain. SI 3 can open the Governing channel and calm the spirit (Shen) and clear the mind as well, which can assist in relieving pain (Tai 1997, p. 135).

The next chapter will present two systematic reviews, the first being a review of randomised controlled trials using SI 3 and the second on published PPT studies.

Chapter 3: Systematic literature review

The determination of the included studies in the following reviews is based on the Australian National Health and Medical Research Council (NHMRC) Hierarchy of Evidence (National Health and Medical Research Council, 1999), which provides a wide indication of bias based on study design. Studies higher on the hierarchy potentially contain less bias than those that are lower on the hierarchy. The randomised controlled trial is on level II while a systematic review of Level II is on Level I. Therefore, the following systematic reviews of randomised controlled trials would be considered as a high level evidence (Coleman et al. 2009).

3.1 The application of SI 3 (*Houxi*) for pain as reported in randomised controlled trials: a systematic review

To evaluate the effect of SI 3 and its clinical application, an English language literature search was conducted using online research databases. The aim was to examine the use and application of SI 3 in acupuncture clinical trials, to identify operational definitions of the location of SI 3, identify details relating to needling retention duration, conditions treated, whether SI 3 was needled unilaterally or bilaterally and whether *deqi* was sought and measured when needling SI 3.

3.1.1 Methods

3.1.1.1 Literature search strategy

Six English language online databases or search engines were searched: Allied and Complementary Medicine Database (AMED), Cochrane Library, EMBASE, MEDLINE, ProQuest Health & Medicine and Google Scholar (from their inception to 14 April 2019) by using various search terms/strategies.

SI 3 is known as “small intestine 3”, “SI3”, “SI 3”, “SI-3”, “Houxi”, “Hou Xi”, “houxi point” and “hou hsi” in English articles, therefore, all the terms were used as part of the search strategy to obtain all related articles in scholarly journals. Other search terms used included “acupuncture” and “clinical trial”.

The following search strategy was used:

	"small intestine 3" OR SI3 OR "SI 3" OR SI-3 OR Houxi OR "Hou Xi" OR "houxi point" OR "hou hsi"
AND	RCT OR "clinical trial*" OR "control clinical trial*" OR "random* clinical trial*"
AND	acupuncture OR "medical acupuncture" OR needl* OR "dry needling" OR "acupoint*" OR acupoint*

In addition, the reference lists of the retrieved articles were hand-searched for further relevant papers.

3.1.1.2 Inclusion and exclusion criteria

The following inclusion criteria were used to identify the research articles:

- Published academic journal articles investigating the clinical application of acupuncture on SI 3;
- Full text articles published in English language;
- SI 3 was used as the main intervention point or as an auxiliary point;
- RCTs on pain including sample pilot studies;
- Conventional manual acupuncture treatment for pain using SI 3 in the treatment group.

The following exclusion criteria were utilised to exclude irrelevant studies including:

- Books, conference proceedings, articles on websites or blogs, thesis and protocols;
- Articles not written in English;
- SI 3 was not mentioned in the manuscript or only mentioned in the reference list;
- Animal experimental studies;
- Observational studies, such as case reports, case series, case-control study, review articles and other human experimental studies excluding RCTs;
- Quasi-randomised trials; and when
- SI 3 was used only in the control group.

3.1.1.3 Data extraction and synthesis

First, the articles were screened by title and abstract according to the inclusion and exclusion criteria. In the second step, the full texts of the selected articles were screened, with further exclusions according to the previously described criteria. Relevant data were then extracted and collected in EndNote X9. EndNote X9 software was used to store the results of the searches and to remove duplicates.

3.1.2 Results

3.1.2.1 Search Result

Abstracts and full text of the articles were screened by two independent reviewers (XQW, YKL), and irrelevant articles were excluded. There were 202 initial records retrieved across the six databases, which were then imported into Endnote software. After screening the abstracts and titles, 7 duplicates were excluded, which resulted in 195 records. Then another 175 further records were excluded for a variety of exclusion reasons (68 records irrelevant to SI 3, 12 records published in non-English language, 1 blog, 4 theses, 1 book sections, 1 conference proceedings, 1 conference abstract, 4 animal studies, 5 RCT protocols, 21 narrative reviews or summary articles, 23 systematic review articles, 11 systematic review plus meta-analysis articles, 3 articles used SI 3 in a placebo group, 1 quasi-randomisation trial, 2 no pain RCTs, 1 article of letter to the editor, 2 studies on laser acupuncture, 7 records about electro-acupuncture, 2 case studies, 3 acupressure studies, 1 embedding needle study, 1 study utilised a special equipment on SI 3). Therefore, 20 articles remained. These records were imported into Microsoft Excel for analysis and assessed for eligibility. In addition, 37 eligible articles were retrieved by manual searching from the reference lists and review articles. Consequently, 57 articles were eligible for the literature review analysis. The PRISMA literature review flow chart is shown in Figure 3.1.

3.1.2.2 Included Studies and Characteristics

A summary of these 57 articles in regards to the year of publications, country of origin, quality of the clinical trials reviewed, study design types of clinical trials, ethical approval prior to the study commencing, sample size, methodology, interventions, number, age of subjects, acupuncturists' experience, and needle sensation (*deqi*), can be found in Table 3.1. In addition, types of conditions treated, operational definitions of the location of SI

3, control groups, effect of pain relief and main outcomes can be found in Table 3.2. All the names of acupoints are based on the World Health Organization, 1993, Standard Acupuncture Nomenclature, 2nd ed, Regional Office for the Western Pacific, Manila.

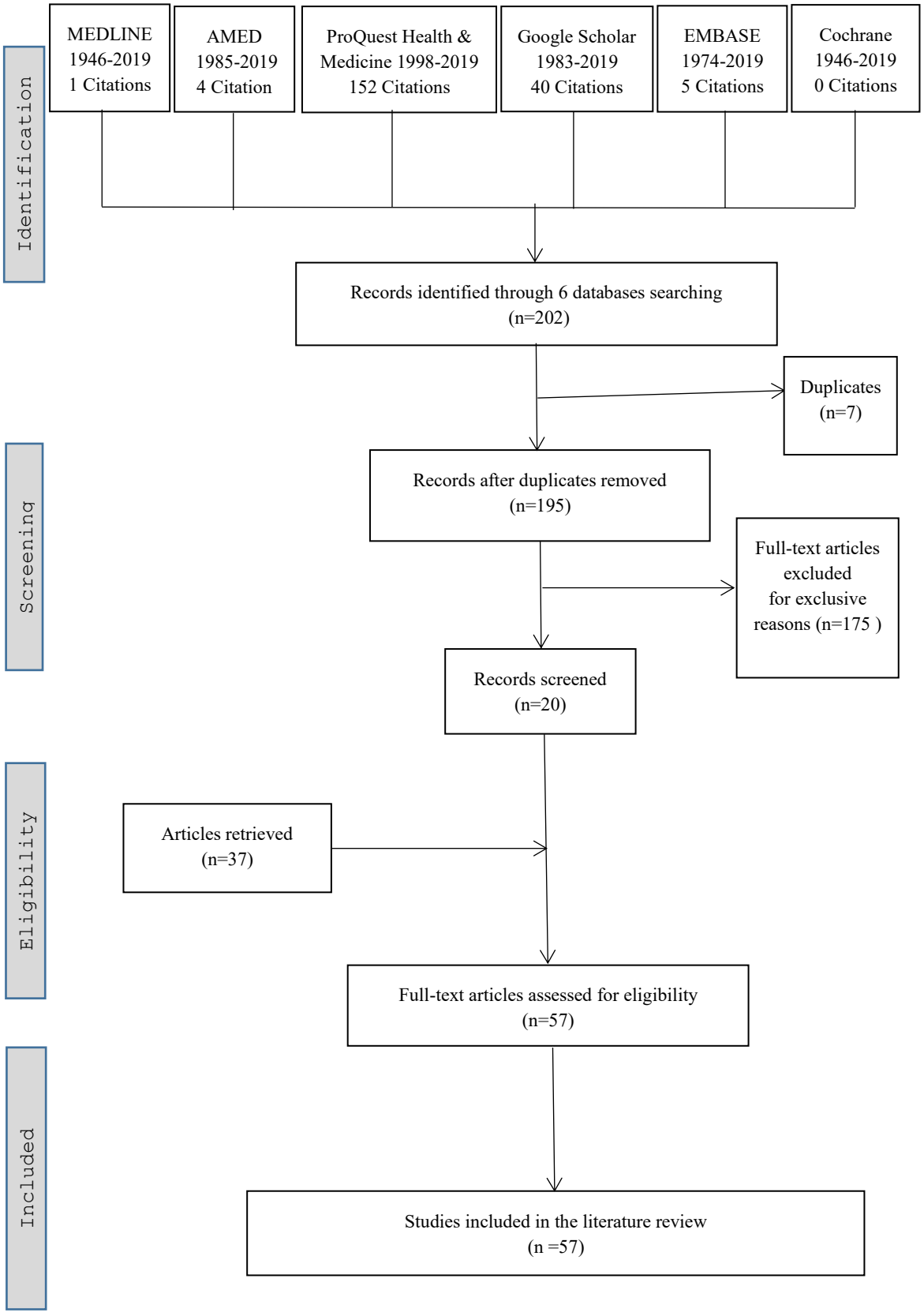


Figure 3.1: PRISMA flow chart of literature searching and article selection process

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Dang & Yang 1998, China	1	Single-centre, randomised, 3 arms parallel-controlled	No	48/ 48, 0	Once daily, 2 weeks, 2 months	CV 17, SP 21, TE 6, GV 12, SI 11, SI 3, GB 39	N/A	(54) 37-75	N/A	20 min	No. (The patient's mind was concentrated at the site of disease)
Sprott 1998, Germany	2	Single-centre, randomised, 3 arms parallel-controlled	No	30/ 30, 0	6 treatments, 2 per week/ 2 months	GV 20, Omega main point, "Darwin" point, HT 7, ST 36, KI 3, LI 4, GB 34, LI 11, LU 9, SI 3, Yaotuidian, KI 7, LR 2, LR 3, Ashi	N/A	(55) 33-73	N/A	N/A	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Kleinhenz et al. 1999, Germany	3	Single-centre, randomised single-blind (patients), 2 arms parallel placebo-controlled	Yes	52/ 45, 7	8 sessions, 4 weeks/ 3 months	TE 15, BL 44, TE 14, Taijian (extra), SI 12, SI 11, LI 15, LI 14, SI 14, SI 9, Jianquan (extra), LI 11, SI 6, TE 3, Symptomatic point, ST 38, GB 34, SI 3	N/A	(33.7 2 ± 7.91)	N/A	N/A	No
Ceccherelli et al. 2001, Italy	1	Single-centre, randomised 2 arms parallel placebo-controlled	No	44/ 44, 0	2 sessions weekly, totally 10 sessions/ 1 & 3 months	SI 9, SI 3, GV 14, TE 15, TE 14, LI 11, LI 15	N/A	40-65	N/A	20 min	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Irnich et al. 2001, Germany	5	Multi-centre, double-blind (observers & patients), randomised (stratified block randomization), 3 arms parallel-controlled	Yes	177/165, 12	5 times over 3 weeks/ 3 months	SI 3, GB 10, GB 60, LR 3, GB 20, GB 34, TE 5, ear point "cervical spine." Active myofascial triggerpoints were located predominantly in the musculus trapezius (nearby GB 20) and levator scapulae (nearby SI 14)	N/A	52.3 ± 13.3	experienced, licensed	30 min	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Irnich et al. 2002, Germany	5	Single-centre, randomised (rolling dice), double-blind (observers & patients), 3 arms sham-controlled crossover	Yes	36/ 34, 2	Once a week, 8 weeks	SI 3, KI 27, Ex 28, LU 7, BL 60, CV 21, CV 22, GV 20, GV 14, LI 4, Ear 'cervical spine', Ear 'stellate ganglion'	N/A	51.9	8 years	30 min	No
Sherman et al. 2002, USA	1	Single-centre, randomised, two-period crossover	Yes	60	Only 1 session	Ashi, BL 23, GV 3, or GV 4; SI 3; BL 40; KI 3	N/A	25-64	experienced, licensed	20 min	No
Sze et al. 2002, China	5	Single-centre, randomised, double-blind (observers & patients), 2 arms parallel-controlled	Yes	106/ 92, 14	A mean of 35 acupuncture sessions, over a 10-week period	LI 15, LI 11, LI 10, LI 4, TE 5 (upper limb), GB 30, GB 34, ST 36, ST 41, BL 60 (lower limb). GB 40, BL 40, ST 32, ST 40, SP 10, KI 3, LU 5, LR 3, PC 6, SI 3, TE 14	N/A	(69.3 ± 9.6)	a well-qualified and experienced acupuncturist	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Wang 2003, China	1	Single-centre, randomised, 2 arms parallel-controlled	No	81/ 81, 0	Once daily, 3 days	EX-UE7, SI 3, TE 3, GV 26	Homolateral point for a unilateral pain and bilateral points for bilateral pains	14-43	N/A	30-40 min	Yes
Kvorning et al. 2004, Sweden	4	Multi-centre, prospective, open, randomised, single blind, parallel-controlled 2 arms	Yes	100/ 72, 28	Twice a week for 2-week, later on no more than once a week/ 3-week	LR 3, GV 20, BL 60, SI 3, BL 22–26	Bilaterally	(30 ± 5.9)	N/A	N/A	Yes
Melchart et al. 2005, Germany	5	Multi-centre, randomised, double-blind (observers & patients), 3 arms parallel-controlled trial	Yes	270/257, 13	12 sessions per patient over eight weeks	Basic points: GB 20, GB 21, LR 3. Optional points: Mainly neck pain: BL 10, 60, or 62; GV 14 or 19; SI 3 or 6.	N/A	(43 ± 13) 18-65	Median 10 years	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Pohodenko-Chudakova 2005, Belarus	1	Single-centre, semi-randomised, 2 arms parallel-controlled	No	150/150, 0	Only once	LI 4 , LI 10 , LI 11 , SI 3, SI 14 , SI 15, ST 2 , ST 10, ST 26, ST 36, BL 11, BL 62, TE 20, GB 1, GB 20 , GB 21, GB 22 , GB 26, GB 38, LU 7 , SP 6, HT 1, HT 5, TE 7, KI 6, TE 3, PC 6	N/A	35-40	N/A	N/A	No
Wayne et al. 2005, USA	5	Single-centre, prospective, randomised, double-blind (observers & patients), 2 arms sham-controlled study	Yes	33/ 24, 9	Up to 20 treatment sessions (mean, 16.9) over a mean of 10.5 weeks	LI 15, LI 14, LI 11, LI 10, LI 4, TE 14, TE 5, TE 3, Ex-UE9, SI 9, SI 4, SI 3, GB 30, GB 31, GB 34, GB 39, GB 40, ST 34, ST 36, ST 41, ST 42, LR 3, Ex-LE10.	Contralateral	(59) 28 - 89	20 years	20-30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Alecrim-Andrade et al. 2006, Spain	5	Single-centre, randomised, double-blind (observers & patients), 2 arms sham-controlled	Yes	31/ 28, 3	16 sessions in 12 weeks/ 24 weeks	Ex-B1, TE 17, TE 20, SP 7, ST 37, LU 5, GB 12, GB 20, GB 21, BL 10, BL 60, SI 3, BL 2, ST 36, GV 23, LI 4, TE 5, GB 34, GB 8, GV 20, LR 3, PC 6,	Bilaterally	32.5 ± 8.0	N/A	N/A	No
Brinkhaus et al. 2006, Germany	5	Multi-centre, randomised (centralized telephone randomization procedure), double-blind (observers & patients), 3 arms parallel-controlled	Yes	298/ 284, 14	12 sessions over 8 weeks/52 weeks	BL 20-34, BL 50-54, GB 30, GV 3-6, Huatojiaji, Shiqizhuixia, SI 3, BL 40, BL 60, BL 62, KI 3, KI 7, GB 31, GB 34, GB 41, LR 3, GV 14, GV 20	Bilateral	(59 ± 9)	3 years	N/A	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Brinkhaus et al. 2006, Germany	2	Multi-centre, single-blind (patients), randomised, parallel-controlled 3 arms	Yes	301	12 sessions, 8 weeks/ 1 year	BL 20-34, BL 50-54, GB 30, GV 3-6, Ex-B2, Ex-B8, SI 3, BL 40, BL 60, BL 62, KI 3, KI 7, GB 31, 34, 41; LI 3, GV 14 , GV 20	Bilaterally	(44) 29-65	3 years	30 (28.4 ± 3.2) min	Yes
Ceccherelli et al. 2006, Italy	5	Single-centre, randomised (previously constructed randomisation table), double-blind (observers & patients), 2-parallel-arm, control	No	70/62, 8	Once a day for 3 days/ once a month	SI 3, TE 5, LI 4, BL 10, GB 20, GV 14, GV 15	Bilateral	25-55	N/A	N/A	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Molsberger et al. 2006, Germany	4	Multi-centre, randomised (centralized telephone randomization procedure), double-blind (observers & patients), 3 arms parallel-controlled	No	1295	10 sessions over 6 weeks/ 90 days	GV 20, LI 4, LR 3 (or LR 2), GB 20 (or BL 10), 0-4 Ashi points, GB 14, GB 8, GB 20, Ex-HN5, GB 41, ST 8, Ex-HN3, GV 23, LI 4, ST 44, BL 2, BL 10, GV 16, GV 14, SI 3, BL 60, LU 7, GV 20, Ex-HN1, LR 3, PC 6	N/A	N/A	2 years	30 min	Yes
Molsberger et al. 2006, Germany	4	Multi-centre, randomised (centralized telephone randomization procedure), double-blind (observers & patients), 3 arms parallel-controlled	No	2201	2 sessions per week, 10 sessions/ 90 days	BL 24-34, BL 36, BL 37, BL 52, BL 54, GB 30, GB 31, GB 34, GB 41, ST 31, ST 32, SI 3	Unilateral	N/A	2 years	30min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Schmid-Schwap et al. 2006,	4	Single-centre, randomised, double-blind (observers & patients), 2 arms placebo controlled	Yes	23/23, 0	Only once	LI 4, SI 2, SI 3	N/A	17-68	N/A	20 min	No
Vas et al. 2006, Spain	4	Multi-centre single-blind (assessors) randomised (simple randomization, sequentially numbered,opaque , sealed envelopes), 2 arms parallel-controlled	Yes	123/ 95, 28	Over 5 sessions in 3 weeks/ 6 months	GB 20, GB 21, LR 3, LI 4, GB 34; BL 10, GV 1 ,SI 3, BL 62; Ear points: Shenmen, Neck, LRer, Kidney, Muscle Relaxation, Occiput, Thalamus.	Bilateral	46.0 ± 13.7	N/A	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Crew et al. 2007, USA	2	Single-centre, randomised 2 arms crossover	Yes	21/19, 2	Twice a week, 6 weeks/ 12 weeks	TE 5, GB 4, GB 34, LI 4,ST 41, KD 3, LI 15, TE 14, SI 10, TE 4, LI 5, SI 5, SI 3, Ex-UE9, LI 3, GV 3, GV 8, BL 23, GB 30, GB 39, SP 9, SP 10, ST 34	N/A	(59) 46-73	licensed	20-25 min	Yes
Itoh et al. 2007, Japan	5	Single-centre, randomised (computerised randomisation program), double-blind (observers & patients), 4 arms sham-controlled	Yes	40/ 31, 9	1 per week, 7 weeks/ 13 weeks	GB 2, GB 21, BL 10, GB 11, S1 2, S1 3; TE 5, LI 4, SI 3	N/A	47-80	7 years	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Ritenbaugh et al. 2008, USA	4	Multi-centre randomised, assessors blinded, 3 arms parallel controlled	Yes	160/ 128, 32	Twice a week for 6 weeks, then once per week for 8 weeks/ 3 months	BL 43, BL 12, SI 3	N/A	25-55	5 years	20-30 min	No
Min et al. 2009, Korea	5	Single-centre, randomised (using a random table generated by SPSS 12.0) double-blind (observers & patients), parallel-controlled 2 arms	Yes	78/ 65, 13	Twice a week, 4 weeks/ 12 weeks	GB 41, SI 3, BL 66, SI 2, ST 36, SI 8	Contralateral	(59.5 ± 5.3)	7 years	20 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Simma et al. 2009, Austria	4	Single-centre, randomised (computer generated random permutation) double-blind (observers & patients), 2 arms placebo-controlled	Yes	23/ 23, 0	Only once	LI 4, SI 3	N/A	18-64	N/A	N/A	No
Yuan et al. 2009, UK	4	Single-centre, assessor-blinded pilot randomised 2 arms parallel-controled	Yes	30/ 29, 1	5 times per week for 2 weeks / 3 months and 1 year	BL 23, BL 24, BL 26, BL 40, Ashi points, Jia Ji, BL 18, BL20, BL 25, BL 27, BL 60, BL 62, GV 3, CV 6, CV 12, KI 3, KI 7, LR 3, GB 34, SI 3, ST 36, SP 6	N/A	18-60	5 years	20-30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Ceccherelli et al. 2010, Italy	4	Single-centre, single-blind (observer), randomised (stratified randomization), parallel-controlled 2 arms	Yes	44/ 36, 8	Only once	SI 3, TE 5, BL 62, GB 20, GV 14, 2 most painful trigger points	Bilateral	29-60	N/A	N/A	No
Molsberger et al. 2010, Germany	4	Multi-centre, randomised (central telephone randomisation) pragmatic, double-blind (patient & statisticians), 3 arms trial	Yes	442/ 360, 82	16 session over 6 weeks/ 3 months	Ashi points, LU 1, LU 2, LI 4, LI 11, LI 14, LI 15, TE 5, TE 13, TE 14, SI 3, SI 9, ST 38, GB 34, BL 58	N/A	25-65	Nationally recognized	21 min	Yes
Sun et al. 2010, China	4	Single-centre randomised (simple randomization) single-blind (patients) parallel-controlled 2 arms	Yes	35/ 34, 1	Twice a week, 3 weeks	GB 20, TE 14, SI 3	Bilateral	31-66	5 years	20 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Ahn et al. 2011, Korea	3	Single-centre, randomised (simple randomization) parallel-controlled 2 arms	No	49/ 46, 3	2 sessions per week, 2 weeks	GB 8, 14, 20, Ex-HN5, TE 5, GB 41, ST 8, YinTang, GV 23, LI 4, ST 44, BL 2, 10, 60, GV 14, 16, SI 3, LU 7, GV 20, Ex-HN1, LR 3, PC 6	Unilateral/ Bilateral	(53.67 ± 10.95)	N/A	20 min	Yes
Johnston et al. 2011, USA	3	Single-centre, randomised, open (non-blinded) parallel-controlled 2 arms	Yes	13/ 12, 1	8 weekly 50-minute acupuncture sessions	GB 20, TE 5, GB 43, SI 3, UB 62, GB 29, GB 30, GB 40	Bilateral	18-65	20 years	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Wang et al. 2011, China	5	Multi-centre, prospective, double-dummy, double-blinded (patients & assessors), randomised (central block randomization) parallel-controlled 2 arms	Yes	140/ 120, 20	3 sessions per week, 4 weeks/ 12 weeks	GV 20, GV 24, GB 13, GV 8, GB20. Additional points were chosen individually depending on different syndromes: TE5, GB3-Shaoyang headache; LI 4, ST 44-Yangming headache; BL 60, SI 3-Taiyang headache; LR 3, GB 40-Jueyin headache; PC 6-nausea and vomiting, LR 3-dysphoria and susceptibility to rage	Bilateral	39.2 ± 10.9	20 years	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Kang et al. 2012, Korea	5	Single-centre, randomised, double-blind (participant-blind, assessor-blind) parallel-controlled 3 arms	Yes	42/ 38, 4	twice a week for 3 weeks, total of 6 sessions/ 4 weeks	TE 17, GB 20, ST 7, ST 6, SI 19, Ex-HN6; LI 4,SI 3; ST 36, BL 60, TE 5, GB 41	Ipsilateral	18-71	6 years	25 min	Yes
Kwak et al. 2012, Korea	4	Single-centre, randomised, double-blind (patients, assessor and analyzer) waiting-list controlled, open label, parallel-group	Yes	40/ 40, 0	3 times a week, 2 weeks	SI 15, SI 14, SI 2, SI 3, SI 5, SI 7, LI 11, BL 10, BL 12, BL 13, BL 14, BL 60, BL 62, BL 66, GB 20, GB 21, GB 40 , GB 41, TE 15, TE 5	N/A	(45.60 ± 8.78)	The practitioner was a licensed oriental medicine doctor with at least 3 years of clinical experience after a 6-year course in oriental medicine education	15 min	Yes
Sun et al. 2012, China	3	Single-centre, randomised, parallel-controlled 2 arms clinical trial	No	60/ 60, 0	6 times a week, 3 weeks	LU 10, LI 15, LI 4, TE 14, TE 3, SI 10, SI 3	N/A	45-75	N/A	20 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Wallasch et al. 2012, Germany	5	Single-centre quasi double-blinded (patients & assessor), randomised (simple randomisation) placebo-controlled	Yes	35/ 27, 8	Once a week, 8 weeks	LI 4, ST 36, TE 5, GB 41, SI 3, BL 62, GV 20, Ex-HN5, TE 23, LR 3, KI 3	Bilaterally	(37.2 ± 9.6)	a licensed acupuncturist according to the standard literature for acupuncture treatment of headache and with a long experience in CM and a history of practicing acupuncture methodology in China	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Wang et al. 2012, China	5	Multi-centre, double-blinded (patients, assessors & statistical analysers), randomised (central block randomization) parallel-controlled 2 arms clinical trial	Yes	150/ 140, 10	1 session/ 3 days	GV 20 , GV 24, ST 8, GB 8, GB 20. TE 5, GB 34, LI 4, ST 44, BL 60, SI 3, LR 3, GB 40, PC 6, LR 3	Bilateral	(37.8 ± 10.6)	20 years	30 min	Yes
Tobbackx et al. 2013, Belgium	4	Single-centre, randomised (simple randomization, sequentially numbered, opaque, sealed envelopes) assessor-blinded crossover	Yes	39/38, 1	Only once	GV 14, CV 1 - CV 7, GB 20, SI 11, GB 21, TE 15, SI 14, BL17, SP10, SI 3, BL 64, TE 5, GB 41, Ex-B8, Ear Zero point, Ear Jerome point, Ear C0 point	Unilateral/ Bilateral	(41 ± 10) 23-57	15 years	20 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Bahrami-Taghanaki et al. 2014, Iran	4	Single-centre, randomised (closed envelopes), participants & statistician blind, 2 arms parallel controlled	Yes	68/ 60, 8	3 times per week, 12 week/ 4-12 weeks	BL 23, BL 25, BL 60, SI 3, BL 24, BL 36, BL 57, BL 37, BL 40, GB 12, GB 26, GB 30, GB 34, GB 39, GB 36, GB 41, ST 4, ST 36, GV 3, GV 4, GV 5, GV 24, GV 20, GV 26	Bilateral	(44.8 ± 13.4) 19-80	an experienced faculty member of the BUCM	20 min	Yes
Ceccherelli et al. 2014, Italy	4	Single-centre, randomised (block randomization) single-blind (assessor & statistical analyzer), 3 arms parallel-controlled	Yes	102/ 90, 12	2 times per week, 6 months	SI 3, TE 5, BL 62, GB 20, GV 14, the 2 most painful trigger points	Bilateral	26-60	5 years	30 min	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Cho et al.2014, Korea	4	Single-centre, assessor-blinded randomised (simple randomization) parallel-controlled 3 arms pilot study	Yes	45/38, 7	3 times a week, 2 weeks	SI 9, SI 10, SI 11, SI 12, TE 14, TE 15, TE 16, TE 17, GB 21, SI 3, SI 4, BL 65.	Bilateral	22-55	3 years	15 min	Yes
Rezvani et al. 2014, Iran	4	Single-centre randomised (a table of random numbers), single blinded (assessor), parallel-controlled 2 arms	Yes	80/ 78, 2	6 sessions given every other day, with 1 week rest between the courses, 3 courses/ 1 month	LI 4, ST 8, ST 36, BL 2, GB 14, TE 5, GB 8, Ex-HN5, SI 3, BL 10, BL 60, GB 20, LR3, KI 1, GV 20, Ex-HN1, LU7, SP 6, LR 2, ST 36, CV 6	N/A	18-65	15 years	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Wen et al. 2014, China	4	Single-centre randomised (envelope method), assessor blinded, parallel-controlled 2 arms	No	300/ 272, 28	5-7 times per week, 4 weeks/ 12 months	LI 16, SI 15, SI 11, LI 15, PC 6, TE 5, LI 10, LI 11, SI 3, LI 4, TE 4	Affected side	(62.3±10.1)	N/A	30 min	No
Wilke et al. 2014, Germany	5	Single-centre randomised (simple randomisation), investigator blinded, 3 arms placebo-controlled crossover	Yes	27/ 25, 2	Only once/ 30 min	GB 20, BL 10, BL 43, TE 15, SI 13, GV 14; TE 5, SI 3, GB 34	Near points-unilateral disease side; far points-bilateral	(33 ± 14) 18-65	licensed	20 min	Yes
Hoseinpour et al. 2015, Iran	2	Single-centre randomised (a table of random numbers), parallel-controled 3 arms	Yes	105/ 105, 0	3 times a week, 3 weeks	GB 20, GB 21, BL 10, GV 14, SI 3, SI 9, SI 11	N/A	(50.32 ± 3.22) 20-55	N/A	15 min	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Kooning 2015, Belgium	3	Multi- centre randomised (simple randomization, sequentially numbered,opaque , sealed envelopes) 2arms crossover trial with blinded assessor	Yes	39/ 39, 0	Only once	GV 14, Huatuojiaji CV 1-CV 7, GB 20, SI 11, GB 21, TE 15, SI 14, BL 17, SP 10, TE 5, GB 41, Ex-B8, Ear Zero point, Ear Jerome point, and Ear C0.	Unilateral/ bilateral	18-65	N/A	20 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
MacPherson et al. 2015, UK	3	Multi-centre 3 arms parallel, open, pragmatic, randomised, controlled trial	Yes	517/ 439,78	once per week initially and once every 2 weeks later, 12 acupuncture sessions or 20 one-to-one Alexander lessons (both 600 minutes total) plus usual care versus usual care alone	GB 20, GB 21, LI 4, LR 3, BL 10, SP 6, SI 3	N/A	(52.0 ± 13.8)	3 years	20 min	Yes
To & Alexander 2015, UK	5	Single-centre, double-blind randomised parallel-controled 2 arms	Yes	35/ 30, 5	Once a week, 6 weeks	LI 4, LI 10, LI 11, LI 14, LI 15, TE 14, LR 3, SI 3, GB 21, SI 12, ST 38	N/A	22-74	4 years	20 min	No

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Deganello et al. 2016, Italy	4	Single-centre, single-blind randomised parallel-controled 2 arms	Yes	53/ 48, 5	Once a week, 5 weeks	LI 4, SI 3, SI 6, GB 34, TB 14, TB 6, LI 15, GB 21	N/A	(60.1 ± 10.7)	10 years	30-45 min	No
Kim et al. 2016, Korea	3	Sigle-center, parallel, pragmatic randomised (block randomization) 2 arms with a 1:1 allocation ratio	Yes	50/ 39, 11	MA: 12-16 sessions over 6 weeks/ 3 months	LI 4, LI 11, TE 5, SI 3, TE 3, ST 36, SP 6, SP 9, LR 3, GB 34, GB 39, BL 40, BL 57, Jiaji points, BL 23	Bilateral	(62.0 ± 9.8)	3 years	20 min	Yes
Zhang et al. 2016, China	4	Single-center single-blind randomised (simple randomisation) parallel-controlled 2 arms	Yes	80/ 64, 16	Once a day, 10 days	TE 3, SI 3, LI 11 , ST 38	Contralateral	25-65	A single experienced acupuncturist	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Kizhakkeveettil et al. 2017, USA	3	Single-centre, no blind, randomised parallel-controled 3 arms	Yes	101/ 98, 3	The frequency of visits was at the discretion of the practitioners / 60 days	BL 18, BL 20, BL 22, BL 23, BL 25, BL 26, BL 28, BL 32, BL 35, BL 40, BL 57, BL 62, SI 3, GB 30, GB 34, Ashi	N/A	(37.2 ± 13.6)	5 years	30 min	Yes
Lewis et al. 2017, Ireland	3	Multi-centre, randomised parallel-controled 3 arms clinical trial,with assessor blinding	Yes	227/ 165, 62	twice a week, 6 sessions/ 6 months, 12 months	TE 14, LI 15, LI 14, LI 10, LU 2, GB 21, LI 4, TE 5, ST 36, ST 38, SI 9, SI 10, SI 11, SI 3	Uunilaterally , on the side of symptoms	(52.08 ± 14.35)	Physiotherapists completed a minimum of 80 hrs training in acupuncture	30 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Uğurlu et al. 2017, Turkey	4	Single-center, randomised, participant-blind, assessor-blind, parallel-controlled 2 arms	Yes	50/ 50, 0	3 sessions in the first week, 2 sessions/ week in the following 2 weeks and 1 session/ week in the following 5 weeks (totally 12 sessions)	LI 4, ST 36, LV 3, GB 41, GB 34, GB 20, SI 3, SI 4, BL 62, BL 10, SP 6, HT 7, GV 20, GV14, KI 27, CV 6, PC 6	N/A	(47.28 ±7.86)	Experienced physician	30 min	Yes
Kang et al. 2018, Korea	5	Single-center, randomised, participant-blind, assessor-blind, parallel sham-controlled preliminary trial with 3 arms	Yes	30/ 28, 2	2 or 3 times weekly for 4 weeks/ 4 weeks	When there was lower abdominal pain, skin dryness, heat in the upper body, or cold in the lower body, SI 3, GB 41, SI 2, and BL 66 were chosen	Both sides and and the contralateral side	(22.5 ± 5.72033)	Traditional Korean medical doctor with clinical experience in acupuncture treatment and more than 10 h of education	15 min	Yes

Table 3.1: Characteristics of the included studies (1)

Author, Publication Year, Country	Jadad' s scale score	Study design	Ethic approved before the study	No. of participants allocated/ assessed, dropouts	Frequency, treatment duration/ follow-up duration	Main acupuncture points	SI3 body sides' selection	Age (mean ± SD) or range	Acupuncturists ' experience	Needling Retention Time (min)	*deqi*
Yüksel et al. 2019, Turkey	1	Single-centre, randomised parallel-controled 3 arms	Yes	63/ 63, 0	Only once	SI 3, SI 4, BL 62, BL 64, BL 65, Ex-HN3	N/A	21-65 (44.6 ± 10.34)	N/A	20 min	No

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Dang & Yang 1998, China	Stomach carcinoma pain/ Neoplasms	1. Filiform needle (n = 16); 2. Point-injection (n = 16); 3. Western medicine (n = 16)	Analgestic effect, QOL	Yes	—
Sprott 1998, Germany	FMS/ Symptoms or signs of the musculoskeletal system	1. AT (n = 10); 2. Placebo (n = 10); 3. No treatment (n = 10)	positive "tender points", pain threshold	Partial	—
Kleinhenz et al. 1999, Germany	Rotator cuff tendinitis/ Symptoms or signs of the musculoskeletal system	1. Acupuncture needle (n = 25); 2. A new placebo-needle (n = 27)	Change in the modified Constant-Murley-score from the baseline; Questionnaires	Yes	—
Ceccherelli et al. 2001, Italy	Shoulder's Myofascial Pain/ Symptoms or signs of the musculoskeletal system	1. Superficial AT (n = 22); 2. deep AT (n=22)	MGPQ	Yes	Proximal to the head of the fifth metacarpal bone at the extremity of the fold evidenced by the palmar flexion of the fingers
Irnich et al. 2001, Germany	Chronic neck pain/ Symptoms or signs of the musculoskeletal system	1. AT (n = 56); 2. Massage (n = 60); 3. Placebo-sham laser AT (n = 61)	VAS ; range of motion (3D ultrasound real time motion), changes of spontaneous pain, motion related pain, global complaints (7 point scale), QOL (SF-36); PPT	Partial	—
Irnich et al. 2002, Germany	Chronic neck pain/ Symptoms or signs of the musculoskeletal system	1. DN (n = 34); 2. Sham laser (n = 34); 3. Non-local AT (n = 34)	VAS; ROM; scored changes of general complaints	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Sherman et al. 2002, USA	LBP/ Symptoms or signs of the musculoskeletal system	1. Standardized acupuncture treatment using real acupuncture needles (n = 30); 2. "treatment" using the toothpick–guidetube simulation at the same acupoints (n = 30).	Perceptions and pain relief measured by a credibility questionnaire	More likely	On the side of the hand
Sze et al. 2002, China	Poststroke motor rehabilitation/ Diseases of the nervous system	1. Standard modalities of treatment + AT (n = 53); 2. Standard modalities of treatment (n = 53)	FMA， BI, FIM, AMT, NIHSS, FMAM,	No	—
Wang 2003, China	Acute lumbar sprain/ Symptoms or signs of the musculoskeletal system	1. AT + cupping (n = 50); 2. Orally administered + ultra-short-wave (n = 31)	Curative effects	Yes	—
Kvorning et al. 2004, Sweden	Pelvic and LBP in late pregnancy/ Symptoms or signs of the musculoskeletal system	1. AT (n = 37); 2. Control group (n = 35)	VAS scorings of pain intensity	Yes	—
Melchart et al. 2005, Germany	Tension-type headache/ Diseases of the nervous system	1. AT (n = 132); 2. Minimal AT (n = 63); 3. Waiting list (n = 75)	Difference in numbers of days with headache between the four weeks before randomisation and weeks 9-12 after randomisation, as recorded by participants in headache diaries	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Pohodenko-Chudakova 2005, Belarus	Cranio-maxillofacial surgical procedures/ Postsurgical pain	1. AT + chemical anaesthesia (n = 20); 2. Chemical anaesthesia (n = 100)	Cardiovascular state (pulse, blood pressure, ECG); serum cortisol	Yes	—
Wayne et al. 2005, USA	Upper-extremity rehabilitation in chronic stroke/ Diseases of the nervous system	1. Active acupuncture intervention (n = 16); 2. Sham acupuncture intervention (n = 17)	UE motor function, spasticity, grip strength, ROM, activities of daily living, QOL, and mood.	No	—
Alecrim-Andrade et al. 2006, Spain	MIG/ Diseases of the nervous system	1. Real AT (n = 16); 2. Sham AT(n = 15)	Reduction percentage; Migraine days	No	With the patient's fist loosely clenched, at the ulnar end of the proximal crease of the fifth metacarpophalangeal joint, on the dividing line between red and white flesh
Brinkhaus et al. 2006, Germany	Chronic low back pain/ Symptoms or signs of the musculoskeletal system	1. At (n = 146); 2. Minimal AT (n= 73); 3. Waiting list control (n = 79)	1. Pain questionnaire; 2. Pain intensity (VAS); 3. Back function (questionnaires of German Society for the Study of Pain)	Partial	—
Brinkhaus et al. 2006, Germany	Low-Back Pain/ Symptoms or signs of the musculoskeletal system	1. AT; 2. Minimal AT; 3. Waiting list control (ratio 2:1:1)	Participating trial physicians and interventions	Most	—
Ceccherelli et al. 2006, Italy	Cervical myofascial pain/ Symptoms or signs of the musculoskeletal system	1. Somatic AT (n = 31); 2. AT + auriculotherapy (n = 31)	MGPQ, VAS	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Molsberger et al. 2006, Germany	MIG & TTH/ Diseases of the nervous system	1. Verum AT; 2. Sham AT; 3. Standard therapy,	Broadly consensual acupuncture protocols for MIG and TTH for verum and sham acupuncture were developed.	Yes	—
Molsberger et al. 2006, Germany	LBP & GON/ Symptoms or signs of the musculoskeletal system	1. Verum AT; 2. Invasive sham AT; 3. Standard therapy	Broadly consensual acupuncture protocols for LBP and GON for verum and invasive sham acupuncture were developed.	Yes	—
Schmid-Schwap et al. 2006,	Craniomandibular dysfunction syndrome/ Symptoms or signs of the musculoskeletal system	1. AT (n=11); 2. Sham laser placebo therapy (n = 12)	SBLjective pain, mouth opening, and muscular tenderness and pain on, pressure (VAS 0-100).	Yes	Hand
Vas et al. 2006, Spain	Chronic uncomplicated neck pain/ Symptoms or signs of the musculoskeletal system	1. AT (n = 61); 2. TENS-placebo (n = 62)	Change in maximum pain intensity related to motion of the neck (pain-VAS); NPQ, ACM, PCM; QOL: SF-36; Treatment credibility	Yes	
Crew et al. 2007, USA	Joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients/ Neoplasms	1. Immediate acupuncture group; 2. Delayed treatment group	BPI-SF, WOMAC index, FACT-G, IL-1β, TNF-α	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Itoh et al. 2007, Japan	Chronic neck pain/ Symptoms or signs of the musculoskeletal system	1. Standard AT (n = 10); 2. Trigger point AT (n = 10); 3. Non-trigger point AT (n = 10); 4. Sham AT (n = 10)	1. Pain scores (VAS); 2. Neck Disability Index	No	—
Ritenbaugh et al. 2008, USA	Neck/shoulder pain or tightness/ Symptoms or signs of the musculoskeletal system	1. Usual care (n = 60); 2. CM (n = 50); 2. NM (n = 50)	1. Worst facial pain; 2. Average facial pain, when the participant was having pain; 3. Effect of pain on activities of daily living; 4. Effect of pain on social activities	Yes	—
Min et al. 2009, Korea	Knee osteoarthritiss/ Symptoms or signs of the musculoskeletal system	1. Sa-am acupuncture (n = 40); 2. Sham acupuncture (n = 38)	1. KWOMAC pain score; 2. KWOMAC stiffness score; 3. KWOMAC function score; 4. KWOMAC total score; 5. SF-36 physical score; 6. SF-36 mental score; 7. SF-36 total score	Yes	—
Simma et al. 2009, Austria	Oromyofacial pain and CMD/ Symptoms or signs of the musculoskeletal system	1. AT (n = 11); 2. Placebo laser therapy group (n = 12)	Pain (VAS)	Yes	—
Yuan et al. 2009, UK	Chronic non-specific LBP/ Symptoms or signs of the musculoskeletal system	1. 2 times/week for five weeks (n = 15); 2. 5 times/week for two weeks (n = 15).	VAS, RMDQ, MYMOP-2, CSQ, PLC questionnaire, SWT, LTF	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Ceccherelli et al. 2010, Italy	CS/ Symptoms or signs of the musculoskeletal system	1. SI 3, TE 5, BL 62, GB 20, GV 14, 2 most painful trigger points (n = 18); 2. SI 3, GV 14, 2 most painful trigger points (n =18)	MPQ; VAS	Yes	Proximal to the head of the V metacarpal on the ulna side of the proximal extremity in the joint after flexion of the wrist; the afferent nerve is the dorsomedial branch of the V digital nerve, C8 dermatome
Molsberger et al. 2010, Germany	Chronic shoulder pain/ Symptoms or signs of the musculoskeletal system	1. Verum AT (n = 154); 2. Sham AT (n = 135); 3. Conventional orthopaedic conservative treatment (n = 135)	VAS score	Yes	—
Sun et al. 2010, China	Chronic neck MPS/ Symptoms or signs of the musculoskeletal system	1. AT (n = 18); 2. SA (n=17)	SF-36; ROM, VAS, SF-MPQ	No	—
Ahn et al. 2011, Korea	Headache, trigeminal neuralgia and retro-auricular pain in facial palsy/ Diseases of the nervous system	1. Traditional Acupuncture (n = 15); 2. Combined Acupuncture (n = 34)	Pain alleviation	Yes	—
Johnston et al. 2011, USA	CRF, myofascial muscle pain/ Neoplasms	1. Usual care plus treatment (n = 5); 2. Usual care only (n = 7)	BFI	Yes	—
Wang et al. 2011, China	Migraine/ Diseases of the nervous system	1. VA (n = 70); 2. Flunarizine (n = 70)	1. Proportion of responders; 2. Change of migraine days, VAS for pain, SF-36, the number of patients with acute medication, AE	Partial	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Kang et al. 2012, Korea	TMDs/ Symptoms or signs of the musculoskeletal system	1. Adjacent point selection group (n = 14); 2. Distant point selection group (n = 14); 3. Combination group (n = 14)	Pain intensity and palpation index in participants with TMD	Yes	—
Kwak et al. 2012, Korea	WAD/ Symptoms or signs of the musculoskeletal system	1. AT (n = 20); 2. waiting-list (n = 20)	VAS, SF-36, ROM, SDS, CMI	Yes	—
Sun et al. 2012, China	Shoulder-hand syndrome due to ischemic stroke/ Diseases of the nervous system	1. Observation group (n = 30); 2. Control group (n=30)	VAS; FMA	Yes	—
Wallasch et al. 2012, Germany	Migraineurs/ Diseases of the nervous system	1. VA (n = 18); 2. PA (n = 17)	Clinical response to VA and PA; f-TCD measurements	Partial	At the end of the transverse crease proximal to the 5th metacarpo-phalangeal joint when hand is half clenched
Wang et al. 2012, China	Acute Migraine Attack/ Diseases of the nervous system	1. TA (n = 75); 2. SA(n = 75)	VAS, SF-MPQ	Yes	—
Tobbackx et al. 2013, Belgium	Chronic WAD/ Symptoms or signs of the musculoskeletal system	1. AT (n = 20); 2. Relaxation therapy (n = 19)	1. Immediate activation of endogenous analgesia i.e., pressure pain sensitivity and conditioned pain modulation; 2. Pain relief and reduced disability level.	Yes	On the ulnar side of wrist, between fifth metacarpal bone and carpal bone 6
Bahrami-Taghanaki et al. 2014, Iran	Chronic LBP/ Symptoms or signs of the musculoskeletal system	1. AT + a pair of confluent points (n = 30); 2. regular AT (n = 30)	VAS	Yes	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Ceccherelli et al. 2014, Italy	Painful cervical myofascial syndrome/ Symptoms or signs of the musculoskeletal system	1. 11 needles (n = 30); 2. 5 needles (n = 30); 3. 3 needles (n = 30)	MPQ, VAS, QOL	Yes	Proximal to the head of the 5th metacarpal, on the ulna side of the proximal extremity in the joint after flexion of the wrist, the afferent nerve is the dorsomedial branch of the 5th digital nerve, C8 dermatome
Cho et al.2014, Korea	Chronic neck pain/ Symptoms or signs of the musculoskeletal system	1. AT + NSAID (n = 15); 2. AT (n = 15); 3. NSAID (n = 15)	1.To determine the feasibility and to calculate the sample size; 2.pain intensity and pain-related symptoms	Yes	—
Rezvani et al. 2014, Iran	Migraine/ Diseases of the nervous system	1. TCA (n = 40); 2. YNSA (n = 40	Frequency and severity of migraine attacks, nausea, the need for rescue treatment, and work absence rate	Yes	—
Wen et al. 2014, China	Omalgia of ischemic stroke/ Diseases of the nervous system	1. Acupuncture group (n = 150); 2. Regular therapy group	Omalgia incidence number; Fugl-Meyer; Rankin Scale	Yes	—
Wilke et al. 2014, Germany	CS/ Symptoms or signs of the musculoskeletal system	1. Dry needling (n = 9); 2. Sham dry needling (n = 8); 3. Placebo laser AT (n = 10)	MPT(i.e. PPT); ROM, VAS	Yes	—
Hoseinpour et al. 2015, Iran	Chronic Cervical Disk Herniation/ Symptoms or signs of the musculoskeletal system	1. Physiotherapy with cervical traction; 2. Acupuncture; 3. Strengthening exercise	VAS; NDI	Partial	—

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Kooning 2015, Belgium	Chronic WAD/ Symptoms or signs of the musculoskeletal system	1. AT (n = 20); 2. Relaxation (n = 19)	Autonomic nervous system parameters (heart rate, skin conductance, and heart rate variability parameters); Endogenous analgesia	Partial	—
MacPherson et al. 2015, UK	Chronic, nonspecific neck pain/ Symptoms or signs of the musculoskeletal system	1. Acupuncture + usual care; 2. Alexander lessons + usual care; 3. Usual care alone	NPQ score; Chronic Pain Self-Efficacy Scale score; QOL	Yes	—
To & Alexander 2015, UK	SIS/ Symptoms or signs of the musculoskeletal system	AT/ Park sham 1. Healthy volunteer (n = 16; 2. SIS patients (n = 19)	Identify the type of needle	N/A	—
Deganello et al. 2016, Italy	Shoulder Pain and Functional Impairment After Neck Dissection/ Symptoms or signs of the musculoskeletal system	1. AT (n = 26); 2. usual care (n = 27)	Constant-Murley score, QOL	Yes	—
Kim et al. 2016, Korea	Symptomatic LSS/ Symptoms or signs of the musculoskeletal system	1. MA ± EA (n = 26); 2. Usual care alone, physical therapy as required (n = 24)	Change in back-specific functional status; Symptoms	No	—
Zhang et al. 2016, China	Chronic shoulder pain/ Symptoms or signs of the musculoskeletal system	1. Contralateral MA (n = 38); 2. Conventional orthopaedic therapy including physical exercise (n = 42)	VAS; Shoulder mobility and QOL included the Jobe test, the Constant-Murley (CM) score, the Disabilities of the Arm, Shoulder and Hand score, SF-36	Yes	On the dorsum of the hand, in the depression proximal to the ulnar side of the fifth metacarpophalangeal joint, at the border between the red and white flesh

Table 3.2: Characteristics of the included studies (2)

Author, Publication Year, Country	Indication/ Diseases ICD-11	Intervention/ Comparator	Main outcomes	Effective for pain relief	Operational Definitions of the Location of SI3
Kizhakkeveettil et al. 2017, USA	LBP/ Symptoms or signs of the musculoskeletal system	1. Acupuncture (n = 33); 2. SMT (n = 36); 3. Integrative acupuncture and SMT (n = 31)	Roland-Morris LBP Disability Questionnaire; NRS	Yes	—
Lewis et al. 2017, Ireland	Subacromial pain syndrome/ Symptoms or signs of the musculoskeletal system	1. Exercise only (n = 73); 2. Exercise & acupuncture (n = 77); 3. Exercise & electro-acupuncture (n = 77)	Oxford Shoulder Score; SPADI; Night pain; Analgesic use; Impact of main functional problem; Two orthopaedic tests (Neer sign, Hawkin's test)	Yes	—
Uğurlu et al. 2017, Turkey	FMS/ Symptoms or signs of the musculoskeletal system	1. TA (n = 25); 2. SA (n = 25)	VAS, FIQ, SF-36, BDI, FSS	Yes	—
Kang et al. 2018, Korea	Atopic dermatitis/ Diseases of the skin	1. Acupuncture twice a week (n = 10); 2. Acupuncture three times a week (n = 10); 3. SA (n = 10)	SCORAD index; VAS (Pruritus) and VAS (Insomnia); EASI and POEM; DLQI, CES-D, and STAXI; Credibility test and PPT	Yes	—
Yüksel et al. 2019, Turkey	FMS/ Symptoms or signs of the musculoskeletal system	1. AT (n = 21); 2. TENS (n = 21); 3. Healthy volunteers (n = 21)	VAS; BDI; FIQ; PPT; qEEG	Yes	—

* The classification of diseases specifically referenced WHO'S International Statistical Classification of Diseases and Related Health Problems - the 11th Revision of the International Classification of Diseases (ICD-11) <http://www.who.int/classifications/icd/revision/en/#>, https://icd.who.int/dev11/l-m/en

Abbreviations of Table 3.1 & Table 3.2:

SCI: Spinal Cord Injury
SF-36: Short Form-36
ROM: range of motion
FMS: Fibromyalgia syndrome
VAS: Visual Analogue Scale
LBP: lower back pain
NIHSS: NIH Stroke Scale
DN: dry needling
IL: interleukin
RA: rheumatoid arthritis
CS: cervical myofascial syndrome
LTF: Lateral Trunk Flexibility
PPT: pressure pain threshold
MPT: Mechanical pain threshold
CMD: craniomandibular disorders
SIS: shoulder impingement syndrome
RMDQ: Roland-Morris Disability Questionnaire
ACR: American College of Rheumatology criteria
VA: verum acupuncture
MGPQ: McGill Pain Questionnaire

iVAS: initial VAS
fVAS: final VAS
PPT: pain pressure threshold
QOL: quality of life
TA: Ture acupuncture
SA: Sham acupuncture
TTH: tension-type headache
SCORAD: SCORing Atopic Dermatitis
DLQI: Dermatology Life Quality Index
NPQ: Northwick Park Questionnaire
SPADI: Shoulder Pain and Disability Index
EASI: Eczema Area and Severity Index
POEM: Patient Oriented Eczema Measure
CSQ: Coping Strategies Questionnaire
NRS: Numeric Rating Scale of pain intensity
EA: ear acupuncture
PA: placebo acupuncture
MIG: migraine
ECG: electrocardiography
MA: manual acupuncture
EA: electroacupuncture
AT: acupuncture treatment
GON: gonarthrosis
BI: Barthel Index
AMT: Abbreviated Mental Test
UE: upper-extremity
CM: Chinese Medicine
NM: Naturopathic Medicine
SMT: spinal manipulative therapy
FIQ: Fibromyalgia Impact Questionnaire
NDI: neck disability index
SC: state-of-the-art specialty care
FSS: Fatigue Severity Scale
AIS: Adolescent Idiopathic Scoliosis
BDI: Beck Depression Inventory
LSS: lumbar spinal stenosis
TCA: traditional Chinese acupuncture
MPS: myofascial pain syndrome
BPI-SF: Brief Pain Inventory-Short Form
CRF: Cancer-related fatigue
EEG: electroencephalography
SF-MPQ: Short-Form McGill Pain Questionnaire
YNSA: Yamamoto new scalp acupuncture
WAD: Whiplash-associated disorder
FIM: Functional Independence Measure
RCT: Randomised controlled trial
SDS: Self-Rating Depression Scale
qEEG: quantitative electroencephalography
TMDs: temporomandibular joint disorders
BFI: Brief Fatigue Inventory
CMI: Cornell Medical Index
STAXI: State-Trait Anger Expression Inventory
KWOMAC: Korean translation of Western Ontario and McMaster Universities Osteoarthritis Index
CA: combined acupuncture which consists of traditional acupuncture and ear acupuncture
FMAM: Fugl-Meyer Assessment of Physical Performance—Motor subsection
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index
TENS: transcutaneous electric nerve stimulation
CES-D: Centre for Epidemiologic Studies–Depression Scale
FACT-G: Functional Assessment of Cancer Therapy-General
f-TCD: functional transcranial Doppler sonography
FMA: Fugl-Meyer Assessment of Physical Performance
MYMOP-2: Measure Yourself Medical Outcome Profile

3.1.2.3 Country of origin

The first listed authors came from fifteen different countries. The first authors of clinical trial reports on SI 3 came from Germany (n = 12) followed by China (n = 9), South Korea (n = 7), USA (n = 6), Italy (n = 5), UK (n = 3), Iran (n = 3), Austria (n = 2), Belgium (n = 2), Spain (n = 2) and Turkey (n = 2). Only one clinical trial was recorded for each of the following countries: Belarus, Ireland, Japan and Sweden (refer to Figure 3.2).

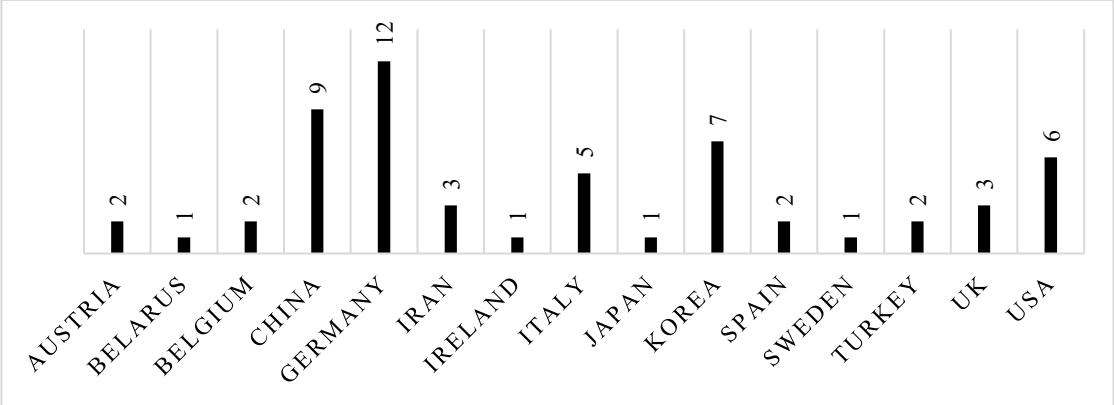


Figure 3.2: Fifteen countries of origin

3.1.2.4 Quality of the clinical trials reviewed

The 57 clinical trials were assessed using the revised Jadad's scale (Jadad et al., 1996; Lee et al., 2008) which assesses three aspects of clinical trials:

1) Randomisation procedure (1 point is given if patients were randomised allocated into the groups, 1 bonus point if the randomization process is appropriate);
2) Drop-out and withdrawal (1 point is given for a clear description of dropouts and withdrawals) and;
3) Blinding (1 point was given for blinding of patient, and an additional 1 point was given if the outcome assessor was blinded).

Therefore, each article could potentially score 0 (lowest quality) to 5 (highest quality). Studies were classified as high quality if they attained a score of 3 or more (Lundh and Gøtzsche, 2008). Figure 3.3 shows that the majority of trials (n=21) scored 4 points. Forty seven clinical trials (82%) scored 3 or more studies and are classified as high quality (refer to Figure 3.4). While it is not possible to blind participating physicians to the treatment used, all the studies had important outcome measures assessed independently and subjects were blinded and therefore has been justified as double-blind.

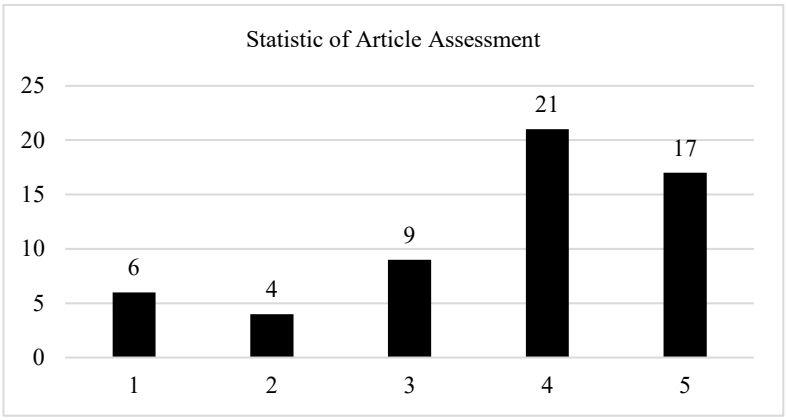


Figure 3.3: Frequency distribution of the modified Jadad's scale scores

3.1.2.5 Ethic approval before the study commenced

Forty six studies had been approved prior to the trial commencing (81% of the 57 RCTs). It appeared that the majority of those acupuncture RCTs had been designed following the international advanced standard.

3.1.2.6 Unilateral or bilateral needling of SI 3

Of the 57 clinical trials, 51% of them (n=29) specified whether SI 3 was needled unilaterally or bilaterally with the majority being bilateral (n=17). Four studies used contralateral needling and three studies were ipsilateral needling of SI 3 selected. In four studies (n=4), a mix of unilateral and bilateral needling of SI 3 were used - homolateral SI 3 for a unilateral pain and bilateral points for bilateral pain (refer to Figure 3.4). Very few studies (n=28) reported any details about which side of the body SI 3 was needled (see figure 1.0.5). In the future, RCTs should be designed to evaluate this concept.

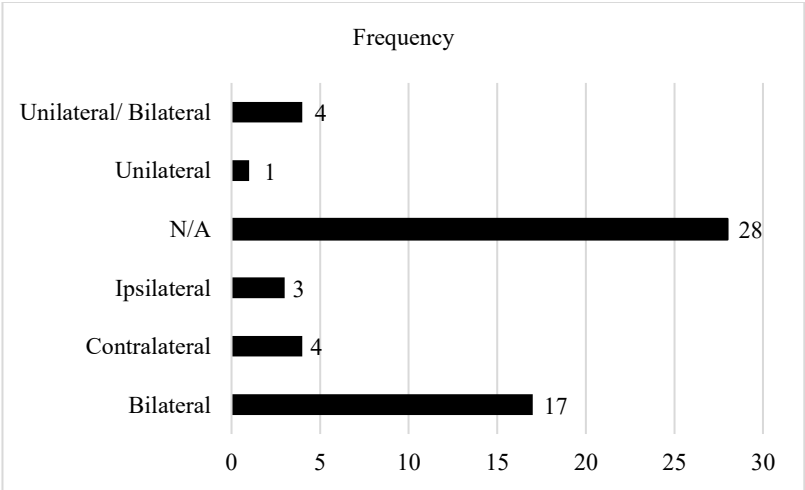


Figure 3.4: Unilateral or bilateral needling of SI 3

3.1.2.7 Needling retention time

The needling retention time varied from 15 to 37.5 minutes. The most common retention time range was 20-30 minutes (n = 42). Nine of the 57 articles did not mention the needling retention time (refer to Figure 3.5). Twenty to thirty minutes can be considered the conventional acupuncture pain relief treatment.

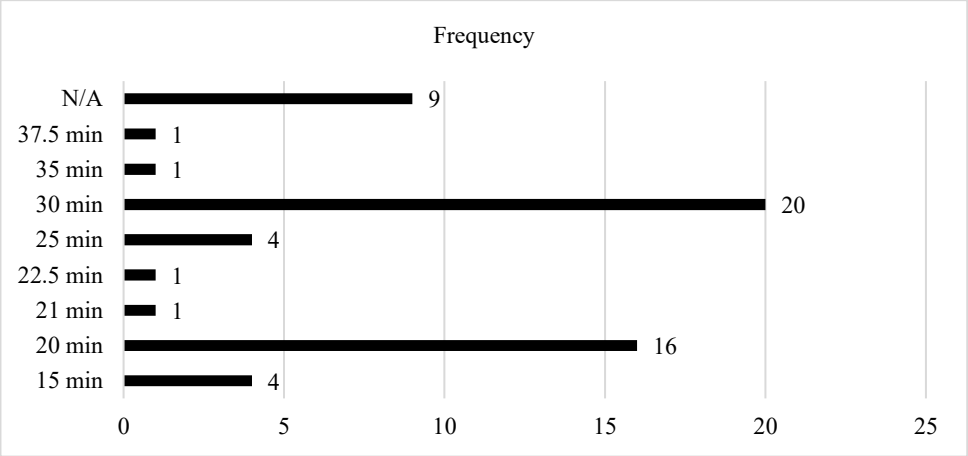


Figure 3.5: Needling Retention Time

3.1.2.8 Needle sensation (*deqi*)

Deqi was sought during needling in 37 clinical trials (65%), while researchers did not mention the term *deqi* in the other 20 trials (35%) (Refer to Figure 3.6). However, one of the 20 trials recorded "The patient's mind was concentrated at the site of disease".

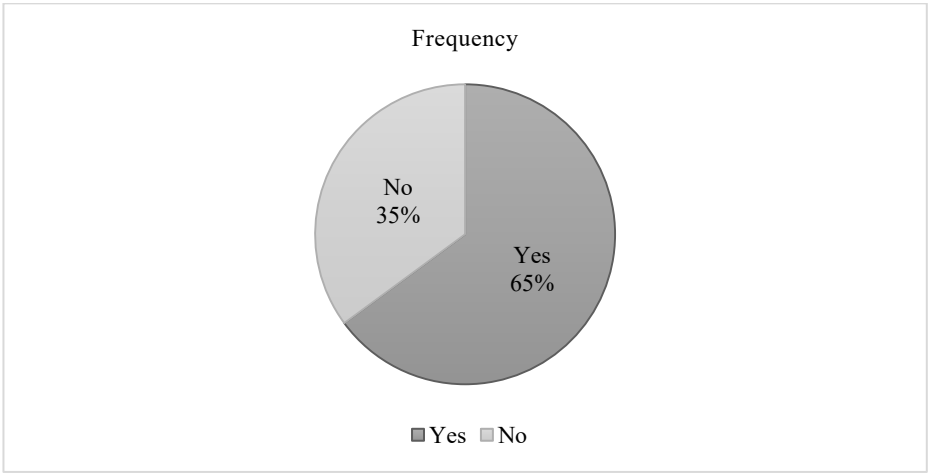


Figure 3.6: Needle sensation (*deqi*) on SI 3 location

3.1.2.9 Type of conditions treated

The pain conditions treated in the clinical trials involving SI 3 were classified according to the International Statistical Classification of Diseases and Related Health Problems

11th Revision (ICD-11) (World Health Organisation 2018). As shown in Figure 3.7, the majority of the conditions treated were symptoms or signs of the musculoskeletal system (n=40) followed by diseases of the nervous system (n=12), neoplasms (n=3). Only one clinical trial was conducted for each of the following conditions: diseases of the skin (n=1) and postsurgical pain (n=1).

Symptoms or signs of the musculoskeletal system (n=40) included lower back pain (n=10), neck and shoulder pain (n=23), cranio-mandibular disorders (n=3), fibromyalgia syndrome (n=3) and knee osteoarthritis (n=1). Therefore, neck, shoulder and lower back pain were the major indication for all treatment regimens.

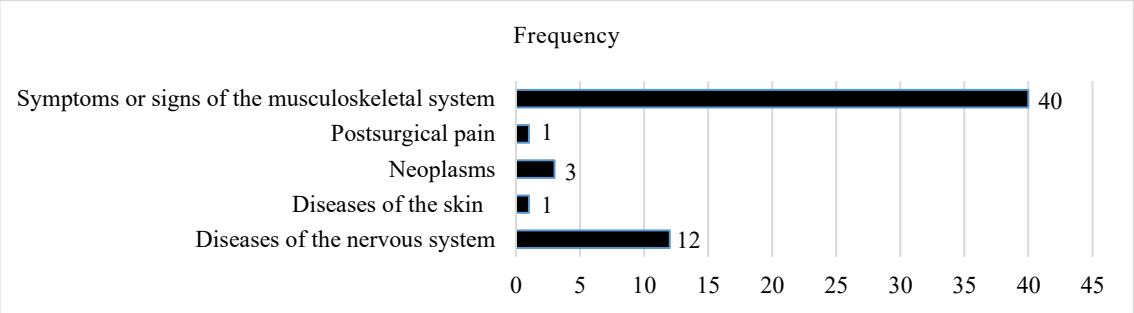


Figure 3.7: Type of pain conditions treated in clinical trials involving the use of SI 3

3.1.2.10 Operational definitions of the location of SI 3

Of the 57 studies, there were only 9 articles that described the operational definition of the location of SI 3. The descriptions can be found in Table 2.

3.1.2.11 Treatment regimen

The frequency of the acupuncture treatment was at the discretion of the practitioners in one trial. Thereby, this trial was not analysed. The graph below (refer to Figure 3.8) shows the number and frequency of the acupuncture treatment for the 56 clinical trials.

The frequency ranged from 1 to 7 treatment sessions per week and most study frequency ranged from 1 to 3 times per week. The total number of treatments ranged from 1 to 48 while most studies ranged from 1 to 16.

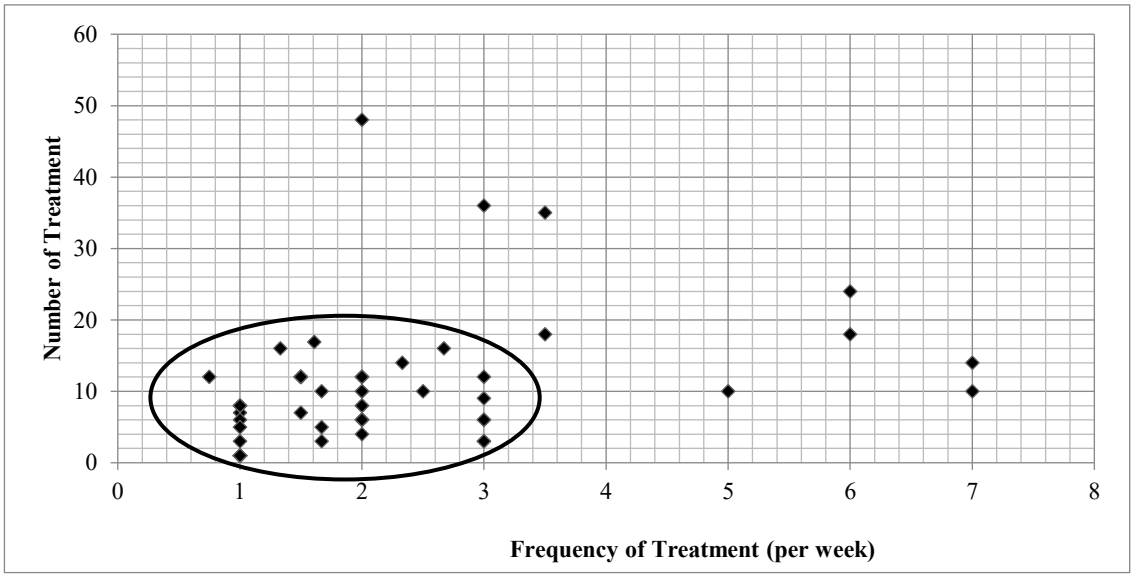


Figure 3.8: Number and frequency of treatments for the 56 clinical trials

3.1.2.12 Effective for pain relief

Of the 57 RCTs, 41 trials achieved effective pain relief, while 6 studies did not show effective pain control with acupuncture (refer to Figure 3.9).

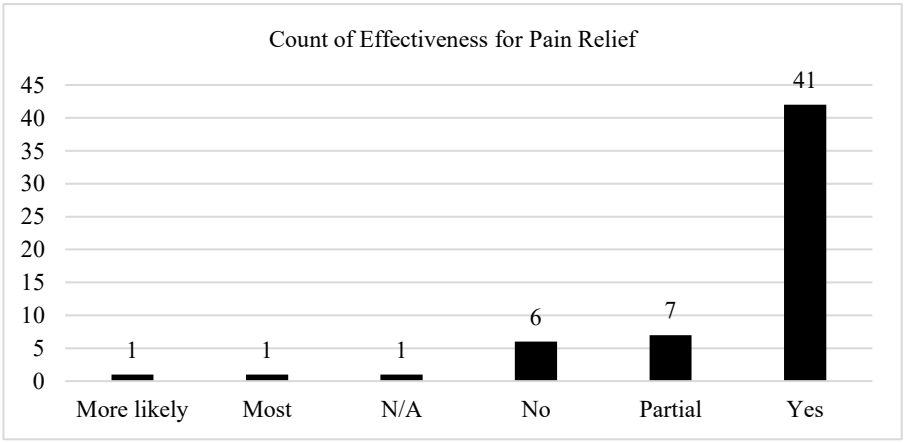


Figure 3.1: Effective for pain relief

3.1.3 Discussion

The aim of this systematic review was to examine and summarise the literature concerning the use of the acupoint - SI 3 on pain syndromes in RCTs and determine the specific effects of SI 3 for the range of pain conditions treated. This study provided a comprehensive analysis of 57 RCTs on pain syndromes using conventional acupuncture to SI 3. Sixteen countries conducted SI 3 trials, which means the acupuncture research on pain syndrome has been widely regarded as a sort of non-pharmacological treatment. Amongst these RCT studies, the number of included participants ranging from 13 to

2,201. In general, the results showed that 72.4% of the studies reduced pain effectively, while 12.1% of studies were partially effective, and six trials demonstrated negative results. This shows promise for SI 3 to play an important role in pain relief. However, most of the trials (84%) did not describe the operational definitions of the location of SI 3, which made hard to evaluate the treatment.

Though 64% of the RCTs sought to elicit *deqi* during the acupuncture treatment, it still requires significant attention to the inclusion of a *deqi* measurement standard as some believed that various factors can influence therapeutic effect of acupuncture treatment, including whether or not the needling sensation appears, the speed of *deqi* radiation, the intensity of *deqi*, different types of sensations as well as propagated sensation along the channels (Hu et al., 2014). Others have argued that whether *deqi* is associated with treatment effect is unclear (Zhou and Benharash, 2014). Indeed it can be argued that practitioners and researchers should pay attention to the relationship between *deqi* and pain relief effectiveness.

There was insufficient data to determine which body side should be selected for needling of SI 3. Thereby, further RCT designs should include this aspect so that patients could attain reliable treatment.

Among the 57 clinical trials reviewed, no study used SI 3 as the sole acupoint in the study. All studies used SI 3 in combination with other acupoints. It is thus difficult to determine the specific effects of SI 3 for the range of conditions treated. Thus there is a need to investigate the specific effect of SI 3 as a sole acupoint. While most studies in this review focused on symptoms or signs of the musculoskeletal system, there is also a great deal of classical Chinese medical texts and modern textbooks that mention the use of SI 3 for a range of musculoskeletal conditions. Further research could investigate the effects of SI 3 on PPT or some other pain challenger instruments.

Furthermore, none of the studies measured *deqi*. In the future studies, *deqi* should be measured both quantitatively and qualitatively.

3.1.4 Conclusion

All the 57 studies used SI 3 in combination with other acupoints. Thus, it is difficult to determine the specific effects of SI 3 for the range of conditions treated. Based on this literature review the author believes further investigation should be made of the specific

effect of SI 3 as a sole acupoint. As most classical and modern textbooks mentioned the use of SI 3 for a range of musculoskeletal conditions, future RCTs could investigate the effects of SI 3 with some certain parameters, such as PPT. In the following section, the author will conduct a systematic review regarding PPT. Furthermore, none of the studies measured *deqi*. In the future studies, *deqi* should be measured both quantitatively and qualitatively.

3.2 Application of pressure pain threshold in acupuncture clinical study: a systematic review of randomised controlled trials

3.2.1 Introduction

The assessment of pain in the diagnosis of disease, the effect of treatment and the resulting prognosis plays an important role in clinical practice. However, it should be reiterated that pain is the patient's subjective feeling. The clinical evaluation of pain is mainly achieved through subjective measurement, using the patient's subjective feelings to quantify the degree of pain. Measures that attempt to do this include the Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MGPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP) (Hawker et al. 2011). Despite this the criticisms of a lack of objective and accurate evaluation methods remain.

The pain threshold measurement is an attempt to objectify the measurement of pain. Pain threshold refers to the intensity of a stimulus that causes the sensation of pain in the body. Human pain threshold can be generally divided into two sorts: one is the minimum stimulus intensity when the human body feels pain or uncomfortable, called pain threshold; the other is the maximum intensity of stimulation that the body can tolerate, called the pain tolerance threshold. Pain threshold refers to the intensity of a stimulus when it is first recognized by the individual as painful. Pain tolerance refers to the amount of pain a person is willing to endure (Martin 2019).

The measurement of human pain threshold is a commonly used method in pain research. The accuracy and reliability of pain threshold measurement directly affect the evaluation of experimental results. Pain threshold can be divided into mechanical pain threshold, temperature pain threshold, chemical stimulation pain threshold and electrical stimulation pain threshold (Schoth et al. 2019). Each type of pain threshold has its own specific

measurement method and equipment. PPT measurement is one of the mechanical pain threshold measures, a popular model for inducing acute, experimental pain. It has been widely used in clinical studies (Maquet et al. 2004), yet there are not many acupuncture clinical trials that measure PPT. PPT is defined as the minimum force applied which induces an uncomfortable feeling, which is one of the mechanical detection thresholds. This measure has proven to be useful in assessing pain symptoms (Park et al. 2011). It has been acknowledged that PPT is a valid and reliable measure (Chesterton et al. 2007). Pressure pain sensitivity however has been shown to be influenced by the anatomical localization of the measurement site and gender.

A dolorimeter is an instrument used to measure pain threshold and pain tolerance. Dolorimetry has been defined as "the measurement of pain sensitivity or pain intensity" (Hawker et al. 2011). Several types of dolorimeters have been developed. Dolorimeters apply steady pressure, heat, or electrical stimulation to an area, or to move a joint or other body part and determine what level of heat or pressure or electric current or amount of movement produces a sensation of pain. Sometimes the pressure is applied using a blunt object, or by locally increasing the pressure on some area of the body, and sometimes by pressing a sharp instrument against the body. There are many types of instruments used for PPT measurement, such as hand held electronic pressure algometer (Pelfort et al. 2015) (Algometer, Somedic Sales, Hörby, Sweden), Vulvalgesiometer (Pukall et al. 2007), Autoalgometry (Lorusso et al. 2018), Force Dial Push Pull Gage to name a few. Digital pressure algometers have become the standard, and computer-controlled pressure algometers are currently being developed and refined.

Acupuncture is increasingly used on pain syndromes, and there is a need for evidence to validate this practice, which is an objective measure of PPT for clinical and research use.

3.2.2 Objective

To date, there have been no systematic reviews of the evidence in this area. The aim of this current review was therefore to review systematically the current clinical evidence concerning the application of PPT as a pain measurement, and to determine safety and efficacy of this approach to further improve the quality of acupuncture research.

3.2.3 Methods

3.2.3.1 Search methods

The search involved relevant databases including MEDLINE, AMED, ProQuest Health & Medicine, Google Scholar, EMBASE and the Cochrane library. The search was conducted on 20 August 2019 using the following parameters: (PPT OR "pressure pain threshold" OR "pain pressure threshold") AND (acupuncture OR needl* OR dry needl*) AND (RCT* or "randomised clinical trial*").

3.2.3.2 Inclusion/exclusion criteria

First, the articles were screened by title and abstract. The following inclusion criteria for relevant articles were used during the initial screening of titles and abstracts: conventional acupuncture randomised clinical trials of certain diseases, written in English language, with no time limitation, on the use of PPT measurement. Exclusion criteria were articles written in other languages, reviews, protocols, case studies or theses, dry needling for trigger points, only the inclusion of electro-acupuncture in the treatment plan.

3.2.3.3 Data extraction, data synthesis and methodological quality assessment

Two reviewers (XQW and CZ) independently selected trials for inclusion, assessed methodological quality, extracted data, and resolved any differences through discussion and examination of study titles, abstracts, and key words and posteriorly the full text. A standardized Microsoft Excel Worksheet was used to determine the eligibility of retrieved studies and collect the date.

A customized form was used to extract data relevant to the review aims, namely: study reference, purpose, study design, diagnosis, study sample, characteristics of the participants, intervention, duration and frequency of treatment in the experimental groups, outcome measures, description of the instrument for measuring PPT and application, *deqi* sensation, manipulation, needle retention time, study result, and conclusion.

The methodological quality of each randomised controlled trial was assessed using the PEDro scale (Moseley et al. 2002) (Appendix 1). A PEDro score between 6 and 10 is indicative of high quality; a score of 4-5 indicates fair quality; and, a score $\leqslant$3 indicates poor quality.

3.2.4 Results

3.2.4.1 Study selection

From the web-based search, 261 articles were identified; MEDLINE (n = 4), AMED (n = 0), ProQuest Health & Medicine (n = 194), Google Scholar (n = 31), EMBASE (n = 7), Cochrane (n = 25). Of these, 10 articles were duplicates and, therefore excluded. Of the 251 potentially eligible articles, 246 were discarded due to the following reasons: conference proceeding (n=29), book chapter, guideline, summaries or commentary (n = 7), abstract (n = 12), poster (n = 6), thesis (n = 4), case reports (n = 3), dry needling or other non-conventional acupuncture intervention trials (n = 28), review paper (n = 88), PPT was not an outcome measure (n = 60), RCT protocol (n = 8) and one trial was not randomised. Therefore, 5 articles (Irnich et al. 2001; Zhang et al. 2011; Schliessbach et al. 2012; Wang et al. 2015; Kang et al. 2018) remained to be included. In addition, 20 eligible articles (Barlas et al. 2000; Karsta et al. 2000; Nabeta & Kawakita 2002; Zaslawski et al. 2003; He et al. 2004; Shen & Goddard 2007; Hübscher et al. 2008; Li et al. 2008; Targino et al 2008; Kumnerddee 2009; Lang et al. 2010; Itoh et al. 2011; Schliessbach et al. 2011; Mavrommatis et al. 2012 Rebhorn et al. 2012; Choi et al. 2013; Loyeung & Cobbin 2013; Tobbackx et al. 2013; Plaster et al. 2014; Zucker et al. 2017) were retrieved by manual searching from the reference lists and review articles. Eventually, 25 RCT articles were included in the review (Figure 3.10).

All the following consequent details refer to table 3.3 and table 3.4.

3.2.4.2 Study characteristics

Tables 3.3 and Table 3.4 summarised the characteristics of included studies. Combining all of the articles, the 25 studies enrolled a total of 1226 participants, including participants with chronic tension-type headache (Karst et al. 2000), migraine (Wang et al. 2015), neck or shoulder pain (Irnich et al. 2001; Nabeta & Kawakita 2002; He et al. 2004), chronic whiplash-associated disorders (Tobbackx et al. 2012), myofascial pain (Shen & Goddard 2007; Kumnerddee 2009), knee osteoarthritis (Mavrommatis et al. 2012; Plaster et al. 2014), plantar fasciitis (Zhang et al. 2011), fibromyalgia (Targino et al. 2008; Zuker et al. 2017), atopic dermatitis (Kang et al. 2018) and eleven studies (44%) with healthy participants (Barlas et al. 2000; Zaslawski et al. 2003; Hübscher et al. 2008; Li et al. 2008; Lang et al. 2010; Itoh et al. 2011; Schliessbach et al. 2011; Rebhorn et al. 2012;

Schliessbach et al. 2012; Bertrand & Cobbin 2013; Choi et al. 2013), which observed some parameters of pain in healthy participants. According to the ICD-11, the subjects in 13 trials (52%) were classified under the condition of symptoms or signs of the musculoskeletal system. Only Kang and his colleagues (2018) conducted a trial on atopic dermatitis, which was not a musculoskeletal disease. Total sample size in each included study ranged from 15 (Shen & Goddard 2007) to 177 (Irnich et al. 2001) and more female participants were involved than male participants.

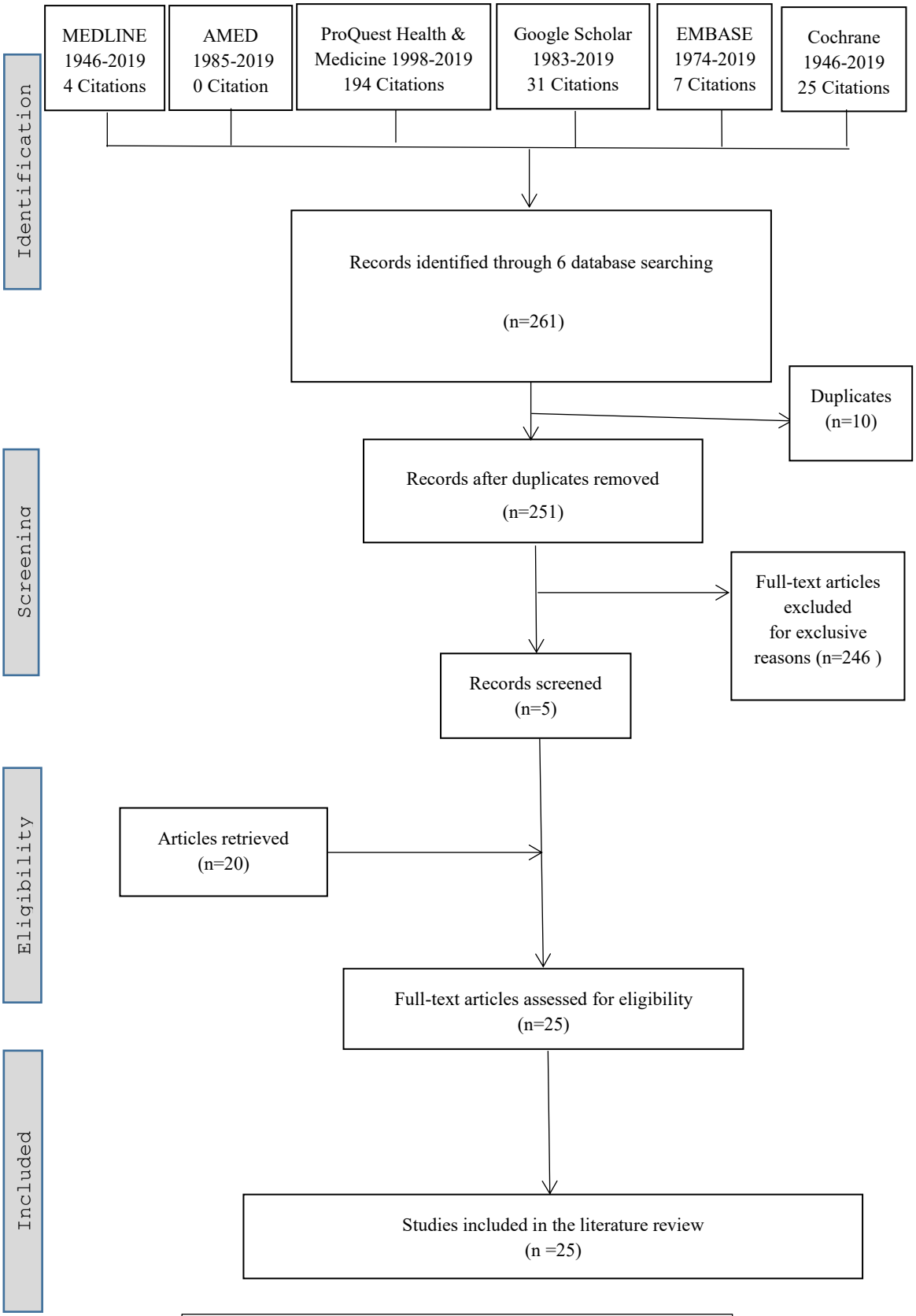


Figure 3.10: Literature review PRISMA flow Chart

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Barlas et al. UK 2000	a placebo-controlled study under blinded (subject) conditions	healthy	48; 24 males, 24 females; (18-40)	(1) control group (20 min rest); (2) placebo group (minimal needling at nonacupuncture points); (3) treatment group 1 (acupuncture at classic acupuncture points), PC 2, CV 11, LU 5, CV 4; (4) treatment group 2 (acupuncture at `tender' points) 5 sessions in one week	elbow range of movement (flexion, extension, relaxed angle), pain (VAS), PPT	no	needles were manually rotated every 5 min, for a period of 15 s per needle on each occasion; rotation took place in an 180° arc at a rate of approximately 2 (alternating) half circles per second (equivalent to a stimulation `cycle' of 1 Hz)	20 min	**9**
Karst et al. Germany 2000	2 arms randomised double-blind (subject and assessor) placebo parallel-controlled trial	chronic TTH	39; (49.0 ± 14.8)	(1) VA; (2) placebo needle GB 20, LI 4, LR 3, GB 8, GB 14, GB 21, GB 41, BL 2, BL 10, BL 60, LU 7, TE 5, ST 8, ST 36, ST 44, GV 20, EXTRA 1 5 weeks, twice a week	pain intensity (VAS); frequency of headache attack; PPT	no	no details	30 min	10

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Irnich et al. Germany 2001	multi-centre, 3 arms randomised, double blinded (patients,observer) placebo parallel-controlled trial	chronic neck pain	177; (18-85)	(1) acupuncture (n=56), SI 3, BL 10, BL 60, LR 3, GB 20, GB 34, TE 5; (2) massage (n=60); (3) sham laser acupuncture (n=61) 5 sessions	maximum pain related to motion (VAS) irrespective of direction of movement; range of motion (3D ultrasound real time motion analyser), pain related to movement in six directions (VAS), PPT, changes of spontaneous pain, motion related pain, global complaints (seven point scale), QOL (SF-36), patients' beliefs	no	no details	30 min	10
Nabeta & Kawakita Japan 2002	2 arms randomised (computerized randomization program) single blind (subject) parallel-controlled trial	neck and shoulder pain and stiffness	34, 10 males, 24 femails; (20-63)	(1) RA (n = 17); (2) SA (n = 17) once a week for 3 weeks	VAS, PPT	yes	sparrow pecking technique (alternate pushing and pulling of the needle five times)	5 min	9

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Zaslawski et al. Australia 2003	4 arms randomised double-blind (subject and assessor) repeated measures trial	healthy	40; (29.9 ± 12.7)	(1) shallow needling of LI 4 with needle manipulation; (2) deep needling of LI 4 without needle manipulation; (3) deep needling of a nonacupoint with needle manipulationl; (4) inactive laser to LI 4	PPT; perceptions of pain; needling sensations; tension; anxiety	yes	needle rotation between the fingers, through a large (540–720◦) angle in a bidirectional manner, first clockwise then anticlockwise. This was repeated nine times, and lasted approximately 5 s. Manipulation was applied every 3 min over a period of 21 min	20 min	10
He et al. Norway 2004	2 arms randomised double-blind (subject and examiner) parallel-controlled trial	neck and shoulder pain	24 female; (20-50)	(1) TG: anti-pain acupoints (n = 14), LI 4, LI 11, GB 31, ExHN, GB 21, BL 12, GV14, SI 15, SI 14 ; (2) CG: placebo-points (n = 10) 10 sessions	intensity of pain, frequency of pain, degree of headache, PPT, blood variables, other treatments in follow-up period	no	rotate every 5 min	30 min	10
Shen & Goddard USA 2007	2 arms single-blind (observer), randomised, parallel-controlled, clinical trial	chronic myofascial pain	15, 1 male, 14 female; (43.1 ± 13.6)	(1) RA (n = 9), LI 4; (2) SA (n = 6)	intensity of pain (NRS), PPT	no	needle was twirled for 5 seconds after 5 minutes into treatment	15 min	9

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Hübscher et al. Germany 2008	prospective, 3 arms randomised (randomization sequence was generated by a computer program (BiAS for Windows 7.0; Department of Mathematics, GoetheUniversity, Frankfort/Mein, Germany) and was retained by the principal investigator until the end of the trial to ensure allocation concealment), parallel-controlled, observer and subject-blinded trial	healthy	22, 10 males, 12 females; (22–30)	(1) RA (n = 7), GB 34, LU 3, LU 5, LI 11, SP 10, *ah shi*; (2) SA (n = 8); (3) control (n = 7)	pain perception (VAS), MPT, PPT, MIVF	yes	no details	15 min	10
Li et al. Australia 2008	4 arms randomised double-blind (subject and evaluator) repeated measures trial	healthy	22, 11 males (28.6 ± 10.8), 11 females; (29.6 ± 8.7)	(1) LI 4 unilaterally; (2) LI 4 bilaterally; (3) LI 11 unilaterally; (4) LI 4 in conjunction with LI 11, both unilaterally	(1) Percentage change in PPT from preintervention baseline measured at the 10 regional sites following every intervention; (2) participants' perceptions of pain; needling sensations; tension during, and anxiety prior to, each intervention; and changes in practitioner behaviour	yes	rotating the needle between the fingers through a large (540—720◦) angle in a bidirectional manner (first clockwise and then anticlockwise) nine times; each manipulation procedure lasted approximately five seconds and was applied every 3 min over a period of 21 min	21 min	10

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Targino et al. Brazil 2008	2 arms randomised single blind (assessor) parallel-controlled trial	fibromyalgia	58 females; (20-70)	(1) acupuncture + tricyclic antidepressants + exercise (n = 34), Ex-HN-3, bilateral LR 3, LI 4, PC 6, GB 34, SP 6; (2) tricyclic antidepressants + exercise (n = 24) 20 sessions	PS (VAS); PPT; QOL (SF-36)	yes	no	20 min	9
Kumnerddee Thailand 2009	2 arms randomised (simple randomization) single blind (measurements) parallel-controlled trial	myofascial back pain	18 males; (20-40)	(1) Thai massage (n = 9); (2) acupuncture (n = 9) 5 sessions, every 2 to 3 days over a 10-day period	PS (McGill, VAS); PPT	no	no details	N/A	9
Lang et al. Germany 2010	3 arms single-blinded (examiner) crossover trial	healthy	24, 12 males, 12 females; (33.1)	(1) MA; (2) LF; (3) HF SP 6, SP 9, ST 36, GB 39	QST (including PPT)	yes	a second stimulation was given midway through the session by rotation of the needle	30 min	9

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Itoh et al. Japan 2011	4 arms randomised (using a computer program (SAMPSIZE V2.0, Blackwell Science, USA), and blocked random-allocation sequence with a block size of four) observer-blinded parallel-controlled trial	healthy	22; 8 male, 14 female; (21.9, 18-28)	(1) control group; (2) skin group (depth of 3 mm: the extensor digital muscle); (3) muscle group (depth of 10 mm: the extensor digital muscle); (4) non-segmental group (depth of 10 mm: the anterior tibial muscle)	PPT & EPT of the skin, fascia and muscle were measured at a point 20 mm distal to the maximum tender point on the second day after the exercise	no	no	30 min	9
Schliessbach et al. Switzerland 2011	3 arms randomised, double blinded (subjects and assessor), placebo-controlled cross-over trial	healthy	45, 22 males (25.7 ± 9.9), 23 females (23.3 ± 2.3); (24.4 ± 7.2)	(1) EA; (2) MA; (3) NPSA LI 4, LI 11	PPT; NRS	yes	rotating the needle in an angle of approximately 180°, both clockwise and anticlockwise, and at the same time lifting and thrusting it 2–3 mm along its vertical axis; This maneuver was performed every 30 seconds during the whole 5 minutes of needling, beginning with LI 4 and followed by LI 11. stimulation of one needle took approximately 5 seconds; results in 10 stimulations per needle and a total of 20 stimulations during the 5 minutes of needling	5 min	10

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Zhang et al. China 2011	2 arms randomised (computer generated random numbers) single-blinded (assessor) parallel-controlled trial	plantar fasciitis	53; (≥18)	(1) treatment group (n = 28), PC 7; (2) control group (n = 25), LI 4 5 times a week for 2 weeks	morning pain (VAS); PPT	yes	slight rotation and thrusting repeated approximately every 5min	30 min	9
Mavrommatis et al. Greece 2012	3-armed, randomised (blocked randomization, computer-generated sequence), single-blind, sham placebo parallel-controlled trial	knee osteoarthritis	120, male 29, female 91; (62.3 ± 9.9)	(1) acupuncture + pharmacological therapy (n = 40); (2) sham acupuncture + pharmacological therapy (n = 40); (3) pharmacological therapy (n = 40) ST 36, SP 9, SP 10, GB 34, Ex-LE 2, Ex-LE 5; LI 4, KI 3, ST 40, SP 6	WOMAC index, WOMAC pain, WOMAC stiffness, WOMAC physical function, VAS; SF-36v2 PCS, SF-36v2 MCS, Algometer PPT	yes	no details	20 min	9
Rebhorn et al. Germany 2012	2 arms randomised, parallel-controlled, double-blinded trial	healthy	50 males; (24.8 ± 2.36, 20-30)	(1) verum acupuncture (n=25): LI 4, HT 7, LI 11, GB 34, LR 3, GV 16, SP 10; (2) sham acupuncture (n=25)	threshold (CDT, WDT, PPT, MPT, CPT, HPT); somatosensory (QST); psychological parameters	no	no details	20-50 min	10

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Schliessbach et al Switzerland 2012	3 arms randomised, double-blind (subject and evaluator) crossover trial	healthy	45, 22 males, 23 females; (24.2 ± 5.7)	(1) acupuncture needling, LI 4; (2) NPSA, LI 4; (3) cold pressor test	pain intensity (NRS); PPT	yes	no details	5 min	10
				(1) acupuncture (n=20); (2) relaxation (n=19)					
Tobbackx et al. Belgium 2012	randomised (sealed envelope) crossover pilot trial with blinded assessors trial	chronic WAD	39, 11 males, 28 females; (23-57, 41 ± 10)	GV 14, Huatuojiaji C1-C7, GB 20, SI 11, GB 21, TE 15, SI 14, BL 17, SP 10, SI 3, BL 64, TE 5, GB 41, Shiqizhuixia, Ear Zero point, Ear Jerome point, Ear C0 point	immediate activation of endogenous analgesia, PPT; disability and pain relief	yes	no details	20 min	9
Bertrand & Cobbin Australia 2013	randomised (stratified randomisation) single blind (subject) within subjects with repeated measures design	healthy	24, 12 males, 12 females ; (18-45)	LI4m+1; LI4m−1; LI4m+21; LI4m−21; NAPm+1; NAPm−1; NAPm+21; NAPm−21	intensities of needling sensation and pain, PPT	yes	rotate the needle for 5 seconds between the thumb and index finger through a large 540–720∘ angle in a bidirectional manner, applied every 3 minutes	21 min	9

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Choi et al. Korea 2013	3 arms randomised (randomisation was done by throwing a dice) single-blinded crossover design trial	healthy	53, 26 males, 27 females; (22.1 ± 2.7)	(1) superficial needling (0.3 cm); (2) deep needling (2 cm); (3) needling with bi-directional rotation SP 6, SP 9, ST 36, GB 39	PPT; acupuncture sensation (VAS, SASS)	yes	rotated 180◦ in a clockwise manner followed by a rotation of 180◦ in an anti-clockwise motion at approximately 1 Hz. This rotation procedure was repeated every minute and carried out five times	5 min	9
Plaster et al. Brazil 2014	randomised double-blind (subject/examiner) parallel-controlled trial	knee osteoarthritis	60; (63, 40-80)	(1) MA (n=30); (2) EA (n=30) LI 4 & LR 3 bilaterally; ST 36, ST 35, SP 10 on the most painful side	Pain intensity; degree of dysfunction (TUG); maximal voluntary isometric contraction; PPT	no	no details	30 min	10
Wang et al. Australia 2015	2 arms randomised (block randomization, 1 : 1 ratio), double-blind (patient and assessor), parallel-controlled trial	migraine	50; (18-80)	(1) RA (n=26), GB 20, EX-HN 5, GB 8, LI 4, GV 20, LR 2, LR 3, KI 3, GB 39, SP 6, GV 23, ST 36, ST 40, CV 12, SP 9, SP 10, Ashi point; (2) SA (n=24) 16 sessions, 20 weeks	days with migraine over four weeks, duration, and intensity of migraine and the number of responders with more than 50% reduction of migraine days; elief medication, quality of migraine, QOL, PPT	yes	needles were inserted transversely, obliquely, or perpendicularly to a depth of 10–30mm depending on the specific locations of acupoints; *deqi* sensation was induced. Needles were retained for 25 minutes, with further stimulation given every 10 minutes	25 min	10

Table 3.3: Acupuncture RCTs using PPT measurement (1)

Study Reference	Study Design	Subject's condition	Subjects n; (age)	Intervention	Outcome measures	*deqi*	Manipulation status	Retention time	PEDro Score
Zucker et al. USA 2017	2 arms randomised single blind (statistician) parallel-controlled	fibromyalgia	114; (48.3 ± 10.2, 24-66)	(1) verum acupuncture (n=59): GV 20, right Ear-Shenmen, left LI 11, right LI 4, left GB 34, left ST 36, left SP 6, and right LR 3; (2) sham acupuncture (n=55): sham points	PS (VAS); needling sensations questionnaire; multiple random staircase method to determine PPT	yes	lifting and thrusting with even rotation (approximately 12 times at 180 degrees clockwise and counterclockwise)	20 min	9
Kang et al. Korea 2018	3 arms randomised (random numbers using the PROC PLAN of SAS 9.2 (SAS Institute Inc., Cary, NC, USA) with a random allocation ratio of the three groups of 1:1:1; random numbers were concealed in opaque envelopes numbered sequentially), sham-controlled double-blinded (statisticians, evaluators, researchers, and participants) preliminary parallel-controlled trial	atopic dermatitis	30; (≥19)	(1) VA1 (n=10), 12 sessions; (2) VA2 (n=10), 8 sessions; (3) SA (n=10) LI 11, ST 36, PC 6 on both sides a 4-week intervention period and a 4-week follow-up	SCORAD, itching and insomnia (VAS), EASI, POEM; DLQI; CES-D, STAXI; BIS, atopic dermatitis pattern questionnaire, cold-heat questionnaire, PPT, credibility test, usage of the rescue medicine, adverse reactions	yes	no details	15 min	10

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Barlas et al. UK 2000	A placebo-controlled study under blinded conditions	Repeated measures and one-way analysis of variance (ANOVA) demonstrated no signi®cant interactive (AB) effects, except for visual analogue scores (P = 0.0483); one factor ANOVA on the second day of the experiment (pretreatment) indicated significant differences between the control and all other groups; however, such differences were not found on any other day of the experiment.	Acupuncture has little effect upon the cardinal signs and symptoms of DOMS, at least under the conditions of the current experiment.	a pressure algometer (Electronic Force Gauge, Salter, West Bromwich, UK), until either the subject reported the sensation to be painful, or the exerted pressure reached 40 N (used as a cut off to avoid bruising)
Karst et al. Germany 2000	Examine the role of muscular mechanisms in chronic tension-type headache	No significant differences between placebo and verum; PPT significantly increased for the verum group.	Peripheral mechanisms - such as increased muscle tenderness - only play a minor role in the pathogenesis of chronic TTH.	algometer (handle with a pressure-sensitive strain gauge situated at the tip and connected to a power supply and an amplifier, tip covered with a probe 0.5 cm2 in area) was held perpendicular to the skin against the temporal region where palpation had shown the anterior part of the temporal muscle to be most prominent (usually 2 cm behind the lateral orbital margin and 2 cm above the temporal line); subjects were instructed to push a button as soon as the pressure became painful. Then the pressure was immediately released; PPTs were expressed in k-pascals

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Irnich et al. Germany 2001	Compare the efficacy of acupuncture and conventional massage for the treatment of chronic neck pain	Acupuncture group showed a significantly greater improvement in motion related pain compared with massage (difference 24.22 (95% confidence interval 16.5 to 31.9), P = 0.0052) but not compared with sham laser (17.28 (10.0 to 24.6), P = 0.327); differences between acupuncture and massage or sham laser were greater in the subgroup who had had pain for longer than 5 years (n = 75) and in patients with MPS (n = 129); the acupuncture group had the best results in most secondary outcome measures; there were no differences in patients' beliefs in treatment.	Acupuncture is an effective short term treatment for patients with chronic neck pain, but there is only limited evidence for long term effects after five treatments.	a digital pressure algometer (kg/cm^2)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Nabeta & Kawakita Japan 2002	Compare the effects of real acupuncture to tender points for neck and shoulder pain and stiffness with those of sham acupuncture.	No statistical difference of VAS scores between acupuncture and sham groups 9 days after the last treatment; however, the acupuncture group showed significant reduction of VAS scores immediately after and/or 1 day after the real acupuncture treatments ($P<0.01$); the effect tended to be prolonged after repeated treatment; PPT tended to increase after real acupuncture treatment but not after sham acupuncture.	Acupuncture applied to tender points appears to have short-term effects on neck and shoulder pain and stiffness, but this study was unable to demonstrate any long-term superiority over sham acupuncture.	a pressure algometer (Yufu-Seiki, F P Meter, with probe of 10 mm)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Zaslawski et al. Australia 2003	Investigate the contribution of two principal features that underlie traditional Chinese acupuncture: site specificity and application of needle manipulation.	Statistically significant increases from preintervention PPT means were obtained at all 10 sites following needling of LI 4 with manipulation compared with one site after needling LI 4 without manipulation. Needling the nonacupoint led to statistically significant increases at six sites when manipulation was present compared with none in the absence of manipulation. No significant changes in mean PPT followed inactive laser. Needling LI 4 with manipulation produced mean increases that were statistically significantly greater than those for the other interventions with one exception: needling the nonacupoint with manipulation was as effective as needling LI 4 with manipulation at one measurement site only.	Both manipulation and site of needling contributed significantly to the elevation of PPT following acupuncture. Distribution of effects on PPT did not support either neural segmental or CM channel theories. Psychological and physiological nonspecific effects appeared to play a minimal role in changes to PPT.	the algometer is a spring loaded pressure gauge attached to a rubber plunger; rate of increase of pressure is kept relatively constant (1 kg/s)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
He et al. Norway 2004	Examine whether acupuncture treatment can reduce chronic neck and shoulder pain and related headache; see whether possible effects were long lasting.	Intensity and frequency of pain fell more for TG than for CG during the treatment period; 3 years after the treatments TG still reported less pain than before the treatments; contrary to what CG, the degree of headache fell during the treatment period for both groups, but more for TG than for CG; 3 years after the treatments the effect still lasted for TG, while the degree of headache for CG was back to the pre-treatment level; PPT of some muscles rose during the treatments for TG and remained higher 6 months after the treatments, which contrasts the situation for CG.	Adequate acupuncture treatment may reduce chronic pain in the neck and shoulders and related headache; the effect lasted for 3 years.	algometry (Algometerw, Somedic production AB, Sollentuna, Sweden) , the probe was placed on the skin above the trigger point and then pressed down with a force increasing at a rate of 30 kPa/s
Shen & Goddard USA 2007	Short-term pain reduction from acupuncture in chronic myofascial pain subjects was evaluated using NRS, VAS, and pain rating of mechanical pressure on the masseter muscle.	There was a statistically significant difference in pain tolerance with acupuncture ($p = 0.027$); there was statistically significant reduction in face pain ($p = 0.003$), neck pain ($p = 0.011$), and headache ($p = 0.015$) with perception of RA.	Pain tolerance in the masticatory muscles increased significantly more with acupuncture than sham acupuncture	a pressure algometer

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Hübscher et al. Germany 2008	Investigate the effects of a standardized acupuncture treatment on symptoms and muscle function in exercise-induced DOMS.	After 72 hours, pain perception (VAS) was significantly lower in the acupuncture group compared to the sham acupuncture and control subjects; MPT and MIVF scores were not significantly different between groups.	Although acupuncture seemed to have no effects on mechanical pain threshold and muscle function, it proved to reduce perceived pain arising from exercise-induced muscle soreness.	a handheld mechanical pressure algometer (manufactured by pdt, Rome, Italy); pressure was applied to each of these points with increasing force at a rate of approximately 1 $kg/cm^2/s$ through the head of the algometer (1-cm diameter) until the subject reported a painful sensation
Li et al. Australia 2008	Compare the effects of unilateral and bilateral needling of the same acupoint, and the effects of individual and combined needling of two distinct acupoints on (PPT).	PPT statistically significant increases ($p < 0.02$ and $p < 0.0001$).	The enhanced effects on PPT by the bilateral compared with the unilateral intervention at LI 4 although limited, do provide some support for the CM assumption that bilateral needling of the same point enhances the treatment effect. There was no support for the assumption that combined needling of points from the same channel should enhance the treatment effect and failure to obtain better effects by combined needling of points from the same channel could result from the interaction occurring during the combined needling.	a simple spring loaded pressure (force) gauge with a rubber plunger; the operator holds the algometer vertically against the skin of the subject and pressure is applied gradually until the subject perceives and reports the initial pressure change to a distinct sensation of discomfort or pain, defined as the PPT

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Targino et al. Brazil 2008	Evaluate the effectiveness of acupuncture for fibromyalgia.	At the end of 20 sessions, patients who received acupuncture were significantly better than the control group in all measures of pain and in 5 of the SF-36 subscales; after 6 months, the acupuncture group was significantly better than the control group in numbers of tender points, PPT at the 18 tender points and 3 subscales of SF-36; after one year, the acupuncture group showed significance in one subscale of the SF-36; at 2 years there were no significant differences in any outcome measures.	Addition of acupuncture to usual treatments for fibromyalgia may be beneficial for pain and QOL for 3 months after the end of treatment; future research is needed to evaluate the specific effects of acupuncture for fibromyalgia	a pressure algometry (Pain Diagnostics, Great Neck) expressed in kgf /cm^2

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Kumnerddee Thailand 2009	Provide preliminary data of comparative effectiveness of TTM and Chinese acupuncture for the treatment of myofascial back pain in young military personnel.	McGill scores decreased significantly in TTM and acupuncture groups ($p = 0.024$ and 0.002, respectively); VAS also decreased significantly ($p = 0.029$ and 0.003, respectively). However, PPT increased significantly in the acupuncture group but not in the TTM group ($p = 0.006$ and 0.08, respectively); when outcomes were compared between the two groups, no significant difference was found in the VAS ($p = 0.115$) and pain pressure threshold ($p = 0.116$), whereas the acupuncture group showed significantly lower McGill scores than the TTM group ($p = 0.039$).	5 sessions of Thai traditional massage and acupuncture were effective in the treatment of myofascial back pain in young Thai military personnel. Significant effects in both groups began after the first session; acupuncture was more effective than Thai traditional massage when affective aspects were also evaluated.	a pressure algometer, the minimal pressure required to produce pain at each point was summarized and recorded in kg

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Lang et al. Germany 2010	Evaluated the immediate effects of different types of acupuncture on thermal, mechanical, and vibratory sensory thresholds.	HPT was increased after MA on the treated and untreated side compared with baseline; low- and high-frequency EA led to a higher MPT on the treated side compared with baseline and manual acupuncture; PPT was increased by all forms of acupuncture on both sides, with individual changes from baseline ranging from 25% to 52%.	There were congruent changes on QST after 3 common acupuncture stimulation methods, with possible unilateral as well as bilateral effects.	a pressure algometer (FDK20, Wagner Instruments, Greenwich, CT) with a range between 2 and 20 kg, the algometer had a rubber tip with a contact area of 1 cm^2; the algometer was pressed to the skin with an increasing ramp of 0.5 kg/s, and the patient was asked to respond verbally as soon as the pressure became painful. This procedure was performed 3 times
Itoh et al. Japan 2011	Determine the effects of depth of needle penetration on muscle pain.	PPT of skin group (depth of 3 mm: the extensor digital muscle) and muscle group (depth of 10 mm: the extensor digital muscle) were significantly higher than the control group, the EPT at fascia of muscle group (depth of 10 mm: the extensor digital muscle) was a significantly higher than control group; no significant difference between the control and other groups.	Acupuncture stimulation of muscle increases the PPT and EPT of fascia. The depth of needle penetration is important for the relief of muscle pain.	a finger type pressure algometer (a probe of 6 mm in diameter)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Schliessbach et al. Switzerland 2011	Investigates effects of brief manual and electrical acupuncture stimulation on PPT compared with NPSA.	PPT rose from 316 kPa (standard deviation [SD] 149) to 398 kPa (SD 157) and 405 kPa (SD184) immediately after acupuncture with manual and electrical stimulation, respectively, and to 380 kPa (SD 175) and 367 kPa (SD 168) after NPSA with simulated manual and electrical stimulation, respectively. During the intervention, EA produced a higher PPT increase than any other procedure ($P< 0.001$). Immediately after, both acupuncture procedures were significantly more effective than NPSA ($P< 0.001$) but did not mutually differ ($P= 0.082$). NRS ratings differed significantly: MA 4.1, EA 2.7, manual NPSA2.5, electro-NPSA 1.2 ($P< 0.001$ except for electroacupuncture vs manual NPSA, $P= 0.271$).	EA produced higher PPT elevation than MA; acupuncture in general showed significantly greater analgesic effect than NPSA; these effects seem to be short lasting (<5 minutes) in the context of only brief acupuncture; the superiority of acupuncture to NPSA provides further evidence for acupuncture-specific analgesic effects	an electronic algometer (Somedic AB, Horby, Sweden) with a probe area of 1 cm^2; pressure was increased from 0 to 1,000 kPa at a rate of 30 kPa/s, until the subject perceived the stimulus as painful

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Zhang et al. China 2011	Determine the efficacy and specificity of acupuncture treatment for plantar fasciitis.	Significant differences in reduction in pain scores, favoring the treatment group, were seen at one month for morning pain (22.6 ± 4.0 versus 12.0 ± 3.0, mean ± SEM), overall pain (20.3 ± 3.7 versus 9.5 ± 3.6) andPPT (145.5 ± 32.9 versus −15.5 ± 39.4)	Acupuncture can provide pain relief to patient with plantar fasciitis, and that PC 7 is a relatively specific acupoint for heel pain	an electronic algometer (SOMEDIC, Sweden)
Mavrommatis et al. Greece 2012	Compared acupuncture combined with pharmacological treatment, sham acupuncture including pharmacological treatment, and pharmacological treatment alone in patients with chronic pain due to osteoarthritis of the knee.	Group (1) exhibited statistically significant improvements in primary and secondary outcome measures, except for Short Form mental component, compared with the other treatment groups.	Acupuncture with etoricoxib is more effective than sham acupuncture with etoricoxib, or etoricoxib alone for the treatment of knee osteoarthritis	a Pain Test FDK 20 Algometer of Warner USA

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Rebhorn et al. Germany 2012	Get evidence for acupuncture analgesia	A significant (P = 0.009) but clinically questionable pain reduction in the verum group for capsaicin-induced pain, which was mainly driven by an effect of CM acupuncture on small pain ratings (max. reduction from 7/100 rating at baseline to 2.5/100 at intervention). Neither pin-prick hyperalgesia, nor allodynia, nor neurogenic flare associated with capsaicin injection, nor pain ratings during the CP test, were significantly different between groups. In addition, there was no placebo response. Attitude towards acupuncture and partial unblinding did not affect the results.	Acupuncture on predefined points has a minor effect on experimental pain in healthy subjects	a handheld blunt pressure gauge device (1-cm^2 contact area) (FDN200; Wagner Instruments, Greenwich, CT, USA)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Schliessbach et al. Switzerland 2012	Investigated the analgesic effect of acupuncture without stimulation compared to NPSA and cold-pressor-induced DNIC	PPT rose from 299 kPa (SD 112 kPa) to 364 kPa (SD 144), 353 kPa (SD 135), and 467 kPa (SD 168) after acupuncture, NPSA, and DNIC test, respectively. There was no statistically significant difference between acupuncture and NPSA at any time, but a significantly higher increase of PPT in the DNIC test compared to acupuncture and NPSA. PPT decreased after the DNIC test, whereas it remained stable after acupuncture and NPSA. Acupuncture needling at low pain stimulus intensity showed a small analgesic effect which did not significantly differ from placebo response and was significantly less than a DNIC-like effectofa painful noninvasive stimulus.	Acupuncture at low pain stimulus intensity did not produce a DNIC-like effect comparable to a classical, painful DNIC test and its effect did not significantly differ from the one induced by NPSA; the penetration of an acupuncture needle by itself, though noxious, seems not to induce an analgesic effect mainly mediated by DNIC.	an electronic algometer (Somedic AB, Horby, Sweden) with a probe area of 1 cm^2 was used. Pressure was increased from 0 to a maximum of 1000 kPa at a rate of 30 kPa/s

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Tobbackx et al. Belgium 2012	Examine whether acupuncture results in activation of endogenous analgesia and relief in symptoms in patients with chronic WAD	Local pressure pain sensitivity at baseline and during conditioned pain modulation decreased significantly more following acupuncture compared with relaxation (time ¥ group interactions: $p < 0.001$), both in the neck and at a site distinct from the painful region; when comparing the effects of acupuncture versus relaxation, no differences were observed on conditioned pain modulation, temporal summation of pressure pain, neck disability or symptom severity (all p-values >0.05).	Acupuncture treatment activates endogenous analgesia in patients with chronic WAD.	an analogue Fisher algometer (Force Dial model FDK 40 Push Pull Force Gage, Wagner Instruments, Greenwich, CT, USA) pressure was gradually increased at a rate of 1 kg/s until the subject reported first onset of pain (the subject said 'stop' at that point); PPT was taken as the mean of two consecutive (30 s in between) measurements

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Bertrand & Cobbin Australia 2013	Examine the effects of needling parameters on *deqi*'s intensity	Immediately after needle insertion, similar levels ofmean needle sensation and of pain were reported independent of intervention; at subsequent measurement times, only 2 interventions (one at LI4 and one at NAP) maintained statistically significantly elevated needle sensation and pain scores and reported higher numbers of needle sensation descriptors; for both, the needle was retained for 21 minutes and manipulated every 3 min; neither intervention differed significantly in terms of levels of pain, and needle sensation or numbers and qualities of needle sensation described.	Initial needling for all eight interventions elicited similar levels of needle sensation and pain; these levels were only maintained if there was ongoing of needle manipulation and retention of the needle; the strength of needle sensation or pain experienced was independent of insertion site.	an algometer

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Choi et al. Korea 2013	Investigated the relationship between acupuncture sensation and analgesic effect according to acupuncture manipulation	Both total acupuncture sensation and increase of the PPT were maximum in needling with rotation, followed by deep needling and superficial needling; both showed significant difference ($p = 0.000$, 0.003); needling with rotation showed significant difference from both superficial needling and deep needling; there was a significant correlation ($p = 0.002$, $p = 0.013$) between the total acupuncture sensation and changes in pressure pain threshold.	Acupuncture sensation and PPT increase according to the depth and rotation of acupuncture; both display significant increase with needle rotation; a significant correlation between acupuncture needling sensation and increase in pressure pain threshold; needle rotation and acupuncture sensation play an important role in verifying the effect of acupuncture.	a PD&T pressure algometer within a range between 2 and 20 kg
Plaster et al. Brazil 2014	Compare the immediate effects of EA and MA on pain, mobility and muscle strength in patients with knee osteoarthriti	Both groups showed a significant reduction in pain intensity ($p < 0.001$) and time to run the TUG test after the acupuncture treatment ($p = 0.005$ for the MA group and $p = 0.002$ for the EA group). There were no differences between the groups regarding pain intensity ($p = 0.25$), TUG test ($p = 0.70$), maximum voluntary isometric contraction ($p = 0.43$) or PPT ($p = 0.27$).	No difference between the immediate effects of a single session of MA and EA on pain, muscle strength and mobility in patients with knee osteoarthritis.	a pressure algometer (Somedic AB, Sweden); perpendicular to the skin and pressed at a rate of approximately 30 kPa/s

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Wang et al. Australia 2015	Evaluate the efficacy and safety of manual acupuncture as a prophylaxis for frequent migraine	Compared with the SA group, the RA group reported significant less migraine days (RA: 5.2 ± 5.0; SA: 10.1 ± 7.1; P = 0.008), less severe migraine (RA: 2.18 ± 1.05; SA: 2.93 ± 0.61; P = 0.004), more responders (RA: 19 versus SA: 7), and increased pressure pain thresholds; no other group difference was found; group differences were maintained at the end of the three-month follow-up, but not at the one-year follow-up.	MA was an effective and safe treatment for short-term relief of frequent migraine in adults; larger trials are warranted	handheld pressure algometer (Wagner, Electronic Engineering Corporation of India); the apparatus consists of a 1 cm in diameter hard rubber tip, attached to the plunger of a pressure (force) gauge; the dial of the gauge is calibrated in kg/cm^2
Zucker et al. USA 2017	Hypothesis that pressure pain tenderness would differentially classify treatment response to verum and sham acupuncture in fibromyalgia patients	Participants who had higher pain pressure thresholds had greater reduction in clinical pain following verum acupuncture while participants who had lower pain pressure thresholds showed better analgesic response to sham acupuncture; patients with lower pressure pain thresholds had exacerbated clinical pain following verum acupuncture. Similar relationships were observed for sensitivity to acupuncture needling.	Acupuncture efficacy in fibromyalgia may be underestimated and a more personalized treatment for fibromyalgia may also be possible	stimulus intensities (in kg/cm^2)

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
Kang et al. Korea 2018	Assess the feasibility of a definitive trial investigating the effects of acupuncture on atopic dermatitis symptoms including itching	SCORAD, VAS (Pruritus), VAS (Insomnia), POEM, DLQI, and EASI were significantly improved in the VA groups; significant BIS mean differences were observed most predominantly in epigastric tenderness and dyspepsia; there was no significant difference between VA1 and VA2 groups in all the main evaluation indices.	Suggest SCORAD (Total) as primary outcome and SCORAD (objective), VAS (Itch), VAS (insomnia), EASI, POEM, and DLQI as secondary outcomes; necessary to compare the differences of general symptoms according to presence of epigastric tenderness or dyspepsia at the screening level.	algometer (Wagner Instruments, Greenwich, CT)

Abbreviations in Table 3.3 and Table 3.4:

BIS: baseline index score
CDT: cold detection threshold
CES-D: Centre for Epidemiologic Studies-Depression Scale
CG: control group
CPT: cold pain threshold
DLQI: Dermatology Life Quality Index
DOMS: delayed-onset muscle soreness
DNIC: diffuse noxious inhibitory controls
EA: electroacupuncture
EASI: Eczema Area and Severity Index
EPT: electrical pain threshold
HF: acupuncture with high-frequency electrical stimulation
HPT: heat pain threshold
LF: acupuncture with low-frequency electrical stimulation
MPT: mechanical pain threshold
NAP: nonacupoint
NDI: neck disability index
NHP: Nottingham health profile
NPSA: nonpenetrating sham acupuncture
NRS: numeric rating scale
POEM: Patient Oriented Eczema Measure
PPT: pressure pain threshold
PS: pain scores
QOL: quality of life
QST: Quantitative sensory testing
RA: real acupuncture
SA: sham acupuncture
SASS: Subjective Acupuncture Sensation Scale
STAXI: State-Trait Anger Expression Inventory
TG: test group
TTH: tension-type headache
TTM: Thai traditional massage
TUG: Timed Up and Go test
VA: verum acupuncture
VAS: visual analog scales
WAD: whiplash-associated disorders
WDT: warm detection threshold
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Table 3.4: Acupuncture RCTs using PPT measurement (2)

Study Reference	Purpose	Reported results	Conclusions	Equipment & operation
MA: manual acupuncture MPS: myofascial pain syndrome MIVF: maximum isometric voluntary force			SCORAD: SCORing Atopic Dermatitis SF-36v2 MCS: Short Form 36 version 2 health survey, mental component SF-36v2 PCS: Short Form-36 version 2 health survey, physical component	

Of these articles, five studies were conducted by German researchers (Karst et al. 2000; Irnich et al. 2001; Hübscher et al. 2008; Lang et al. 2010; Rebhorn et al. 2012), while four were in Australia (Zaslawski et al. 2003; Li et al. 2008; Bertrand & Cobbin 2013; Wang et al. 2015). There were two articles of PPT applied in conventional acupuncture RCTs published respectively in Brazil (Targino et al. 2008; Plaster et al. 2014), Switzerland (Schliessbach et al. 2011; Schliessbach et al. 2012), USA (Shen & Goddard 2007; Zuker et al. 2017), Japan (Nabeta & Kawakita 2002; Itoh et al. 2011) and Korea (Choi et al. 2013; Kang et al. 2018). There was only one acupuncture RCT of PPT in the following countries: Thailand (Kumnerddee 2009), China (Zhang et al. 2011), Belgium (Tobbackx et al. 2012), UK (Barlas et al. 2000), Norway (He et al. 2004) and Greece (Mavrommatis et al. 2012).

Regarding to the intervention comparison, conventional manual acupuncture needling was compared to: placebo, sham needling, sham laser or control (Barlas et al. 2000; Karst et al. 2000; Irnich et al. 2001; Nabeta & Kawakita 2002; He et al. 2004; Shen & Goddard 2007; Hübscher et al; Schliessbach et al. 2011; Rebhorn et al. 2012; Schliessbach et al. 2012; Wang et al. 2015; Kang et al. 2018), massage (Irnich et al. 2001; Kumnerddee 2009), pharmacological therapy or exercise (Targino et al. 2008; Mavrommatis et al.2012), electroacupuncture (Lang et al. 2010; Schliessbach et al. 2011; Plaster et al. 2014), cold pressor test (Schliessbach et al. 2012) and relaxation (Tobbackx et al. 2012). Moreover, in five studies, the location of acupuncture points (Zhang et al. 2011; Bertrand & Cobbin 2013), depth of insertion and manipulation (Zaslawski et al. 2003; Itoh et al. 2011; Choi et al. 2013) were also compared.

According to the outcome measures, PPT was the primary outcome in fourteen studies (Barlas et al. 2000; Nabeta & Kawakita 2002; Zaslawski et al. 2003; He et al. 2004; Shen & Goddard 2007; Hübscher et al. 2008; Li et al. 2008; Lang et al. 2010; Itoh et al. 2011; Schliessbach et al. 2011; Rebhorn et al. 2012; Tobbackx et al. 2012; Bertrand & Cobbin 2013; Choi et al. 2013). The other eleven trials employed PPT as a secondary outcome (Karst et al. 2000; Irnich et al. 2001; Targino et al. 2008; Kumnerddee 2009; Zhang et al. 2011; Mavrommatis et al. 2012; Schliessbach et al. 2012; Plaster et al. 2014; Wang et al. 2015; Zuker et al. 2017; Kang et al. 2018). In addition, pain intensity was the primary outcome in most of studies (Table 3.3).

3.2.4.3 Quality of included literature

All 25 published papers were RCTs. The quality of the 25 articles was assessed with the PEDro scale (Moseley et al. 2002) (Appendix 1). All articles had a high score demonstrating good methodological quality. Twelve articles were assessed as a score of 10 and thirteen were evaluated as a score of 9. The blinding of subjects and the researcher administering the interventions were the most common criteria not met. This is partially due to the face-to-face delivery style of the intervention making it difficult to blind the person providing and receiving the acupuncture. As all included RCTs were conventional acupuncture intervention experiments, the acupuncturists were not applicable as blinded therapists who administered the therapy for these studies. Thus, no articles could be assessed as reaching the maximum score of 11 because of the criterion number 6 (see Appendix 1). Twelve trials were double blind (subject and assessor) reached a score of 10 while thirteen studies conducted as single blind designed obtained scores of 9.

As these 25 studies were published after 2000, all trials attained the approval of human research ethic committee. Twenty-four of these trials were conducted at a single site. Only one study was multi-centre research.

3.2.4.4 *Deqi*

Among the studies, 16 (64%) indicated the elicitation of *deqi* (Nabeta & Kawakita 2002; Zaslawski et al. 2003; Hübscher et al. 2008; Li et al. 2008; Targino et al. 2008; Lang et al. 2010; Schliessbach et al. 2011; Zhang et al. 2011; Mavrommatis et al. 2012; Schliessbach et al. 2012; Tobbackx et al. 2012; Bertrand & Cobbin 2013; Choi et al. 2013; Wang et al. 2015; Zucker et al. 2017; Kang et al. 2018) as a successful mark of treatment. However, 9 trials (36%) did not document *deqi* sensation (Barlas et al. 2000; Karst et al. 2000; Irnich et al. 2001; He et al. 2004; Shen & Goddard 2007; Kumnerddee 2009; Itoh et al. 2011; Rebhorn et al. 2012; Plaster et al. 2014). No study concerned the measurement of the *deqi* sensation during acupuncture.

3.2.4.5 Acupuncture manipulation

There were 13 trials (52%) that did not describe the needling manipulation in their study protocols while 12 acupuncture RCTs (48%) did record the details of acupuncture manipulation during their treatment (Table 3.3). The acupuncture researchers applied needle rotation or twirling manipulation during the interventions in 9 studies (36%).

There were 2 studies (8%) that adopted manipulation of lifting and thrusting with rotation. Only one Japanese study used a sparrow pecking technique (alternate pushing and pulling of the needle five times) (Nabeta & Kawakita 2002).

3.2.4.6 Needle retention time

Of the 25 RCTs, only one trial from Thailand did not mention the needling retention time in their study (Kumnerddee 2009). Two acupuncture experiments in healthy participants conducted by Schliessbach and his colleagues designated 5 minutes of needle retention, while the retention time of the other 22 RCTs (88%) ranged between 15 minutes to 30 minutes (refer to Table 3.3).

3.2.4.7 Analgesic effect

Regarding the DNIC-like effect, Schliessbachand and his colleagues (2012) found that the penetration of an acupuncture needle did not induce an analgesic effect mainly mediated by DNIC. Three articles (12%) reported minor effects of manual acupuncture (Barlas et al. 2000; Karst et al. 2000; Rebhorn et al. 2012). Twenty one of the 25 RCTs (84%) demonstrated the significant efficacy of acupuncture in eliciting analgesia (refer to Table 3.4). The intensity of pain in VAS or NRS and the frequency of pain were evaluated in all 25 studies.

3.2.4.8 Algometry

All the articles in this review concerned PPT using an algometer. The algometer is an essential equipment for the outcome measurement, however, not all the study papers detailed the algometer used in the study.

Four trials applied electronic algometer (Barlas et al. 2000; Schliessbach et al. 2011; Zhang et al. 2011; Schliessbach et al. 2012) while one study employed a digital pressure algometer (Irnich et al. 2001). It was supposed that the simple handheld mechanical pressure algometer was used in other studies (refer to Table 3.4). Most of the algometers used in the 25 trials were made in USA and Sweden, with only a few from UK, Japan and Italy (refer to Table 3.4).

To summarise the description of the algometer in the RCTs, it is a handheld mechanical pressure algometer with a pressure-sensitive spring loaded strain gauge situated at the tip and connected to a power supply and an amplifier. The tip is covered with a rubber blunt probe 0.5 cm^2 in area. The operator holds the algometer “vertically against the skin of the

subject and pressure is applied gradually until the subject perceives and reports the initial pressure change as a distinct sensation of discomfort or pain" (Li et al. 208).

3.2.5 Discussion

Algometry has been used to measure pain with reliable results (Kinser et al. 2009; Escalona-Marfil et al. 2020). This systematic review summarised 25 high quality conventional acupuncture RCTs that utilised PPT measures. Acupuncture researchers in non-Asian countries have paid more attention to PPT in their study design compared to Asian based researchers.

PPT has been used in a range of studies on musculoskeletal disease, such as chronic tension-type headache, migraine, neck or shoulder pain, chronic whiplash-associated disorders, plantar fasciitis, myofascial pain, knee osteoarthritis, fibromyalgia, even for the measurement of epigastric tenderness in atopic dermatitis. Furthermore, PPT can be applied in the healthy human experimental study on pain in the acupuncture research.

Only one trial was a multi-centre study. The majority of the RCTs in this review were conducted using small sample sizes. The manual acupuncture was an effective intervention for pain modulation. However, in terms of the diversity of needling retention time, manipulation status, measurement site and presence of *deqi*, it remains unclear which parameter actually affects the change observed for PPT.

3.2.6 Conclusion

PPT is a commonly used approach in manual therapies and other research areas. However, it has not been employed in acupuncture studies comprehensively. In addition, the relationship between PPT and some relevant parameters in the acupuncture study on pain has only been explored occasionally. More high quality studies that utilise PPT measures are needed for acupuncture randomised control trials.

Chapter 4: Methods: a protocol for a randomised controlled study

4.1 Study design

The current study is a prospective crossover design with repeat measures. The study involved three different interventions: (a) needling SI 3 with manipulation ($SI3m^{+}$), (b) needling SI 3 without manipulation ($SI3m^{-}$) and (c) Sham Laser (SL). All participants received all three interventions in a randomly ordered sequence from a random number table using an envelope method that was stratified by gender (Sjölund & Persson 2007; Chesterton et al. 2003) to match as closely as possible the sequence. Each sequence was printed on a slip of paper and sealed into an individual envelope marked F (female) or M (male). Prior to commencing the first session, the subjects chose one of the available envelopes and this determined their unique sequence of interventions. Each subject completed the three intervention sessions with a duration of at least one-week washout period between each intervention session (Strudwick et al. 2007). The three interventions were renamed for the individual session recording sheets (rose, tulip and daisy) so that only the acupuncturist administering the interventions knew the actual intervention the subject received. This allowed blinding of the researcher taking the PPT measures and the person analysing the data at the completion of the study. The study workflow can be seen below in Figure 4.1.

This document has been prepared in accordance with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 (Chan et al. 2013) (see Appendix 2) and follows the principles of the CONSORT and STRICTA (MacPherson et al. 2010).

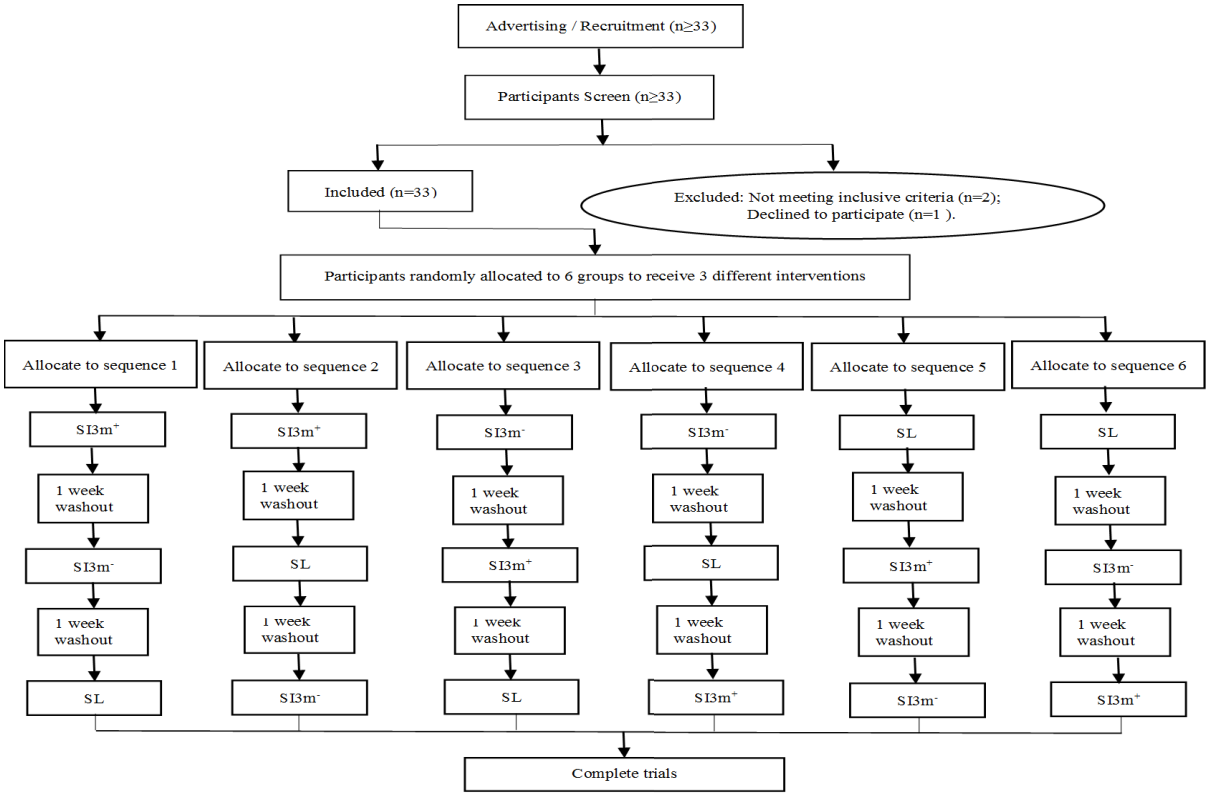


Figure 4.1: Study schedule: 33 eligible participants will be randomly allocated into six sequences with a 1:1:1:1:1:1 ratio. Assessments will be performed immediately before and after each treatment. Wash-out period between interventions is at least one week. $SI3m^{+}$, SI 3 with manipulation; $SI3m^{-}$, SI 3 without manipulation; SL, sham laser acupuncture.

4.2 Protocol Version

The protocol used in the study is identified as Issue date: 4th. October 2018 Version 3

4.3 Research team roles and responsibilities

See Appendix 3.

4.4 Background and rationale

4.4.1 Mechanisms

There are two plausible explanations on how SI 3 treat pain symptoms in Chinese Medicine according to the classic and modern textbooks. Please refer to Section 2.9.

In modern electro-acupuncture treatment, SI 3 was selected due to its location along nerves innervating affected muscle group in some diseases (Shanghai College of Traditional Medicine 1992). This neural modulation might play a role in relaxing the muscle channels.

Several neurological explanations have revealed the mechanism of acupuncture partially. Some scientists interpreted the qi as the electrical depolarization or energy in Channels, which are actually nerve fibres (Mann 1983), (Mann 1992). Needling at specific acupoints, which are the nerve endings, triggers neurotransmission to the cortical area of the brain. It has been believed that the endocrine and autonomic nervous systems are activated by these cortical activities (Cho et al. 2000) and subsequently stimulate and facilitate the healing process of the body (Mann 1983), (Mann 1992).

4.4.2 Existing knowledge

According to both ancient and modern textbooks, SI 3 is indicated for the treatment of pain-related conditions at different parts of the body (head, shoulder, lower back, neck, hands and feet) indicating that SI 3 may have a general analgesic effect.

4.4.3 Need for a trial

Even though traditional and modern textbooks mentioned the use of SI 3 for pain-related conditions, no studies have been conducted to date to investigate the effects of SI 3 on PPT. Among 57 clinical trials reviewed, no study used SI 3 as a sole acupoint. All the studies used SI 3 in combination with other acupuncture points. It is thus difficult to determine the specific effects of SI 3 for the range of conditions treated. There is thus the

need to investigate the specific effect of SI 3 as a sole acupuncture point. As most classical and modern textbooks mentioned the use of SI 3 for a range of musculoskeletal conditions, this project will investigate the effects of SI 3 on PPT. Furthermore, none of the studies measured *deqi*. This study will also measure if *deqi* as experienced, both qualitatively and quantitatively, when SI 3 is needled.

4.4.4 Explanation for the choice of comparators

Since this study aims to investigate a single acupuncture point, that of SI 3 instead of different therapies for a certain condition, therefore an active control is not needed. To date, the acupuncture treatment has not been shown beyond a doubt to be superior to placebo due to the selection of quality control. Although the first description of the location of SI 3 was in the Ling Shu as a site on the surface of the body (Unschuld 2016), the Yellow Emperor's Classic of Medicine also recorded the "needling depth in acupuncture" (Ni 1995, p. 186), which meant the acupoint is a three-dimensional structure. In addition, the complicated network of channels and collaterals, which comprise of twelve main channels, luo collaterals, small collaterals, superficial collaterals, twelve divergent channels, the fifteen divergent collaterals and dermatomes of the channels (Ni 1995), means that the choice of a non-acupoint or the use of minimally inserted acupuncture as a placebo comparator could result in confounding the study outcome. Therefore, the sham laser control, was selected as a suitable control.

According to traditional Chinese acupuncture, needle manipulation techniques should be appropriate for treating pain syndromes (Auteroche et al. 1992). Thus, the acupuncture point SI 3 with standardised manipulation or without manipulation, were selected as comparator interventions.

4.5 Study setting

The study site setting was the University of Technology Sydney (UTS) Chinese Medicine Clinic, at the UTS City Campus, CB04, Level 2 (Street level, Harris Street). The clinic is a teaching facility where students of Chinese Medicine treat patients under supervision and where academic research may be conducted. There are four separate treatment rooms with 4 treatment couches within each room. Each couch has a full-length curtain that can be drawn for patient privacy. Each room has a sliding door that may be closed for further privacy. The clinic is air-conditioned to ensure a standard temperature. Each treatment

room has a sink for hand washing. There are chairs with arms available for seated treatments. The clinic also has two consultation rooms that were used for confidential conversations such as recruitment interviewing and completion of outcome measurement forms.

4.6 Participants

For the present trial, all potential healthy participants matching the eligible criteria underwent a face-to-face screening interview including Trial Entry Assessment and Health Evaluation. The individual who administered the acupuncture interventions and sham laser was a qualified acupuncturist with over 35-years clinical practice.

4.7 Sample size

Sample size was calculated using GPower version 3.1.9.2 (a free downloaded software). The significance level was fixed at 0.05 by convention and the power was fixed between 0.8 and 0.95 by convention. For this cross-over trial, it had been determined prospectively that $\alpha = 0.05$ and $1-\beta = 0.80$, and one tail test according to the previous studies (Loyeung 2013; Zaslawski 2006), we anticipated that effect size is 0.5. Thus, 27 participants were required. To compensate for a potential of 20% dropout, it was planned to enroll 33 participants in the study.

4.8 Recruitment

Recruitment strategies aimed to achieve adequate participant enrolment to reach target sample size. Applicants were screened and recruited until the target sample size of 32 participants was achieved. Since 31 participant's the data have been collected completely, the 33$^{rd.}$ participant was not recruited. The enrolment period was four months in duration.

Recruitment commenced in November 2018 after the UTS Human Research Ethics Committee (HREC) had given approval. An Information Sheet which included a description of the study and an outline of each participant's involvement (tests, intervention and questionnaires), the recruitment period and researchers' contact details had been prepared. Advertising for participants occurred through flyers around the university and through staff notices and social media. Individuals (not necessarily UTS

students) known to the PhD student were approached on occasions and could be perceived as convenience recruiting. An email using information from the Information Sheet (Appendix 4) was circulated to all UTS students, staff and UTS sporting clubs. An A4 UTS Science poster based on the information sheet was posted on noticeboards throughout the University (see Appendix 5). Information sheets were available at the UTS Chinese Medicine Clinic.

Those interested contacted the research student by email or telephone. The Project Information Sheet and the Consent Form (Appendix 4) was sent to the interested individual if they still expressed interest after the initial contact.

4.9 Eligibility criteria

Participants provided written, informed consent before any study procedures occurred (see Appendix 4 for Informed Consent Form)

4.9.1 Inclusion criteria

Patients eligible for the trial complied with all of the following inclusion requirements at randomization: (1) healthy pain-free volunteers regardless ethnic background (Kim et al. 2017); (2) age 18-70 years old (both male and female participants); (3) right-handedness; (4) no medical history of chronic musculoskeletal disorder; (5) no diagnosis of pain caused by any diseases in the seven days before study entry; (6) non-smokers; (7) acupuncture practitioners and students of acupuncture were not excluded; (8) willingness to give written informed consent and willingness to participate and comply with the study.

4.9.2 Exclusion criteria

Participants matching any of the following items were excluded: (1) depression or sleep disorders, complications of severe systemic diseases, such as cardio or cerebrovascular diseases, diabetes, kidney diseases, central or peripheral nervous system or digestive system diseases; (2) regular use of analgesic or other drugs (that may dampen pain perception); (3) haemophilia and use of anticoagulant medication (that may interfere with blood clotting); (4) chronic consumers of sedatives, especially benzodiazepine or antidepressants (inhibiting the reuptake of serotonin, will not be enrolled in the study for the possible interference of the drugs on acupuncture action mechanisms); (5) pregnancy or menses; (6) alcohol abuse and/or drug abuse; (7) people highly dependent on medical

care; (8) people with a cognitive impairment, an intellectual disability or a mental illness; (9) needle phobia; (10) allergy to metal; (11) any type of acupuncture, massage, cupping, guasha or physio intervention used in the seven days before study entry; (12) enrolled in other investigational studies.

From previous studies, it is known that there are individual differences in pain threshold. The most frequently mentioned differences are gender differences, age differences and psychological and physiological states. Therefore, the eligibility criteria were chosen according to the following influencing factors of PPT measurement:

- Age: Lautenbacher et al. investigated 20 young (mean age 27.1 years) and 20 elderly (mean age 71.6 years) subjects. Their results confirmed and extended previous findings by showing that pressure pain thresholds decrease with age (Lautenbacher et al. 2005). Therefore, subjects' ages should be consistent as far as possible in order to make PPT measurements comparable.
- In order to produce reliable results and to minimize variation, handedness should be standardized (Brennum et al. 1989).
- Psychological and physiological state: The pain threshold is closely related to the psychological and physiological state of the subject. In a large sample (424 subjects) clinical trial, Chiu et al. found that poor sleep and depression were independently associated with a reduced PPT (Chiu et al. 2005). Another study submitted for publication in 2003 also shed a new light on the relationship between PPT sensitivity and distress (Giesecke et al. 2003). Therefore, psychological factors have a great influence on the measurement of pain threshold. Additionally, in some physiological states, the pain threshold also changes. The digital algometer was performed to measure PPT for research and clinical use in people with and without neck pain (Walton et al. 2011). Many psychological and physiological factors can affect the pain threshold, such as drugs, smoking, alcohol, caffeine and exercises. PPT measures increased significantly after the contraction of the quadriceps (Kosek & Ekholm 1995). Consuming coffee, tea, alcohol (Wolff, Hardy & Goodell 1940), smoking and exercise should be considered in order to eliminate confounding factors in the study of pain threshold. In a study of reliability of the conditioned pain modulation paradigm, assessments were completed on knee pressure-pain threshold during painful conditioning. Twenty healthy adult volunteer participants were also asked to refrain from

consuming caffeine, alcohol, nicotine, and undertaking strenuous exercise for a period of 4 hours before each session (Lewis et al. 2012). In Walton's study, caffeine intake within the past 6 hours or vigorous exercise within the past 24 hours was captured to evaluate its role as a potential moderator of PPT (Walton et al. 2011). Caffeine is the main ingredient of coffee, tea and even colas (Corti et al. 2002; Dulloo et al. 1999; Goyal, Bishnoi & Agrawal 2011). Smoking had differential pain threshold effects depending on the pre-smoke nicotine level. Smoking a cigarette after 12 hours of deprivation led to a significant pain threshold increase (Pauli et al. 1993). The refraining time was due to the total clearance time in human body. However, due to its complexity and non-significance, it cannot be considered in any study. Therefore, they can be considered as potential confounding factors.

Study participants were retained in the trial whenever possible to enable follow up data collection and prevent missing data.

4.10 Randomization and allocation

4.10.1 Sequence generation

In this crossover study, a random sequencing of the three interventions for each subject was achieved using an envelope method that was also stratified by gender to match as closely as possible the sequencing by gender. The random number was generated from the website – RANDO.ORG (see Appendix 6). Each sequence was printed on a slip of paper and sealed into an individual opaque envelope marked F (female) or M (male). At the beginning of their first session, the subjects were asked to choose one of the available envelopes and this determined their unique sequence of interventions. Each subject completed the three intervention sessions with a duration of at least one week between each intervention session. The three interventions were renamed for the individual session recording sheets (rose, tulip and daisy) to blind the PPT collecting the PPT measures and only the acupuncturist knew the actual intervention the subject received.

4.10.2 Allocation concealment mechanism

Upon receipt of an applicant's consent and personal details form, an identification (ID) number was allocated in numerical order to the participant beginning at 1. The ID number

was used on all documentation (medical history, questionnaires, assessment forms and treatment sheets) during the study period to preserve confidentiality. Only the research student and principal investigator were aware of the name of the participants and their ID numbers. The participants' identity features such as name, date of birth and consent forms were kept separate from the data.

4.10.3 Implementation

The research student (XQW) allocated the participants ID number, completed the enrolment procedure and recorded the assignment to interventions.

4.11 Blinding (masking)

All participants were followed up to give opportunity for feedback and reporting of post-treatment adverse reactions and harms.

Study participants and the outcome assessor were blinded after assignment to interventions. Due to the nature of the acupuncture intervention, it was difficult to blind the acupuncturist. Researchers did not disclose the allocation status of the participant at the follow up assessments. A researcher entered data into the computer on separate datasheets so that the researchers can analyse data without having access to prior information about the allocation. Trial participants were aware they would receive three different interventions but did not know what they were specifically or the sequence they would receive them. A curtain was drawn between the participant's body and right arm, so the participant could not visually see the intervention procedures of acupuncture or the sham laser. A suitably qualified acupuncturist was requested to administer the acupuncture using a standardised technique but did not do any measures or assessments. The acupuncturist did not know the participants' names and identifying information. Assessments regarding the trial outcomes were conducted by an assessor blind to treatment allocation. The assessor had undertaken assessment training.

Once a participant has concluded their involvement in the study, and if the participant requested to know their own results of their measure, they could contact the researcher. The details could then be released to the participant only. The Investigator had to report all code breaks (with reason) if they occurred on the corresponding case report form (Appendix 7).

4.12 Data collection, management, and analysis

4.12.1 Primary measures

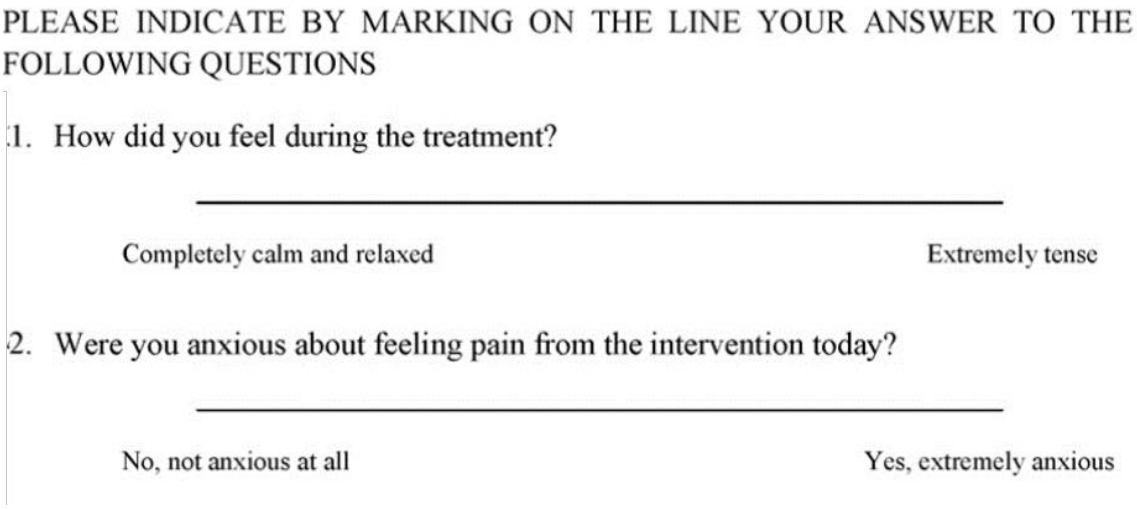
The primary outcome measure was the PPT measurements. These were recorded once at each acupoint at each time point. Three measures were taken prior to the administration of each intervention and three taken following the intervention. The mean was calculated for each of the three measures both pre and post intervention. There was only one algometer (WAGNER, FPK 20) (see 4.14.1.2) used to reduce the risk of requiring recalibration. The assessor was trained and experienced in using the algometer. Appendix 8 shows the Data Collection Form.

4.12.2 Additional measures relating interventions

Secondary outcome measures were needling sensation is defined for the subjects as any sensation other than needling pain. Participants' perceptions of needle sensation (*deqi*) and pain were assessed via a VAS which comprises of a 100mm long non-segmented line, where participants will be required to mark an × on the line rating their *deqi* between no sensation/pain to excruciating sensation/pain (State Insurance Regulatory Authority 2014) (refer to Appendix 8).

In addition, participants were asked to write a description of the sensations of needling and of the type of pain perceived and their responses (Li et al. 2008). The 100mm VAS was used to record subject perceptions relating to the 21 min intervention period for each experimental session (Figure 4.2).

Finally the Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS) was also used to collect the participant's perception of *deqi* sensations and generate a MASS *Deqi* index (MDI) for analysis (see Figure 4.3) (Kong et al., 2007).


PLEASE INDICATE BY MARKING ON THE LINE YOUR ANSWER TO THE FOLLOWING QUESTIONS

1. How did you feel during the treatment?

Completely calm and relaxed — Extremely tense

2. Were you anxious about feeling pain from the intervention today?

No, not anxious at all — Yes, extremely anxious

Figure 4.2: The 100mm VAS used to record subject perceptions relating to the 21 min intervention period for each experimental session

MASS for *deqi*. Place a mark (×) on the line below to indicate your current level of *deqi*.

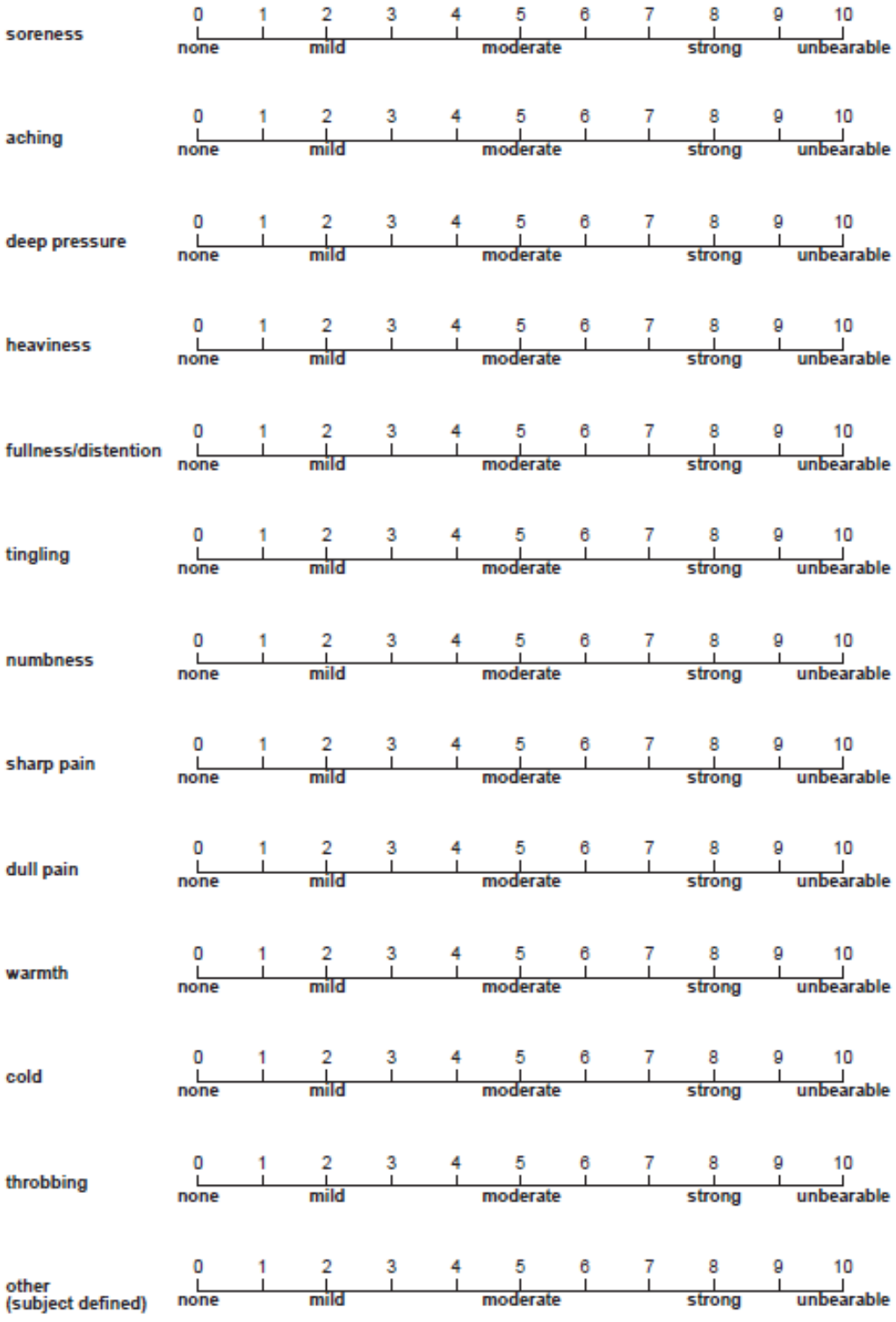


Figure 4.3: MASS data collection form

4.12.3 Participants' retention

Participants were offered a small financial remuneration for their participation in the study. It was a $15 transportation fee for each intervention session to support retention and participation during the study.

In the event of withdrawal from the study, any data collected for that participant was kept and noted as 'incomplete' as part of the findings. Participants were notified that even with withdrawal from the study; data collected to date will be retained and may be used as part of the study findings.

In the event of withdrawal from the study, there was a one-week follow up for that participant to offer opportunities to report adverse events and harms.

4.12.4 Data management (see Appendix 9):

A research data management plan was developed in accord with the Australian National Data Service (ANDS). ANDS was supported by the Australian Government through the National Collaborative Research Infrastructure Strategy Program and the Education Investment Fund (EIF) Super Science Initiative. The research data management plan had been stored on the UTS Research Data Catalogue, STASH.

Data locations and forms were stored securely in password UTS computer and backed up by uploading to CloudStor daily. This data was only accessible to the research student, principal supervisor. Paper based data was stored in key lockable cabinets, within a locked room in Chinese medicine clinic at UTS, only accessible to the research student, principal supervisor and co-supervisor. Backup data was stored in a 7.5 GB USB flash disk once a week, only accessible to the research student and principal supervisor.

4.12.5 Statistical methods

4.12.5.1 Statistical methods for analysing primary and secondary outcomes.

Data was initially entered into EXCEL. IBM SPSS Statistics 26 for Windows version 10 was used to analyse the quantitative data. The main analyses involved various forms of analysis of variance, Chi-square tests and Pearson's correlation. The significance levels were set at $p < 0.05$. In addition, post hoc analysis was conducted to identify statically differences between categories.

4.12.5.2 PPT measurements

For each subject and intervention session, all PPT values were described as a percentage of the mean pre-intervention value, the mean of the three PPT measures obtained prior to administration of the intervention. This was calculated using the following formula:

$$\text{mean} = \frac{\text{PPT } \left(\frac{\text{g}}{\text{cm}^2}\right) \text{ for this site}}{\text{mean preintervention PPT } \left(\frac{\text{g}}{\text{cm}^2}\right) \text{ at this site}} \times 100$$

This data transformation was applied in view of the range of baseline PPT measures encountered both between subjects and also with respect to the same subject across the ten regional measurement sites. Extensive checking of the appropriateness of both the transformation and the model tested in General Linear Model (GLM) was undertaken for the present research and has also been completed in related research studies at UTS. Further, it has been reported in a related study that baseline PPT is not a useful predictor of the percentage change following an active intervention (Yuan 2002). Comparisons were made both within each intervention across all ten PPT measurement sites, and between the three interventions for each individual PPT measurement site.

4.12.5.3 Needling sensation and pain intensity scores

Scores were measured on the 100 mm VAS for each of these variables. Analyses include one way analysis of variance, Pearson's product moment correlation coefficient.

The MASS (Kong et al., 2007) was used to measure the sensory responses elicited by the two interventions (acupuncture and mock laser). The MASS is a revised version of an earlier quantitative assessment tool, the Subjective Acupuncture Sensation Scale (SASS) (Kong et al., 2005), developed in a previously reported pilot study. The scale includes 12 descriptors (soreness, aching, deep pressure, heaviness, fullness/distension, tingling, numbness, sharp pain, dull pain, warmth, cold, and throbbing), each represented using a 10-point Likert scale rating from 'no sensation' (0) to 'unbearable' (10). To quantify the total intensity of *deqi* experienced by each individual, the MDI was calculated by the following formula:

$$\text{MASS Index} = \frac{\sum_{i=1}^{n} (1/2)^i \, R_i}{1 - (1/2)^n}$$

The MDI is calculated as a weighted average of the intensity of *deqi* sensory responses elicited during the intervention using an exponential smoothing (Kong et al., 2007). This index is considered convenient to create a single value to quantitatively summarise the full multivariate breadth and depth of acupuncture sensory responses (Bai et al., 2009).

4.13 Intervention

Following is a description of each of the three interventions with sufficient details to allow replication, including how and when each procedure was administered.

4.13.1 Protocol

Eligible applicants were randomly allocated in equal proportions to three intervention groups with six sequences; each group will receive three interventions in different sequences. A qualified acupuncturist with over 35 year's clinical practice conducted acupuncture interventions. The three intervention groups were:

- Needling SI 3 without manipulation ($SI3m^-$).
- Needling SI 3 with manipulation ($SI3m^+$).
- Sham Laser (SL) on SI 3.

The six sequences were:

- $SI3m^+$, followed by a washout period of at least one week, followed by the $SI3m^-$, followed by a washout period of at least one week, followed by the SL intervention to the same local acupoint.
- $SI3m^+$, followed by a washout period of at least one week, followed by the SL, followed by a washout period of at least one week, followed by the $SI3m^-$ to the same local acupoint.
- $SI3m^-$, followed by a washout period of at least one week, followed by the $SI3m^+$, followed by a washout period of at least one week, followed by the SL to the same local acupoint.
- $SI3m^-$, followed by a washout period of at least one week, followed by the SL, followed by a washout period of at least one week, followed by the $SI3m^+$ to the same local acupoint.
- SL, followed by a washout period of at least one week, followed by the $SI3m^+$, followed by a washout period of at least one week, followed by the $SI3m^-$ to the same local acupoint.
- SL, followed by a washout period of at least one week, followed by the $SI3m^-$, followed by a washout period of at least one week, followed by the $SI3m^+$ to the same local acupuncture point.

A washout period between interventions was required so that physical responses have returned to baseline.

4.13.2 Procedure – approximately 60 minutes

Each intervention procedure was approximately 60 minutes in duration. After having been given information on the purpose and process of the trial and signing the participant informed consent, the participant was scheduled to arrive at a specific time at the UTS Chinese medicine clinic. On arrival participants were asked to complete a short registration form (see Appendix 10) including participants' personal information and current health questionnaires to confirm the absence of new exclusion criteria (e.g. recent injury/illness/medicine) which may inadvertently alter results or pose a risk of harm to the participant. Any new exclusion criteria led to either rescheduling the patient, or release from the study. This took approximately 10 minutes. Participants were then taken to a treatment area and asked to lie prone (face down) on a treatment couch (Figure 4.4). A curtain was drawn between the participant's body and right arm. The acupuncturist was positioned on the side where the arm was exposed while the assessor taking the PPT measures was on the other side during the data collection phases of pre and post PPT measures. The data collector left the room during the intervention phase of the study. In this way, both the assessor and the participants were blind to the needling intervention (sham laser and the SI 3 interventions with or without manipulation). Three rounds of pre-treatment outcome measurements were taken (PPT) across the ten measurement sites. Acupuncture was then administered to the participant's SI 3 on the right hand. The duration of needling was 21 minutes, as per previous similar clinical trials (Loyeung 2013; Szabo 2007; Yuan 2002; Zaslawski 2006). Three rounds of post-treatment outcome measurement were taken (PPT, *deqi*, participants' perceptions concerning each intervention period) across the same ten measurement sites. The procedure of participation refers to Appendix 11.

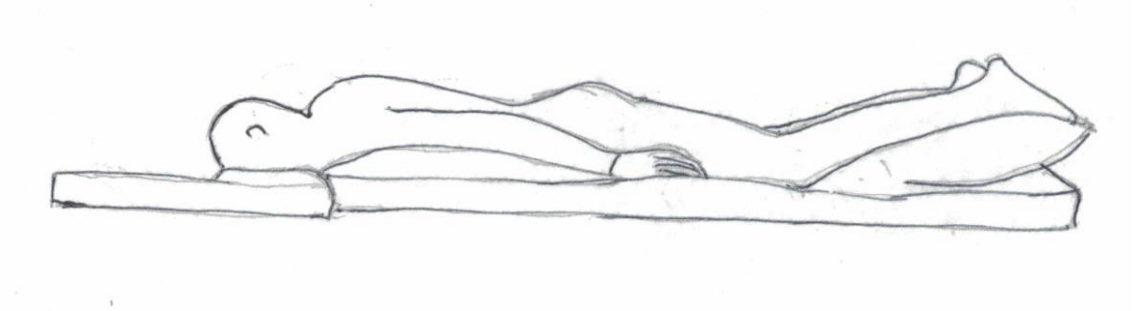


Figure 4.4: Lying prone position

4.13.3 Intervention protocol

4.13.3.1 Acupuncture treatment protocol

A single-use, stainless steel, sterile filiform with guide tube 0.22 mm × 25 mm (C&G; Helio Supply Co. Pty Ltd.) needle was inserted at the acupuncture point SI 3 in the right hand. The acupuncturist inserted the needle perpendicularly (90^{o}) to the skin and to a depth of approximate 7.5-12.5 mm (Chu, Yeh & Wood 1979; Davis et al. 1975; Rogers & Rogers 1995; Shanghai College of Traditional Medicine 1992).

In the "with manipulation" ($SI3m^{+}$) group, once the needle was inserted to the appropriate level the needle was manipulated to obtain *deqi*. The needle was manipulated by holding the needle at the handle and rotating the needle between the thumb and index finger through a 540°-720° angle in a bidirectional manner (neutral supplementation and drainage) with a speed of 2-4Hz, - for five seconds or to patient tolerance. This was applied just after needle insertion and at every three minutes. The needle was retained for 21 minutes. Following the needle retention period the needle was withdrawn and pressed with a cotton ball for 1 minute.

In the "without manipulation" ($SI3m^{-}$) group following insertion of the needle to the appropriate depth there was no attempt to explicitly obtain *deqi*. Just after needle insertion and at every three minutes, the acupuncturist rested the hand in the same position as for the $SI3m^{+}$ intervention and lightly moved his fingers next to the acupuncture needle to mimic movements that would accompany needle manipulation. This is referred to as 'simulated manipulation'.

The control intervention was inactive laser therapy which was applied with an inactive laser probe resting lightly on the skin at the right side SI 3. The low level laser unit (Microlase, Melbourne, Australia) had the laser diode (gallium aluminum arsenide) removed. Sham laser must have either light or sound to indicate functionality. Participants were warned about the "harmfulness" of laser to the eyes and the laser should be held away from them. The laser probe rested lightly on the skin above SI 3 for 20 seconds every 3 min. The unit emitted a regular audible beep during each such period of 'stimulation'.

4.13.3.2 Acupoint

The acupuncture point SI 3 location was as illustrated and described in "WHO Standard Acupuncture Point Locations in the Western Pacific Region" (World Health Organisation 2009) (see Figure 2.4).

4.13.3.3 The control intervention

Laser protocol: Inactive laser therapy will be given with a laser probe which is rested lightly on the skin at the right side SI 3. The low level laser unit (Microlase, Melbourne, Australia) has had the laser diode (gallium aluminium arsenide) removed.

4.13.4 Criteria for discontinuing or modifying allocated interventions for a given trial participant (See Appendix 12)

4.13.5 Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (See Appendix 13)

4.13.6 Relevant concomitant care and interventions that are permitted or prohibited during the trial (See Appendix 14)

4.14 Outcome

The schedule of outcome measures data administration and collection time points are presented in Table 4.1.

Table 4.1: Schedule of enrolment, interventions, and assessments

Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of the trial. This is a randomised cross-over controlled trial which includes at least one-week washout period. In the baseline period, recruited patients will be screened according to the inclusion criteria and exclusion criteria; then, eligible participants will give informed consent and receive a Trial Entry Assessment. After allocation, the patients will receive acupuncture with manipulation, acupuncture without manipulation, or sham laser. The outcome assessments - PPT, is measured before and after the intervention in each visiting session. In addition, the *deqi* - VAS, *deqi* - MASS, needling pain - VAS and subjects' perceptions concerning each intervention period - Questionnaire will also be evaluated after the intervention each time. Adverse events will be recorded in the Incident Adverse Reaction Harms Reporting Form (Appendix 7) at any time during the experiment.

	STUDY PERIOD								
	Enrolment	**Allocation**	**Post-allocation**						**Close-out**
TIMEPOINT	**Pre-Intervention**		**Day 1**		**Day 8**		**Day 15**		**Day 22**
	- Day 7	**0**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Follow up**
RECRUITMENT									
Information sheets	×								
Trial Entry Assessment	×								
ENROLMENT:									
Trial Entry Assessment	×								
Eligibility screen	×								
Informed consent	×								
Health Evaluation	×								
Allocation		×							
INTERVENTIONS:									
SI3m^{+}		●						●	
SI3m^{-}		●						●	
SL		●						●	
ASSESSMENTS:									
PPT			×	×	×	×	×	×	
***Deqi* -VAS**				×		×		×	
***Deqi* - MASS**				×		×		×	
Needling pain - VAS				×		×		×	
Subjects' perceptions concerning each intervention period - Questionnaire				×		×		×	
REPORTING:									
Adverse reaction	●	●	●	●	●	●	●	●	●
Incident	●	●	●	●	●	●	●	●	●

At the first time visit clinic, the participant will complete a Registration Form (see Appendix 9). On arrival at any of the clinic visits, the participant was asked to inform the investigator of any changes of his/her health. PPT readings and self-report assessment

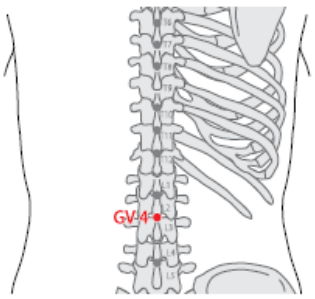
were entered directly into the Data Collection Form (see Appendix 8). This form was sorted by participant number (no personally identifying information). Information was duplicated into the Excel Worksheet on a password secured computer.

4.14.1 Primary subjective outcome measure

With increasing attention to the pain, the pain threshold has become an important part of the pain related studies. Pressure pain threshold (PPT) at defined sites were measured as kilograms of force. PPT measurements were taken once at each acupoint at each time point.

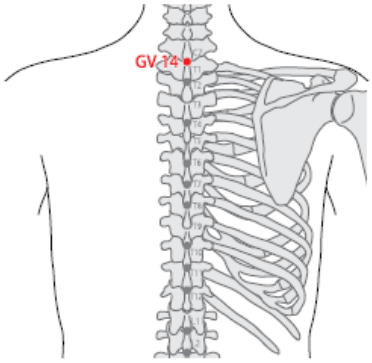
4.14.1.1 PPT measurement sites

PPT was measured at ten regional acupoint locations: GV 4 (*Mingmen*), GV 14 (*Dazhui*), SI 11^{R} (*Tianzong*), SI 11^{L}, GB 21^{R} (*Jianjing*), GB 21^{L}, HT 7^{R} (*Shenmen*), HT 7^{L}, BL 60^{R} (*Kunlun*) and BL 60^{L} by a trained assessor. The locations of the acupuncture points are showed in Figure 4.5, 4.6, 4.7, 4.8, 4.9, 4.10 and described in Table 4.2 (WHO 2009). Each point was located by the research student and confirmed by a co-investigator. Each point was marked with a non-toxic semi-permanent pen. The order of site measurement was HT 7^{R}, SI 11^{R}, GB 21^{R}, GV 14, GB 21^{L}, SI 11^{L}, GV 4, HT 7^{L}, BL 60^{R}, and BL 60^{L}. This same sequence of measurement was used throughout all pre and post-intervention cycles. There were standardised rest periods between repeated measurements made at the same site of approximately 2 minutes.



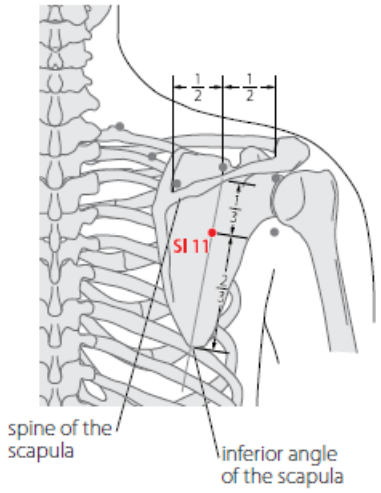
GV4

Figure 4.5: Location of GV 4 (WHO 2009), P. 205



GV14

Figure 4.6: Location of GV 14 (WHO 2009), P. 210



SI11

Figure 4.7: Location of SI 11 (WHO 2009), P. 93

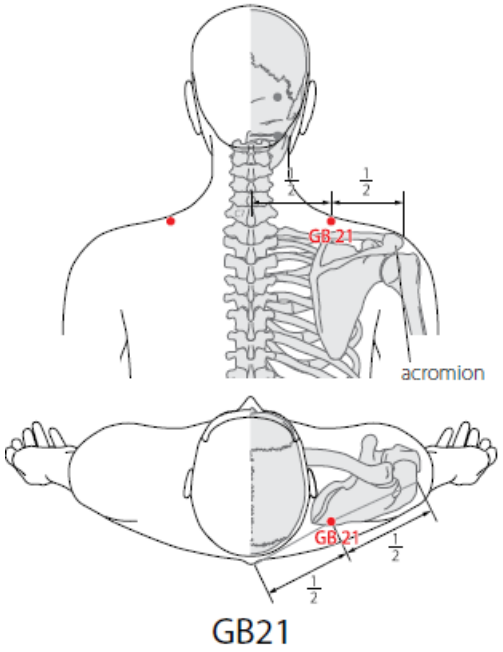


Figure 4.8: Location of GB 21 (WHO 2009), P. 182

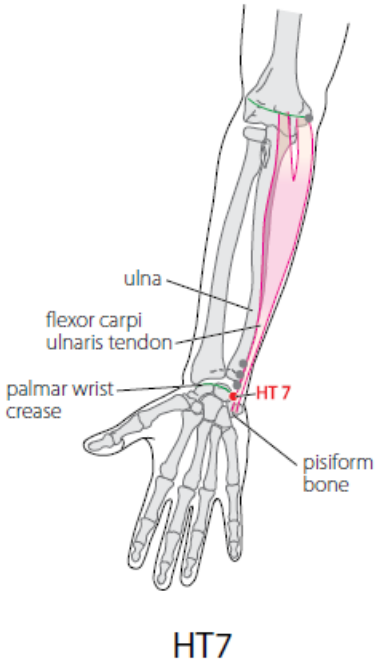
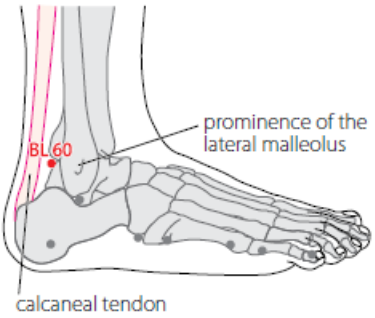


Figure 4.9: Location of HT 7 (WHO 2009), P. 85



BL60

Figure 4.10: Location of BL 60 (WHO 2009), P. 129

Table 4.1: Description of the anatomical location of the ten measurements sites, including their respective methods of location and their channel or segmental relationships to SI 3 (Rogers and Rogers 1989, WHO 2009)

Site	Anatomical location (WHO 2009)	Location method (Aird, Cobbin & Rogers 2002), (Loyeung & Cobbin 2013)	Channel/segmental regions (Chapple 2013), (Marieb & Hoehn 2013), (Loyeung & Cobbin 2013)
GV 4	In the lumbar region, in the depression inferior to the spinous process of the second lumbar vertebra (L2), on the posterior median line.	Anatomical landmark	Dermatome: distal segmental region of L2 Channel: Governor Vessel
GV 14	In the posterior region of the neck, in the depression inferior to the spinous process of the seventh cervical vertebra (C7), on the posterior median line. Note 1: When the head is in a neutral position while the subject is seated, the most prominent site on the posterior aspect of the neck is the spinous process of the seventh cervical vertebra (C7). Forward flexion of the neck may facilitate palpation of the C7 spinous process. Note 2: Slight rotation of C7 can be palpated by rotating the head with the neck slightly flexed.	Anatomical landmark	Dermatome: distal segmental region of C8 Channel: Governor Vessel
SI 11 (R, L)	In the scapular region, in the depression between the upper one third and lower two thirds of the line connecting the midpoint of the spine of the scapula with the inferior angle of the scapula.	Proportional (elastic method)	Dermatome: distal segmental region of T3 Channel: Small Intestine channel
GB 21 (R, L)	In the posterior region of the neck, at the midpoint of the line connecting the spinous process of the seventh cervical vertebra (C7) with the lateral end of the acromion.	Proportional (elastic method)	Dermatome: distal segmental region of C2,3 C5,6 Channel: Gall Bladder channel
HT 7 (R, L)	On the anteromedial aspect of the wrist, radial to the flexor carpi ulnaris tendon, on the palmar wrist crease. Note: In the depression radial to the proximal border of the pisiform bone, on the palmar wrist crease.	Anatomical landmark	Dermatome: same segmental region of C8 Channel: Heart channel
BL 60 (R, L)	On the posterolateral aspect of the ankle, in the depression between the prominence of the lateral malleolus and the calcaneal tendon.	Anatomical landmark	Dermatome: To epidermis, dermis, and subcutaneous tissue: S1 via the sural nerve Channel: Bladder channel

4.14.1.2 Algometer

PPT protocols have been based on those published by Dr David Walton (Walton et al. 2011). The device used was a mechanical pressure algometer (FDK20, Wagner Instruments, Greenwich, CT) using the methods described by Andrew A. Fischer (Fischer 1987) which was also used and detailed in all previous PPT studies at UTS (shown in Figure 4.11). In preparation for testing, the investigator practiced applying force until the force was applied consistently at a rate of approximately 50kPa/second. This was

accomplished by applying increasing pressure on a flat surface, while the investigator listened to a clock second hand counting for 5 seconds.

After marking the acupoints with a semi-permanent pen, instructions were given to the participant "I'm going to begin applying pressure to this acupuncture point. I want you to tell me the moment the sensation changes from comfortable pressure to slightly unpleasant pain". The PPT measurement result of each acupoint (noted as kgf) was recorded in the data collection form (Appendix 8).

Figure 4.11: Wagner FPK algometer

4.14.2 Additional subjective outcome measures relating interventions

The additional measures were the participants' perceptions of needle sensation (*deqi*) and pain.

Participants' perceptions of needle sensation (*deqi*) (measured as the Visual Analogue Scale, VAS score, Massachusetts General Hospital Acupuncture Sensation Scale, MASS & a perceptions' questionnaire) is defined for the subjects as any sensation other than needling pain.

Participants' perceptions of needle sensation (*deqi*) and pain were assessed via a visual analogue scale (VAS) which comprises of a 100mm long non-segmented line, where participants were required to mark a × on the line rating their *deqi* between no sensation/pain to excruciating sensation/pain (State Insurance Regulatory Authority 2014).

The Massachusetts General Hospital acupuncture sensation scale (MASS) is another important measure of *deqi*. The scale includes 12 descriptors: soreness, aching, deep pressure, heaviness, fullness/distension, tingling, numbness, sharp pain, dull pain, warmth, cold, throbbing, and a subject defined "other" (Kong et al. 2007). The Data Collection Form is in Appendix 5.

In addition, participants were asked to write a description of the sensations of needling and of the type of pain perceived and their responses (Li et al. 2008). The 100mm VAS was used to record the participant's perceptions related to the 21 min intervention period for each experimental session (measured using the VAS score & a perceptions' questionnaire).

4.15 Participant timeline:

The time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants are shown in Table 4.1 and Figure 4.10.

The trial consisted of a one (1) week pre-intervention stage (-1), a three-week intervention phase and a two-week follow up phase. The total trial period was five weeks (35 days). As shown measurements were undertaken at four time-points for each group:

PPT: Baseline scores (the mean of three measures) was obtained immediately before intervention (pre-intervention) and immediately after the intervention (post-intervention), (again the mean of three successive measures) with approximately 25 minutes between each phase.

Self-report Assessments: At pre and post interventions.

Applicants were assessed for eligibility/suitability to the trial using the Initial Health Information Questionnaire (Appendix 8) and sign the consent form (Appendix 4) in the recruitment interview. This form has a short list of strategic questions such as "do you have a phobia of needles", "are you pregnant or planning to become pregnant in the next 3 months" with "yes" "no" answer boxes. The purpose of the Initial Health Questionnaire was to confirm eligibility and resolve any exclusion criteria prior to participation in the study. This was used in conjunction with the information sheet and the informed consent form (Appendix 4). Applicants who are suitable for enrolment were allocated to six different sequences and scheduled for their experimental visits.

For the details of the procedure of participation, please see the Appendix 11.

All participants were followed up to give opportunities for feedback and reporting of post-treatment adverse reactions and harms. Appendix 6 is Incident Adverse Reaction Harms Reporting Form.

The reason for the control group selection is illustrated in Section 4.4.4. For the details of monitoring and harms of this trial, please see the Appendix 15.

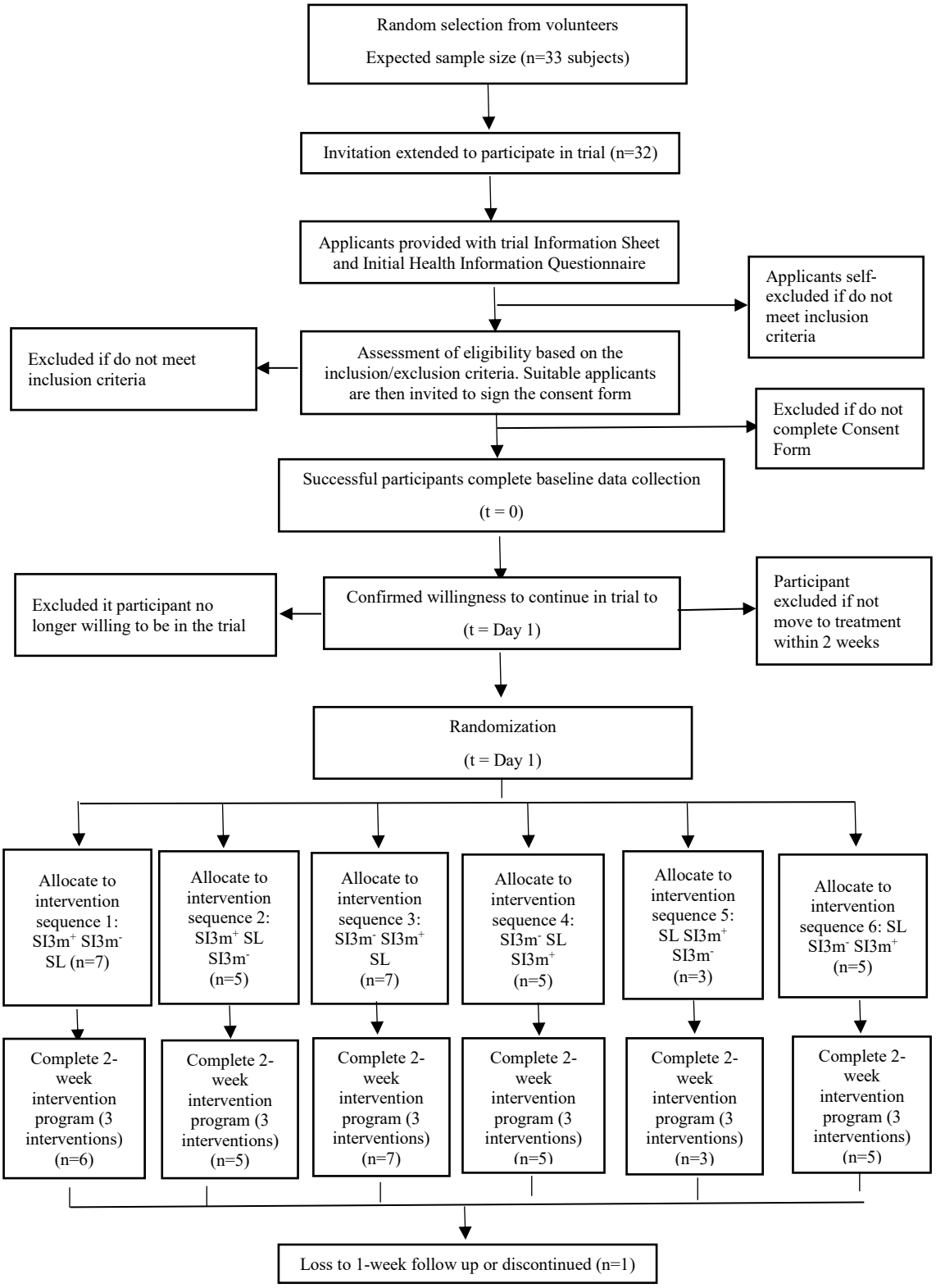


Figure 4.12: Diagram showing flow of participants

4.16 Ethics and dissemination

An application was made to the UTS HREC. The Human Ethic Application ID of this study is ETH18-2294 and was approved by UTS HREC on 9 November 2018. The study was completed by April 2019. For the details of ethical approval process and dissemination, please see the Appendix 16. Appendix 17 is a form for project change management. Appendix 18 is an explanation of technical terms used. Appendix 19 is Standard Operating Procedures, which had been submitted to the UTS HREC.

4.17 Summary

Pain is a common public health problem that presents to the clinic. The results of this pilot study will focus on PPT changing in healthy participants. In addition, this study will observe the influence of different acupuncture intervention on SI 3 to *deqi* and needling pain.

The SI 3 (*Houxi*) acupoint is the Shu point of five Shu points (special points of the 12 meridians, located distal to the elbows and knees, namely well, brook, stream, river and sea points), which belongs to the small intestine channel. According to the theory of Five-Shu points, the Shu point (SI 3) is responsible for diseases related to neck, shoulders, arms or back pain. PPT measurement on 10 regional sites across the body will show SI 3's site specificity on pain relief.

To improve the reliability and repeatability of study results, strict quality control must be enforced. In this trial, quality control will be strengthened not only from participants' enrolment and acupuncture manipulation but also from data acquisition and analysis.

In conclusion, SI 3 is an effective acupoint to manage pain, but the influence on site specificity and application of needle manipulation is still unclear. This trial is the first prospective study to explore the effects of the acupoint SI 3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain with high-quality randomised control.

Chapter 5 Results of a prospective crossover trial

5.1 Characteristics of participants

Between November 2018 and March 2019, 32 healthy volunteers were enrolled in the study. One participant discontinued treatment prematurely due to scheduling difficulties within the first 3 weeks of treatment. The characteristics of thirty-one of 32 participants are presented in Table 5.1. The mean age was 41.9 years with a mean BMI (body mass index) of 23.3 kg/m^2.

Table 5.1: Characteristics of healthy particpants

Characteristics	Frequency
Number	31
Age, years	
Mean	41.9
Median ± SD	43 ± 14.0
Range	19-66
Gender	
Female	16
Male	15
Height, cm	
Mean	167.36
Median ± SD	166 ± 9.0
Range	153-186
Weight, kg	
Mean	65.81
Median ± SD	61.7 ± 14.6
Range	45-107
BMI, kg/m^2	
Mean	23.2
Median ± SD	22.5 ± 3.8
Range	17.6-32.0
Acupuncture experience	
Naïve	10
Had Experience	21

Data of one subject (subject ID was 10) was excluded from analyses as they only attended the first session.

5.2 Variation depending on PPT

It would be determined whether each intervention can affect PPT and which intervention, and measurement site, had the biggest statistical mean %PPT change.

5.2.1 PPT measurements

For each subject and intervention session, all PPT values are described as a percentage of the mean pre intervention value. This was calculated using the following formula:

$$\text{mean} = \frac{\text{PPT } \left(\frac{\text{g}}{\text{cm}^2}\right) \text{ for this site}}{\text{mean preintervention PPT } \left(\frac{\text{g}}{\text{cm}^2}\right) \text{ at this site}} \times 100$$

This data transformation was applied in view of the range of baseline PPT measures encountered both between subjects and also with respect to the same subject across the ten regional measurement sites. Extensive checking of the appropriateness of both the transformation and the model tested in General Linear Model (GLM) was undertaken for the present research. Furthermore, it had been reported in a related study that baseline PPT is not a useful predictor of the percentage change following an active intervention (Yuan 2002).

Comparisons were made:

1) within each intervention across all ten sites, and
2) between the three interventions at each individual measurement site.

A statistical change for the within intervention comparison means that there was a statistical significant increase or decrease in mean %PPT from the pre intervention baseline within that one particular intervention. A statistical change for the between intervention comparison means that the intervention produced a statistical significant difference for the post intervention mean %PPT scores when compared to the pre intervention scores for the other interventions.

In this regional PPT study, there were four variables: (1) the dependent variable, PPT, which was the mean %PPT; (2) the independent variable, time, which has two categories: "pre intervention" and "post intervention"; (3) the independent variable, intervention, which has three categories: "$SI3m^-$", "$SI3m^+$" and "SL"; and (4) the independent variable measurement site, which has ten categories: "$SI11^R$", "$SI11^L$", "GV4", "GV14", "$BL60^R$", "$BL60^L$", "$HT7^R$", "$HT7^L$", "$GB21^R$", "$GB21^L$".

5.2.2 Homogeneity test of variance

Because the statistical results of this study were focused on mean values, the central limit theorem (Riffenburgh 2012, p. 88) was applied. No matter what the distribution of

original data (may be normal, but may also be not), multiple sampling from raw data, and obtaining more samples, each sample can be calculated to obtain a corresponding statistics (e.g., mean). If the number of cases is more than 30 of each sample, the distribution of these statistics, such as a mean, is close to normal. Thirty-one samples in a crossover experiment have been collected, which means 31 random samples have been drawn several times. In addition, each intervention group had the same number of people (n = 31). Thus, the distribution was considered as normal. Therefore, a two-way analysis of variance (ANOVA) using the GLM was conducted using IBM SPSS Statistics version 26.

5.2.3 To compare and contrast the effects on PPT of three interventions (needling intervention without manipulation, needling intervention with manipulation and sham laser) to the acupoint SI 3

5.2.3.1 Within intervention comparisons en bloc - Post intervention changes in mean %PPT

The 95% confidence intervals (CI) and adjusted significance levels are shown in Table 5.2 for the three intervention en bloc (with differentiating each measurement site) (refer to Appendix 20). As shown in Table 5.2 and Figure 5.1, significant increases in mean %PPT were observed for two of the three interventions ($p < 0.0001$ for both $SI3m^-$ and $SI3m^+$ needling interventions) while no significant increase was observed for the sham laser intervention ($p > 0.1$). For the three interventions, mean PPT changes ranged from 23.7% ($SI3m^+$) to 0.2% (SL). Statistical significant p values are shown in bold.

Table 5.2: Mean percentage change in PPT from pre intervention mean (baseline) for the three interventions

Intervention	Number of subjects	Mean %PPT change	Median	SD	95% CI	p value (adjusted)
$SI3m^-$	31	16.1	15.2	19.5	14.0 to 18.3	**< 0.001**
$SI3m^+$	31	23.7	22.1	21.1	21.4 to 26.1	**< 0.001**
SL	31	0.2	0	12.2	-1.1 to 1.6	0.3

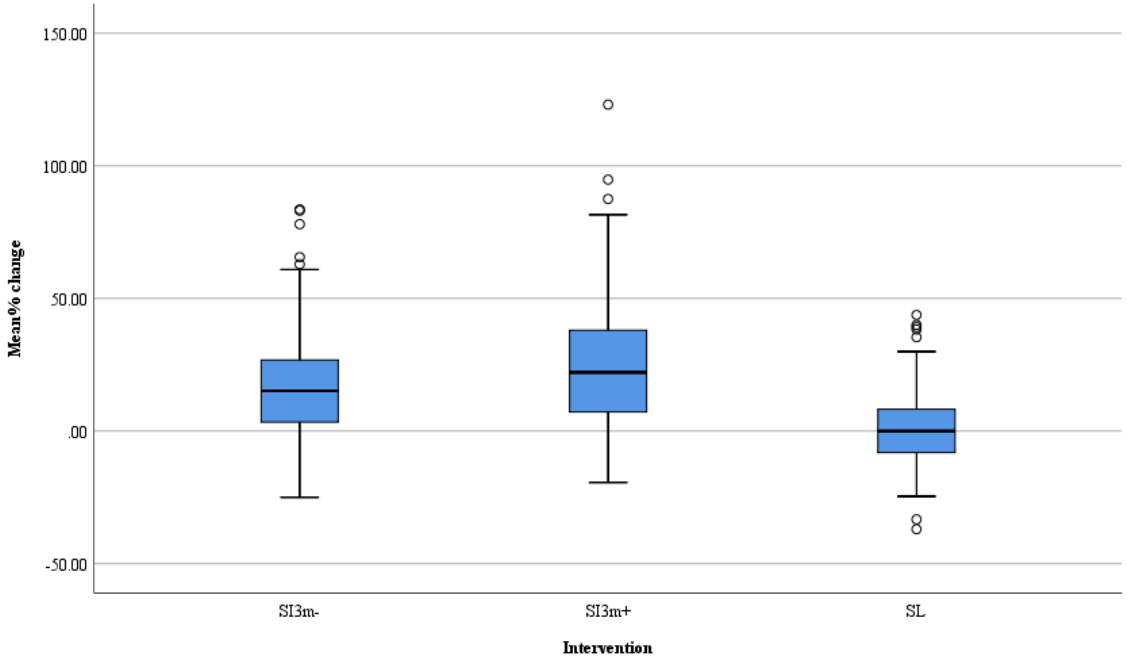


Figure 5.1: A boxplot for mean percentage %PPT change from pre intervention scores for the three interventions from pre-intervention scores

5.2.3.2 Between intervention comparisons en bloc - Post intervention changes in mean %PPT

While it had been shown there were significant main effects obtained for the en bloc analysis for within intervention comparison (refer to Appendix 21), it was also noted that the significant effects were for intervention and regional site that were responsible for the change ($p < 0.001$). In addition because the two acupuncture interventions significantly increased the mean %PPT from pre-intervention scores (baseline), it was therefore necessary to determine whether there was a difference between each intervention for the mean %PPT changes observed. Table 5.3 shows the between intervention (en bloc) differences and significance levels following post hoc analysis. It was found that the $SI3m^+$ intervention produced significantly greater changes in mean %PPT than the $SI3m^-$ intervention and that both needling interventions ($SI3m^+$ and $SI3^-$) produced significantly greater mean %PPT increases than the sham laser control (refer to Appendix 22 for the SPSS output).

Table 5.3: Between intervention scores and significance levels for mean %PPT (en bloc)

Intervention pair		Difference	CI	p value
$SI3m^-$ with	$SI3m^+$	-7.6	-10.9 to -4.2	**< 0.001**
	SL	15.9	12.5 to 19.2	**< 0.001**
$SI3m^+$ with	$SI3m^-$	7.6	4.2 to 10.9	**< 0.001**
	SL	23.5	20.1 to 26.8	**< 0.001**
SL with	$SI3m^-$	-15.9	-19.2 to -12.5	**< 0.001**
	$SI3m^+$	-23.5	-26.8 to -20.1	**< 0.001**

*. Comparisons found significant are shown with 95% confidence intervals (CI) and adjusted p values in bold font.

5.2.3.2 Within intervention comparisons by site- Post intervention changes in mean %PPT

Tables 5.4, shows that significant increases in mean %PPT from baseline were observed at all ten measurement sites following both the needling interventions of $SI3m^-$ and $SI3m^+$ but not for any of the ten sites for the SL control intervention. The range observed for the $SI3m^+$ intervention was 15.5% ($HT7^R$) to 32.6% (SI11L). With respect to the $SI3m^+$ interventions at the ten regional PPT measurement sites, significant mean %PPT increases were observed at all ten sites: $HT7^R$ 15.5%, $SI11^R$ 24.5%, $GB21^R$ 20.3%, GV14 24.4%, $GB21^L$ 20.2%, $SI11^L$ 32.6%, GV4 31.6%, $HT7^L$ 22.6%, $BL60^L$ 22.7% and $BL60^R$ 22.7% ($p < 0.0001$ in all cases).

The mean %PPT at Site GV4 following the $SI3m^+$ intervention was the second largest increase observed, which was 31.6% and very similar to score for SI11L. Figure 5.2, Figure 5.3 and Figure 5.4 show three bar charts reflecting the mean %PPT changes following the three different interventions at each of the ten sites.

The $SI3m^-$ intervention produced ten significant mean %PPT increases that ranged from 6.0% ($HT7^R$) to 24.5% (GV4). The increases from baseline for the $SI3m^-$ intervention at the 10 measurement sites were: 6.0% at site $HT7^R$ ($p < 0.05$), 13.6% at site $SI11^R$ ($p < 0.0001$), 10.7% at site $GB21^R$ ($p < 0.0001$), 17.4% at site GV14 ($p < 0.0001$), 17.1% at site $GB21^L$ ($p < 0.0001$), 22.5% at site $SI11^L$ ($p < 0.0001$), 24.5% at site GV4 ($p < 0.0001$), 16.5% at site $HT7^L$ ($p < 0.0001$), 15.2% at site $BL60^L$ ($p < 0.0001$) and 17.9% at site $BL60^R$ ($p < 0.0001$).

In contrast, there were no significant changes from pre intervention mean %PPT observed following the sham laser intervention at any of the ten PPT measurement sites, with mean % changes ranging from -1.2 to 3.3. As shown in Figure 5.2 and Figure 5.3, both acupuncture intervention to SI 3 on the right increased the mean %PPT on all different regional sites, but especially on GV4, $SI11^{L}$. These two sites showed the increases of all ten measurement body sites following the $SI3m^{-}$ and $SI3m^{+}$ interventions.

Table 5.4: Mean percentage change in PPT from pre intervention mean at the ten regional measurement sites for the three SI 3 interventions

Regional site	$SI3m^{-}$ (n = 31)		$SI3m^{+}$ (n = 31)		SL (n = 31)	
Acupoint	mean	SD	mean	SD	mean	SD
$HT7^{R}$	**6.0***	**18.3**	**15.5****	**18.2**	-1.2	13.7
$SI11^{R}$	**13.6****	**17.8**	**24.5****	**20.4**	2.7	12.5
$GB21^{R}$	**10.7****	**19.5**	**20.3****	**20.4**	3.3	10.3
GV14	**17.4****	**18.3**	**24.4****	**23.6**	1.1	11.9
$GB21^{L}$	**17.1 ****	**17.9**	**20.2****	**19.0**	1.0	10.6
$SI11^{L}$	**22.5****	**19.8**	**32.6****	**22.2**	0.8	13.5
GV4	**24.5****	**20.5**	**31.6****	**27.7**	0.1	15.4
$HT7^{L}$	**16.5****	**17.9**	**22.6****	**16.7**	-0.9	10.7
$BL60^{L}$	**15.2****	**18.8**	**22.7****	**20.6**	0.7	13.2
$BL60^{R}$	**17.9****	**21.6**	**22.7****	**17.6**	1.4	9.6

Adjusted significance levels are shown: *$p < 0.05$, ** $p < 0.0001$. Statistical significant effects are shown in bold.

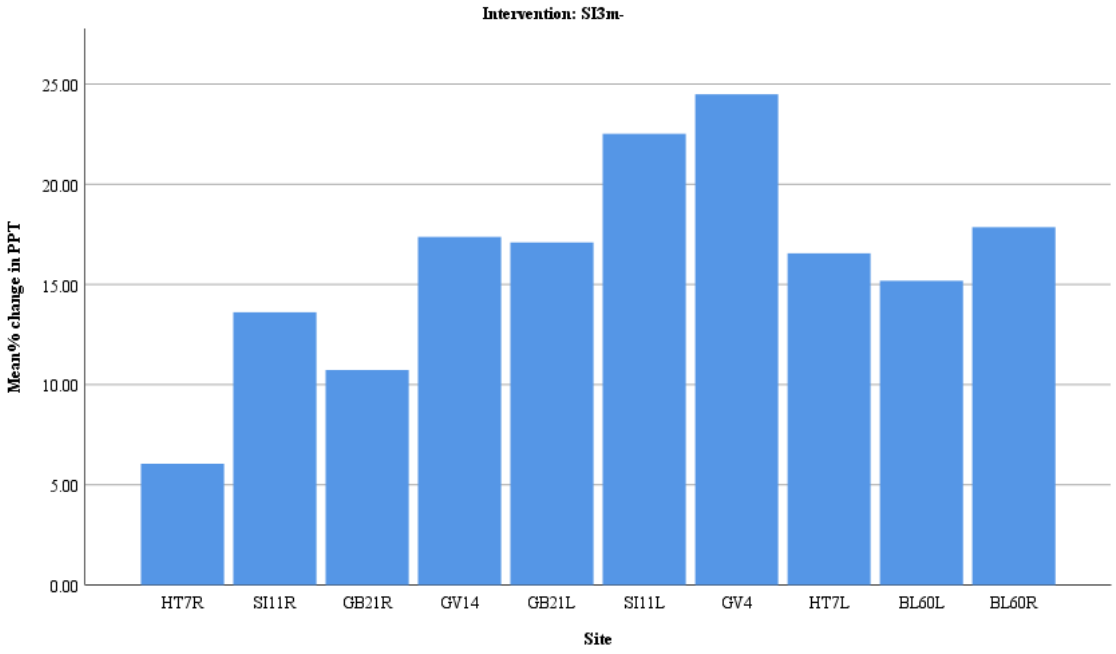


Figure 5.2: Mean percentage change in PPT from pre intervention for the ten regional sites by SI3m$^-$

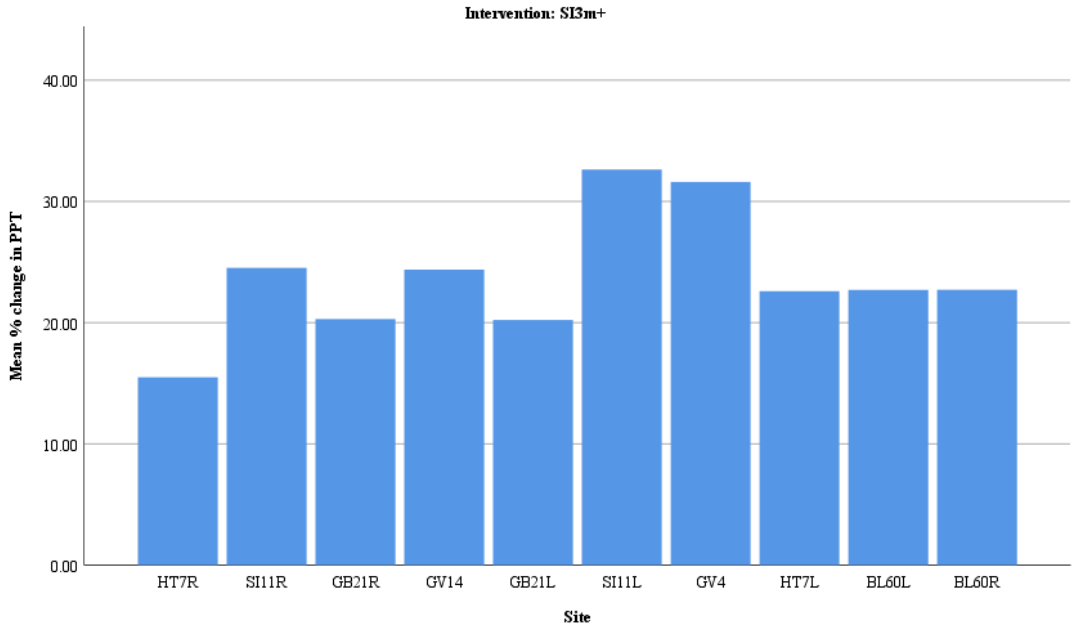


Figure 5.3: Mean percentage change in PPT from pre intervention for the ten regional sites by SI3m$^+$

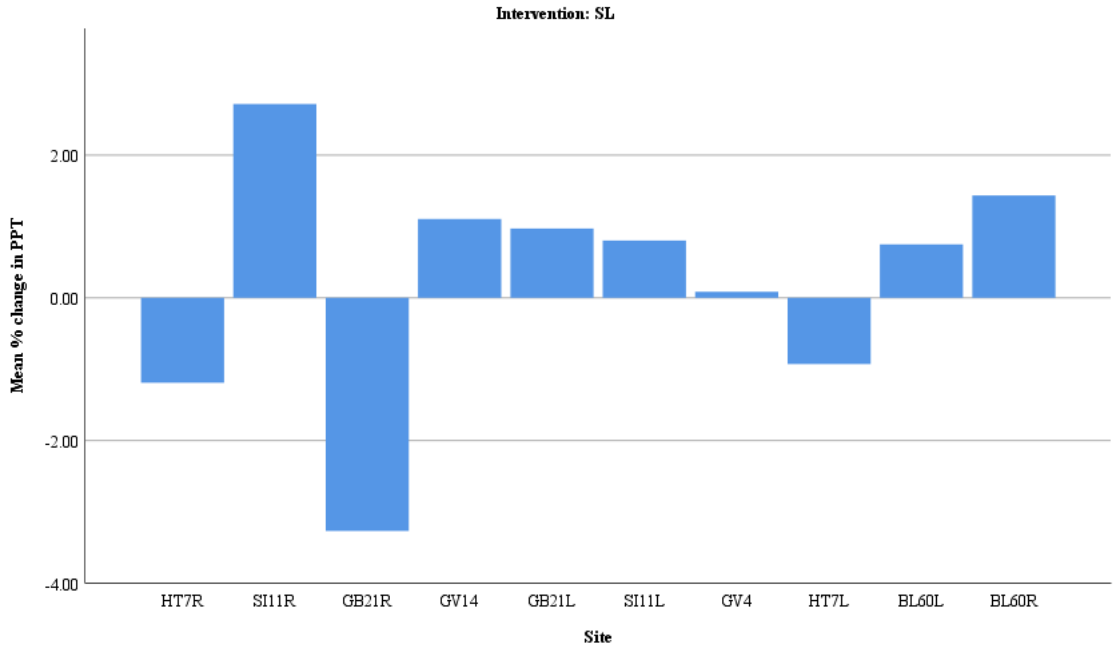


Figure 5.4: Mean percentage change in PPT from pre intervention for the ten regional sites by SL

5.2.3.3 Between intervention comparisons by ten regional sites

The between comparison changes at ten different regional measurement sites are shown for all three interventions in Tables 5.5 (refer to Appendix 23 for SPSS output). The post intervention changes in regional PPT were statistically significantly greater for $SI3m^{+}$ than for sham laser intervention at all the ten sites ($p \leq 0.001$). For the $SI3m^{-}$ intervention changes were significantly greater than SL at nine sites ($p < 0.05$) the exception being for the site $HT7^{R}$ ($p = 0.285$). While the needling at $SI3m^{+}$ produced higher scores at all ten regional sites compared to those following $SI3m^{-}$ it was only statistically significant at only one site - $SI11^{R}$ ($p = 0.038$).

Table 5.5: Comparison of the mean percentage change in PPT and associated 95% confidence intervals at the ten regional measurement sites between the $SI3m^-$, $SI3m^+$ and SL interventions

Sites	Intervention Pair		
	$SI3m^-$ with $SI3m^+$	$SI3m^-$ with SL	$SI3m^+$ with SL
$HT7^R$	p = 0.076 -19.7 to 0.8	p = 0.216 -2.9 to 17.5	**p = 0.001** **6.5 to 26.9**
$SI11^R$	**p = 0.038** **-21.3 to -0.5**	**p = 0.038** **0.5 to 21.3**	**p < 0.001** **11.4 to 32.2**
$GB21^R$	p = 0.080 -20.0 to 0.9	**p = 0.006** **3.5 to 24.5**	**p < 0.001** **13.1 to 34.0**
GV14	p = 0.303 -18.3 to 4.2	**p = 0.002** **5.0 to 27.5**	**p < 0.001** **12.0 to 34.5**
$GB21^L$	p = 0.731 -13.0 to 6.7	**p = 0.001** **6.3 to 26.0**	**p < 0.001** **9.4 to 29.1**
$SI11^L$	p = 0.093 -21.5 to 1.3	**p < 0.001** **10.3 to 33.1**	**p < 0.001** **20.4 to 43.2**
GV4	p = 0.407 -20.3 to 6.1	**p < 0.001** **11.2 to 37.6**	**p < 0.001** **18.3 to 44.7**
$HT7^L$	p = 0.276 -15.4 to 3.3	**p < 0.001** **8.1 to 26.8**	**p < 0.001** **14.2 to 32.9**
$BL60^L$	p = 0.226 -18.3 to 3.3	**p = 0.005** **3.7 to 25.2**	**p < 0.001** **11.2 to 32.7**
$BL60^R$	p = 0.502 -15.2 to 5.4	**p = 0.001** **6.1 to 26.7**	**p < 0.001** **11.0 to 31.6**

Only those comparisons found significant are shown together with 95% confidence intervals (CI) and adjusted p values in bold font.

5.2.4 Nonparametric test

The above analyses in Section 5.2.3 were based on the population normality and homogeneity of variance, which have been explained in Section 5.2.2. Meanwhile, homogeneity tests were conducted to exam the sensibility of the data (refer to Table 5.6). The Levene's test showed that the homogeneity of variance assumption was not achieved ($p < 0.001$). Therefore, it was decided that a Friedman test should also be performed.

Table 5.6: Levene's test of equality of error variances*

Dependent Variable: Mean% change

F	df1	df2	Sig.
2.729	29	900	< 0.001

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.
* Design: Intercept + Intervention + Site

The results of the Friedman test indicated that significant differences did exist in mean percentage change in PPT across interventions en bloc ($p < 0.001$) (refer to Table 5.7 and Table 5.8), While the results of SL comparison with $SI3m^-$ ($p < 0.001$), $SI3m^+$ ($p < 0.001$) remained statistically significant however for the Friedman test it was found that there was a statistically significant difference between $SI3m^-$ and $SI3m^+$ ($p = 0.001$), the two needling interventions.

Table 5.7: Nonparametric tests hypothesis test summary by interventions

	Null Hypothesis	Test	Sig.	Decision
1	The distributions of $SI3m^-$, $SI3m^+$ and SL are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	**< 0.001**	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is 0.050.

Table 5.8: Related-samples Friedman's two-way analysis of variance by ranks summary – $SI3m^-$, $SI3m^+$ & SL

Total N	310
Test Statistic	201.763
Degree Of Freedom	2
Asymptotic Sig.(2-sided test)	**< 0.001**

Table 5.9 Mean % PPT pairwise comparisons by interventions

Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig*
SL - $SI3m^-$	0.805	0.080	10.020	**< 0.001**	< 0.001
SL - $SI3m^+$	1.102	0.080	13.715	**< 0.001**	< 0.001
$SI3m^-$ - $SI3m^+$	-0.297	0.080	-3.695	**< 0.001**	0.001

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.

Asymptotic significances (2-sided tests) are displayed. The significance level is 0.05.

* Significance values have been adjusted by the Bonferroni correction for multiple tests.

In addition, it could be seen from the output that the consequence of the Friedman test is significant by site ($p < 0.001$) (refer to Appendix 24). Respectively, the intervention $SI3m^-$ $p < 0.001$, the intervention $SI3m^+$ $p = 0.001$ and intervention SL $p = 0.340$, which indicated that acupuncture on right SI 3 could result in different change in %PPT at ten different human regional sites. However, sham laser had no different effect amongst ten regional sites.

Hence, the nonparametric test demonstrated the same results as two-way ANOVA. ANOVA showed the accuracy of the date consequence, while Friedman test examined the sensitivity of the %PPT change in this prospective crossover trial. The change of needling pain will be analysed in the next section.

5.3 Comparison of the effects on needling pain intensity scores among the three interventions (needling intervention without manipulation, needling intervention with manipulation and sham laser) to the acupoint SI 3

To examine the influence of the three different interventions on needling pain intensity scores when stimulating the acupoint site SI 3 on the right hand, additional analyses were completed that involved the following comparisons:

Participants' perceptions of needling pain were measured using a Visual Analogue Scale (VAS), for the comparison between $SI3m^-$, $SI3m^+$ and SL (n = 31).

5.3.1 Needling pain (VAS) in three different interventions without differentiating gender

Each of the 31 healthy participants were randomly administered the three different interventions – $SI3m^-$, $SI3m^+$ and SL (refer to Table 5.10) and asked to rate the pain their

experienced on each of the three occasions (n = 93). Among the interventions, there were 48 intervention occasions administered to females and 45 intervention occasions to males (refer to Table 5.11).

Table 5.10: Needling pain scores (VAS)

Intervention	Mean	Std. Deviation
$SI3m^-$ (n = 31)	24.4	24.7
$SI3m^+$ (n = 31)	32.2	21.0
SL (n = 31)	8.6	17.8

Table 5.11: Needling pain scores (VAS) by gender

Gender	Intervention	Mean	Std. Deviation
Female	$SI3m^-$ (n = 16)	18.1	18.8
	$SI3m^+$ (n = 16)	34.9	17.8
	SL (n = 16)	12.8	21.8
Male	$SI3m^-$ (n = 15)	31.1	28.9
	$SI3m^+$ (n = 15)	29.3	24.3
	SL (n = 15)	4.0	11.2

Table 5.10 and Table 5.11 indicate that subjects in general felt a mild level of pain. The sham laser intervention interestingly also resulted in very minor level of pain reported despite no active stimulation other than resting the probe on the skin surface. However, the VAS needling pain was significantly different amongst the different interventions ($p < 0.001$). Therefore, a multiple comparison statistical analysis of needling pain (VAS) was conducted. Table 5.12 shows that there were significant increased pain reported after acupuncture compared to sham laser for both $SI3m^-$ ($p = 0.014$) and $SI3m^+$ ($p < 0.0001$). However, there was no significant difference in reported VAS pain between $SI3m^-$ and $SI3m^+$ ($p = 0.463$). Figure 5.5 shows the difference of needling pain within three interventions.

There was no significant difference between genders ($p = 0.912$) for the needling pain score (see Appendix 25 for SPSS output).

Table 5.12: Multiple comparisons of needling pain VAS

Dependent Variable: Needling Pain VAS
Tukey

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig (p).	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
$SI3m^-$	$SI3m^+$	-7.8	5.5	0.326	-20.8	5.2
	SL	15.8*	5.5	**0.013**	2.8	28.8
$SI3m^+$	$SI3m^-$	7.8	5.5	0.326	-5.2	20.8
	SL	23.7*	5.5	**<0.001**	10.6	36.7
SL	$SI3m^-$	-15.8*	5.5	**0.013**	-28.8	-2.8
	$SI3m^+$	-23.7*	5.5	**<0.001**	-36.7	-10.6

Based on observed means.
The error term is Mean Square (Error) = 461.123.
* The mean difference is significant at the 0.05 level.
Adjusted p values in bold font

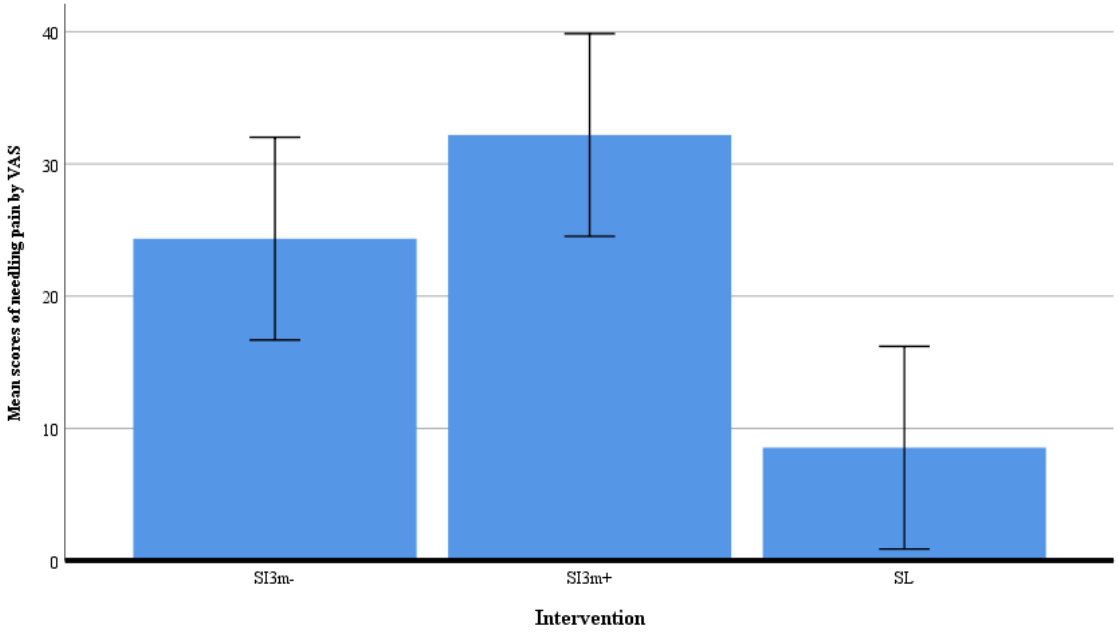


Figure 5.5: Means of needling pain (VAS) for the three different interventions without differentiating gender

5.3.2 Needling pain (VAS) in three different interventions according to gender

As shown in table 5.13, the needling pain reported using the VAS had no significant difference ($p > 0.05$) between $SI3m^-$ and $SI3m^+$ for both male and female participants. For male subjects, the needling pain reported during both $SI3m^-$ and $SL3m^+$ was significantly different from the sham laser intervention ($p < 0.05$). For female healthy participants, $SI3m^-$ when compared with SL had no significant difference in VAS pain ($p > 0.05$), while the comparison between $SI3m^+$ and SL did show a significant difference

($p < 0.05$). Figure 5.4 shows the mean scores for pain (VAS) associated with the three different interventions across the two genders.

Table 5.13: Mean needling pain (VAS) concerning gender during the three needling interventions

Gender	Intervention Pair		
	$SI3m^-$ with $SI3m^+$	$SI3m^-$ with SL	$SI3m^+$ with SL
Male	p = 1.000 -18.9 to 22.5 (CI)	**p = 0.007** **6.4 to 47.8 (CI)**	**p = 0.012** **4.6 to 46.0 (CI)**
Female	p = 0.056 -34 to 0.3 (CI)	p = 1.000 -11.9 to 22.4 (CI)	**p = 0.007** **5.0 to 39.3 (CI)**

p values is in bold font

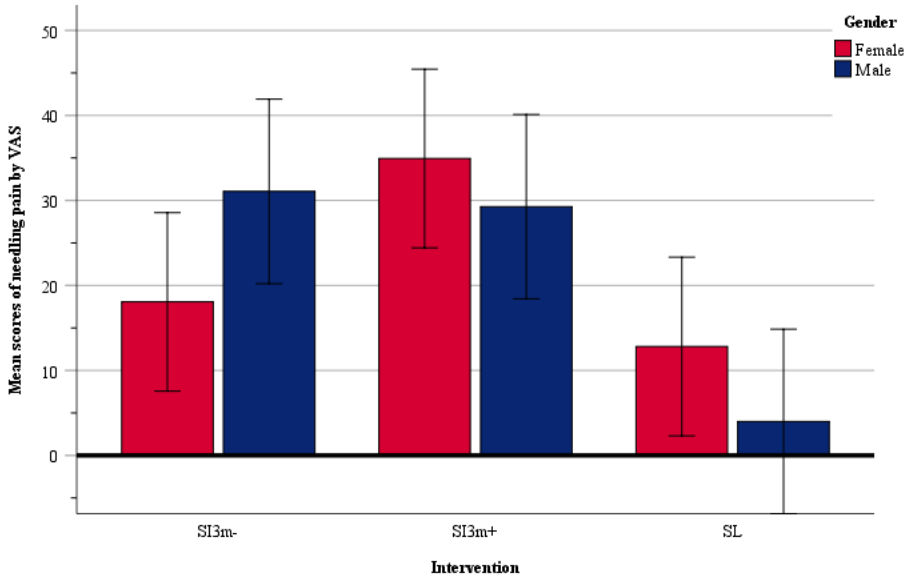


Figure 5.6: Means scores of needling pain (VAS) for the three different interventions by gender

5.3.3 Nonparametric test for needling pain

As illustrated in Section 5.2.2, this thirty-one sample crossover experiment could apply a two-way ANOVA without the homogeneity test for variance. However, according to the Table 5.14, p-value < 0.05, it was concluded that the variances were not all equal. Therefore, a Friedman test was conducted (refer to Appendix 26). The results of the Friedman test indicate that significant differences do exist in needling pain across

acupuncture interventions, χ^2 (2, N = 31) = 26.92, p < 0.001, and that sham laser appeared to induce less pain.

Table 5.14: Levene's test of equality of error of needling pain VAS variances

F	df1	df2	Sig.
2.683	5	87	0.026

5.4 To compare and contrast the effects on needling sensation (*deqi*) of three interventions (needling intervention without manipulation, needling intervention with manipulation and sham laser) to the acupoint SI 3

In order to examine the influence of three different interventions on needling sensation (*deqi*) when needling SI 3, additional analyses were completed that involved the following comparisons:

1. Participants' perceptions of needle sensation (*deqi*) measured using the VAS score, comparing SI3m$^-$, SI3m$^+$ and SL (n = 31).

2. Participants' perceptions of needle sensation (*deqi*) measured using the MASS comparing SI3m$^-$, SI3m$^+$ and SL; (n = 31).

5.4.1 VAS needling sensation (*deqi*) scores

The reported mean VAS needling sensation scores (Table 5.15, Figure 5.7) were higher than those reported for VAS pain. Table 5.15 shows there were significant difference among interventions (p < 0.001) in VAS scores of *deqi* while there no significant difference between genders (p = 0.781) (refer to Table 5.16 and Figure 5.8).

Table 5.17 shows that the two SI 3 needling interventions produced similar mean VAS needling sensation scores for both the male and female participants (p > 0.05). Furthermore, when compared with SL, both SI3m$^-$ and SI3m$^+$ interventions produced significantly higher *deqi* VAS scores (p < 0.005).

Table 5.15: Mean scores of needling sensation (VAS)

Dependent Variable: *deqi* VAS

Intervention	Mean	Std. Deviation	n
SI3m$^-$	37.4	31.0	31
SI3m$^+$	45.0	27.6	31
SL	12.7	22.9	31

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	17751.189[a]	3	5917.063	7.835	< 0.001
Intercept	93263.469	1	93263.469	123.497	< 0.001
Intervention	17692.452	2	8846.226	11.714	**< 0.001**
Gender	58.738	1	58.738	0.078	0.781
Error	67211.972	89	755.191		
Total	178475.000	93			
Corrected Total	84963.161	92			

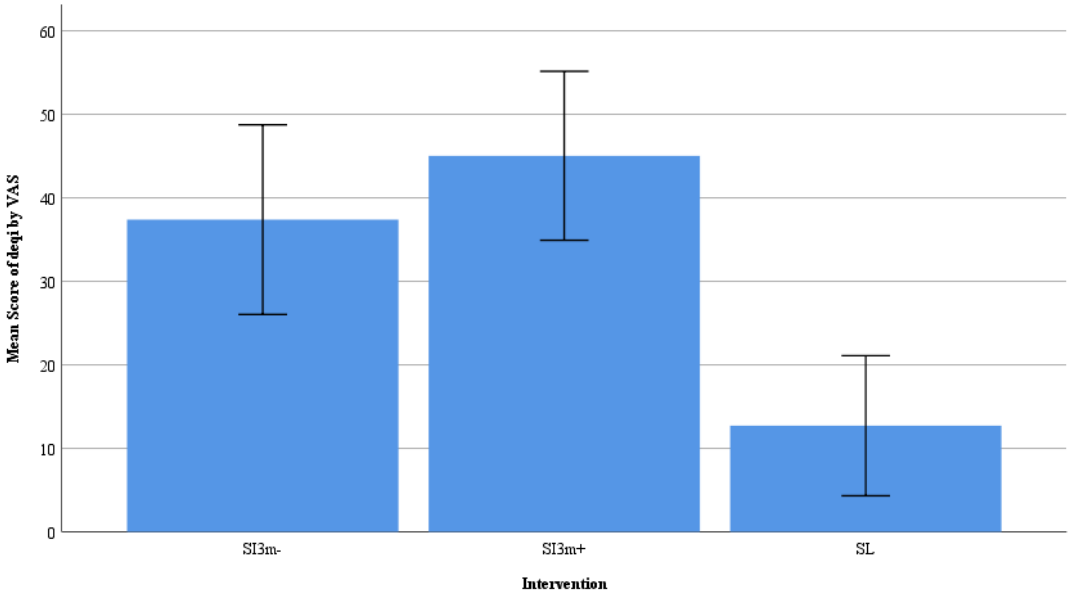


Figure 5.7: Means of *deqi* VAS

Table 5.26: Mean score of needling sensation (VAS) by gender

Gender	Intervention	Mean	Std. Deviation	n
Female	SI3m$^-$	33.9	30.3	16
	SI3m$^+$	50.1	19.2	16
	SL	13.4	21.7	16
Male	SI3m$^-$	41.1	32.3	15
	SI3m$^+$	39.7	34.3	15
	SL	11.9	24.8	15

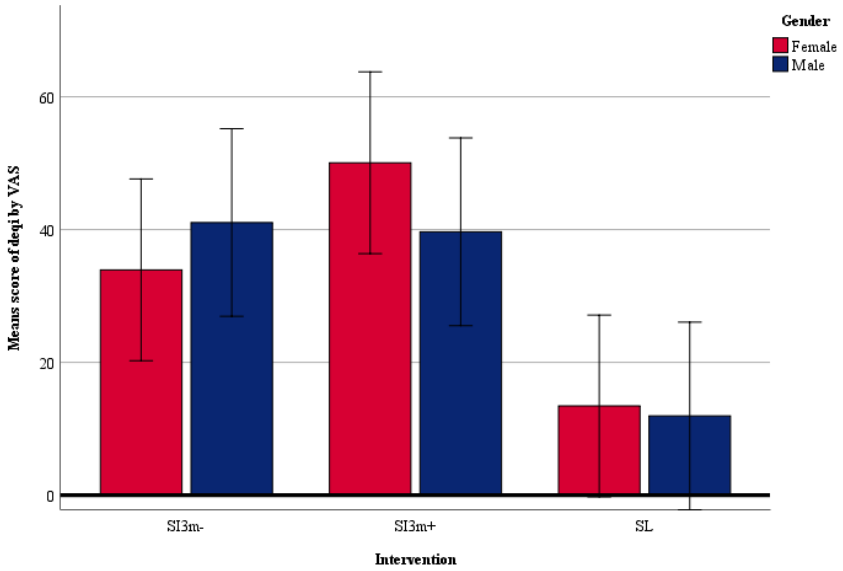


Figure 5.8: Means of *deqi* VAS by genders

Table 5.17 (Post Hoc Tests, Tukey) demonstrates that both acupuncture interventions resulted in statistically significant higher VAS *deqi* scores compared to sham laser ($p<0.002$ for both cases). As shown in Table 5.18 (Post Hoc Tests, Tukey) and Figure 5.8, when comparing both SI3m$^-$ and SL3m$^+$ with SL interventions, the male scores were significantly higher than the SL intervention ($p < 0.05$ in both cases), which was same as the combined gender comparison ($p < 0.05$). However, for the female scores there were no significant differences ($p > 0.05$) between SI3m$^-$ and SL ($p = 0.155$), only when comparing the SI3m$^+$ with SL interventions was there a statistically significantly higher scores ($p < 0.001$). There was no statistically difference when comparing the two needling interventions of SI3m$^-$ and SL3m$^+$ for the VAS of *deqi* scores for either gender ($p > 0.05$ in both cases).

Table 5.17: Comparison of mean VAS for needling sensation (*deqi*), each recorded on 100mm VAS by subjects for the 21 minutes of each of the three needling interventions

Intervention pair		Mean Difference	95% CI	p value
$SI3m^-$	$SI3m^+$	-7.7	-24.3 to 9.0	0.520
$SI3m^-$	**SL**	**24.7**	**8.0 to 41.3**	**0.002**
$SI3m^+$	**SL**	**32.3**	**15.7 to 49.0**	**< 0.001**

The confidence intervals (CI) and the adjusted p values from Post Hoc Tests are included. Statistical significant effects are shown in bold.

Table 5.18: Comparison of mean VAS for needling sensation (*deqi*), each recorded on 100mm VAS by subjects for the 21 minutes of each of the three needling interventions by gender

Intervention pair		Mean Difference	95% CI	p value
Male				
$SI3m^-$	$SI3m^+$	1.4	-25.9 to 28.7	1.000
$SI3m^-$	**SL**	**29.1**	**1.9 to 56.4**	**0.034**
$SI3m^+$	**SL**	**27.7**	**0.5 to 55.0**	**0.045**
Female				
$SI3m^-$	$SI3m^+$	-16.1	-36.9 to 4.6	0.155
$SI3m^-$	SL	20.5	-0.3 to 41.3	0.053
$SI3m^+$	**SL**	**36.6**	**15.9 to 57.4**	**< 0.001**

The confidence intervals (CI) and the adjusted p values from Post Hoc Tests are included. Statistical significant effects are shown in bold.

Given the thirty-one samples it was feasible to employ the two-way ANOVA without the homogeneity test for variance (refer to Section 5.2.2). Nevertheless, regarding the Table 5.19 ($p = 0.009$, $p < 0.05$), the data did not meet the stringent assumptions of a two-way ANOVA. Thus, it was decided that a Friedman test should be performed. The results from the Friedman test is similar to the ANOVA results, in that it did not reveal any statistical difference between $SI3m^-$ and $SI3m^+$ as well ($p = 0.465$).

Table 5.19: Levene's test of equality of error variances* of *deqi* (VAS)

Dependent Variable: *deqi* VAS

F	df1	df2	Sig.
3.301	5	87	0.009

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

* Design: Intercept + Intervention + Gender

The next section will compare *deqi* measured by MASS to see whether there is any different results compared to those from the VAS.

5.4.2 MASS *deqi* Index (MDI)

The calculation equation for the generation of the MDI by gender has been tabled in Section 4.12.5.3. Table 5.20 and Figure 5.9 show the mean MASS response for the three interventions in relation to MDI during the intervention period. The mean MDI scores ranged for the two needling interventions ranged from 3.3 to 4.9 while the sham laser intervention range was 1.2-1.7. Participants reported that the SI3m$^-$ and SI3m$^+$ interventions produced significantly greater MDI scores during the acupuncture intervention than sham laser to the acupoints ($p < 0.01$) (see Table 5.21). There were no significant differences in mean MASS measured between the SI3m$^-$ and SI3m$^+$ interventions ($p > 0.05$). Interestingly, no significant difference was observed in mean MDI scores among female subjects ($p > 0.05$). This was similar to the *deqi* VAS scores.

Table 5.20: Mean scores of MDI

Dependent Variable: MDI

Gender	Intervention	Mean	Std. Deviation	n
Male	SI3m$^-$	3.3	2.4	15
	SI3m$^+$	4.5	2.5	15
	SL	1.2	1.7	15
Female	SI3m$^-$	3.3	2.6	16
	SI3m$^+$	4.9	2.3	16
	SL	1.7	2.5	16

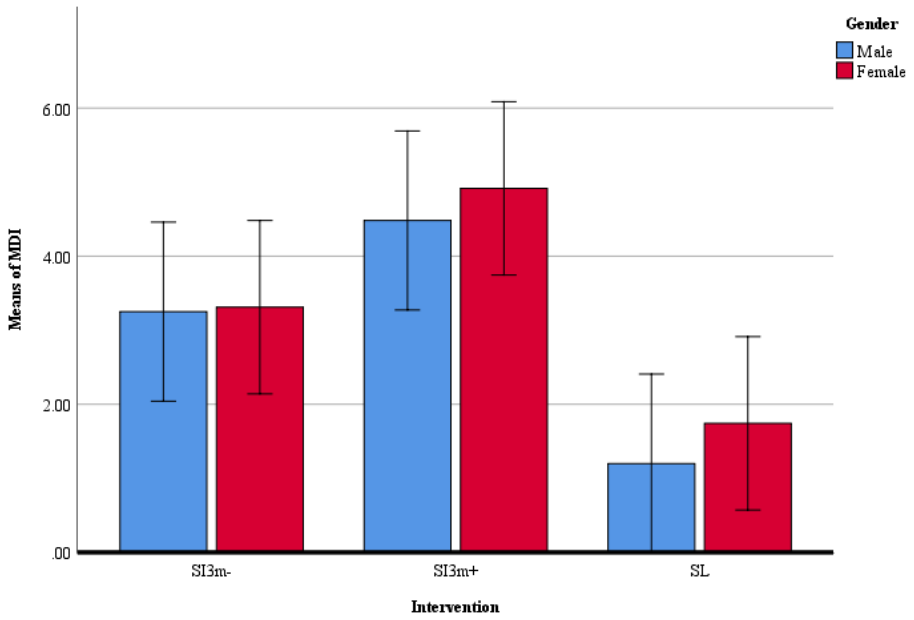


Figure 5.9: Mean MDI scores of the three interventions

Table 5.21: Comparison of mean MDI for the three needling interventions by gender

Intervention pair		Mean Difference	95% CI	p value
Male				
$SI3m^-$	$SI3m^+$	-1.2	-3.3 to 0.8	0.415
$SI3m^-$	**SL**	**2.1**	**0 to 4.1**	**0.047**
$SI3m^+$	**SL**	**3.3**	**1.3 to 5.3**	**0.001**
Female				
$SI3m^-$	$SI3m^+$	-1.6	-3.8 to 0.6	0.218
$SI3m^-$	SL	1.6	-0.6 to 3.7	0.237
$SI3m^+$	**SL**	**3.2**	**1.0 to 5.3**	**0.002**
Total				
$SI3m^-$	$SI3m^+$	-1.4	-2.9 to 0	0.055
$SI3m^-$	**SL**	**1.8**	**-0.4 to 3.2**	**0.009**
$SI3m^+$	**SL**	**3.2**	**1.8 to 4.7**	**0.0001**

The confidence intervals (CI) and the adjusted p values from Post Hoc Tests are included. Statistical significant effects are shown in bold.

As showed in Table 5.22 below, the difference in MID is the homogeneity test for variances are equal ($p > 0.05$). Therefore, two-way ANOVA was appropriate.

Table 5.22: Levene's test of equality of MDI error variances

		Levene Statistic	df1	df2	Sig.
MDI	Based on Mean	1.152	5	86	0.340
	Based on Median	0.576	5	86	0.718
	Based on Median and with adjusted df	0.576	5	79.701	0.718
	Based on trimmed mean	1.146	5	86	0.342

5.5 Other perceptions

This section explored the following four perceptions of participates in another questionnaire during three different interventions.

5.5.1 How did you feel during the treatment?

As shown in Table 5.23, compared to needling pain (Table 5.10) and needling sensation (Table 5.15), the participants' experience of "feeling tense" was much lower during the three interventions. Table 5.23 and Figure 5.10 show that participants felt tenser during

the needling interventions (18.3 and 17.2) compared to the sham laser (11.1) Table 5.24 demonstrates that the homogeneity of variance for "tense feeling" had not been violated ($p > 0.05$). Table 5.25 illustrates that the main effects for intervention are not significant ($p = 0.318$). Therefore, the type of intervention they received did not influence the sensation of "feeling tense" for the participants. Because there were no significant differences observed between the three groups ($p > 0.05$), post-hoc analyses were not required.

Table 5.23: Descriptive statistics of "feeling tense"

Intervention	Mean	Std. Deviation	n
SI3m$^-$	18.3	22.5	31
SI3m$^+$	17.2	18.2	31
SL	11.1	19.1	31

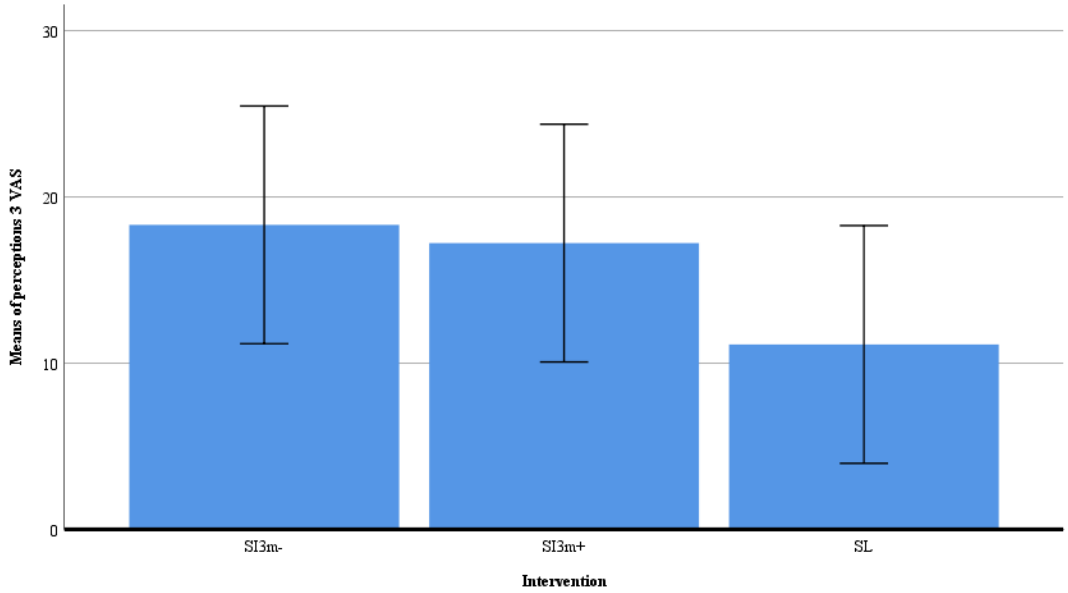


Figure 5.10: Mean VAS score concerning "feeling tense" during the three needling interventions

Table 5.24: Levene's test of equality of error variances[a,b] of "feeling tense"

		Levene Statistic	df1	df2	Sig.
Perceptions 3 VAS	Based on Mean	1.015	2	90	0.366
	Based on Median	0.736	2	90	0.482
	Based on Median and with adjusted df	0.736	2	76.345	0.482
	Based on trimmed mean	1.017	2	90	0.366

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Dependent variable: Perceptions 3 VAS

b. Design: Intercept + Intervention

Table 5.25: Analysis of Mean VAS scores regarding "feeling tense" during the three needling interventions

Dependent Variable: Perceptions 3 VAS

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	931.247[a]	2	465.624	1.160	0.318	0.025
Intercept	22514.075	1	22514.075	56.105	0.000	0.384
Intervention	931.247	2	465.624	1.160	0.318	0.025
Error	36115.677	90	401.285			
Total	59561.000	93				
Corrected Total	37046.925	92				

a. R Squared = 0.025 (Adjusted R Squared = 0.003)

5.5.2 Were you anxious about feeling pain from the intervention today?

Table 5.26 and Figure 5.11 show that the three interventions produced similar mean VAS scores for the participants' feeling of anxiety prior to receiving the interventions. The mean VAS scores of feeling anxious were much lower than needling pain, needling sensation and tense feeling (refer to Table 5.10. Table 5.15 and Table 5.23). Table 5.27 shows that the homogeneity of variance for the question associated with anxious was equal ($p > 0.05$). Table 5.31 illustrates that difference between the intervention was not significant ($p = 0.733$) regarding whether the participants felt anxious.

Since there was no significant differences between the three interventions ($p > 0.05$), post-hoc analyses were not required.

Table 5.26: Descriptive statistics of "feeling anxious" during the three interventions

Dependent Variable: Perceptions 4 VAS

Intervention	Mean	Std. Deviation	n
SI3m$^-$	7.5	14.3	31
SI3m$^+$	9.5	15.2	31
SL	6.6	15.8	31
Total	7.9	15.0	93

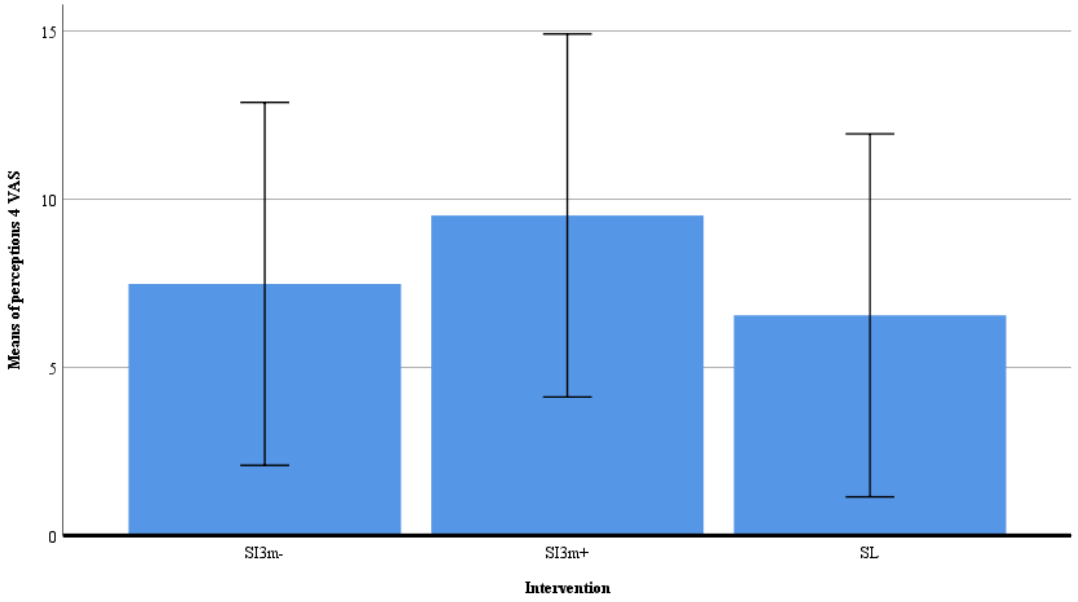


Figure 5.11: Mean score concerning anxiety feeling during the three needling interventions

Table 5.27: Homogeneity of variance anxiety feeling

				Levene Statistic	
Perceptions 4 VAS	Based on Mean			0.159	
	Based on Median			0.283	
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	142.731[a]	2	71.366	0.312	0.733
Intercept	5730.108	1	5730.108	25.067	< 0.001
Intervention	142.731	2	71.366	0.312	0.733
Error	20573.161	90	228.591		
Total	26446.000	93			
Corrected Total	20715.892	92			

5.6 Correlation amongst PPT, needling pain and *deqi*

5.6.1 Correlation between PPT and needling pain

5.6.1.1 Correlation between PPT and needling pain reported following SI3m$^-$ and SI3m$^+$

When the correlation for the two acupuncture interventions were combined and calculated, as seen from the scatterplots in Figure 5.12, there was no linear relationship between PPT and needling pain. Table 5.28 also shows the correlation coefficient and its associated significance value ($r = 0.158$, $p > 0.05$). Therefore, needling pain scores as reported using the VAS were not associated with higher mean percentage change of PPT for both acupuncture with manipulation and without manipulation.

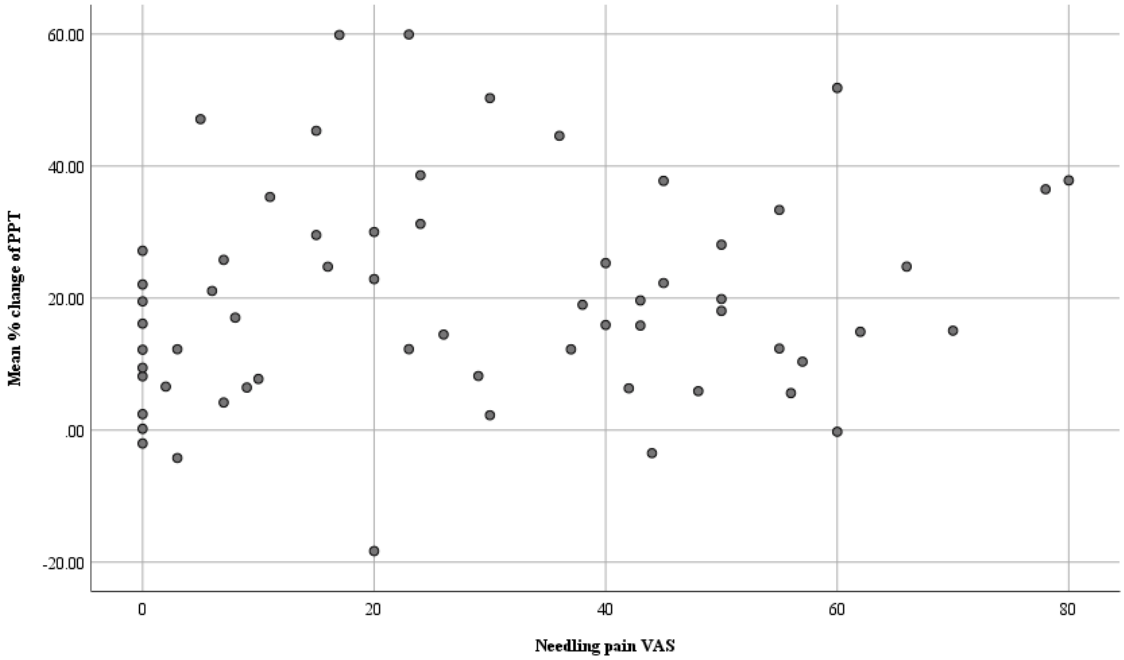


Figure 5.12: Scatterplots of relationship between PPT and needling pain by two different acupuncture interventions

Table 5.28: Correlations between PPT and needling pain by two acupuncture interventions

		mean % change of PPT	Needling Pain VAS
mean % change of PPT	Pearson Correlation	1	0.158
	Sig. (1-tailed)		0.108
	n	63	63
Needling Pain VAS	Pearson Correlation	0.158	1
	Sig. (1-tailed)	0.108	
	n	63	63

5.6.1.2 Correlation between PPT and needling pain by SI3m-

Figure 5.13 shows the relationship between PPT and needling pain when only acupuncture to SI 3 without manipulation was examined. These scatterplots demonstrate that there was no linear relationship between PPT and needling pain, which also can be seen in Table 5.29 ($r = 0.180$, $p > 0.05$). Thus, needling pain scores by VAS were not associated with higher mean percentage change of PPT.

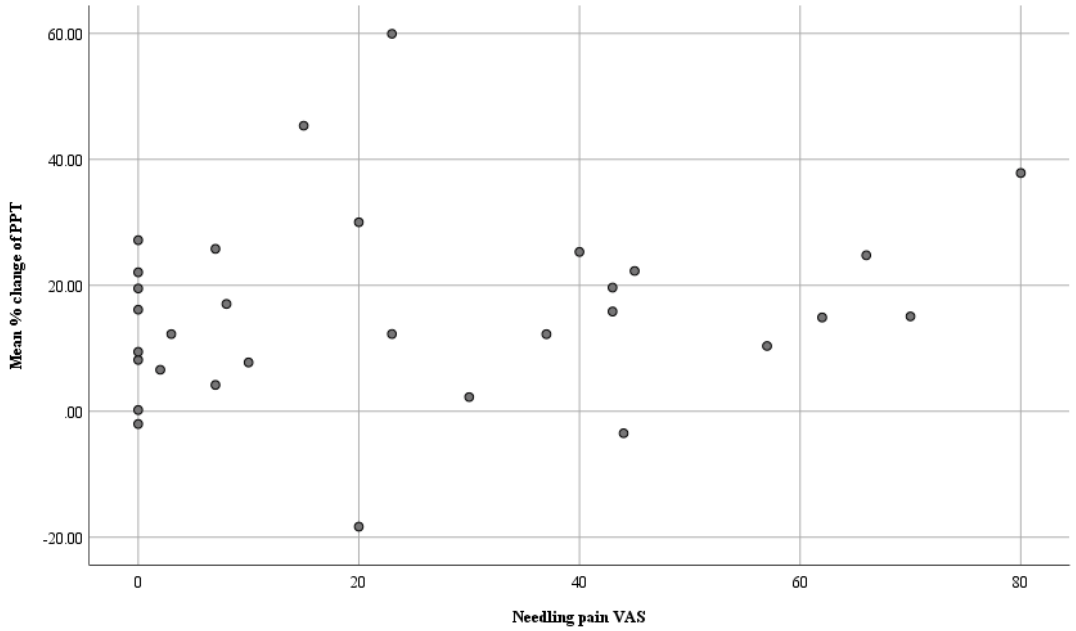


Figure 5.13: Scatterplots of relationship between PPT and needling pain by acupuncture intervention without manipulation

Table 5.29: Correlations between PPT and needling pain by acupuncture intervention without manipulation

		mean % change of PPT	Needling Pain VAS
mean % change of PPT	Pearson Correlation	1	0.180
	Sig. (1-tailed)		0.166
	n	31	31
Needling Pain VAS	Pearson Correlation	0.180	1
	Sig. (1-tailed)	0.166	
	n	31	31

5.6.1.3 Correlation between PPT and needling pain by SI3m^{+}

The scatterplots in Figure 5.14 shows there was no linear relationship ($r = 0.050$, $p > 0.05$) between PPT and needling pain when acupuncture on SI 3 with manipulation was examined (see Table 5.30).

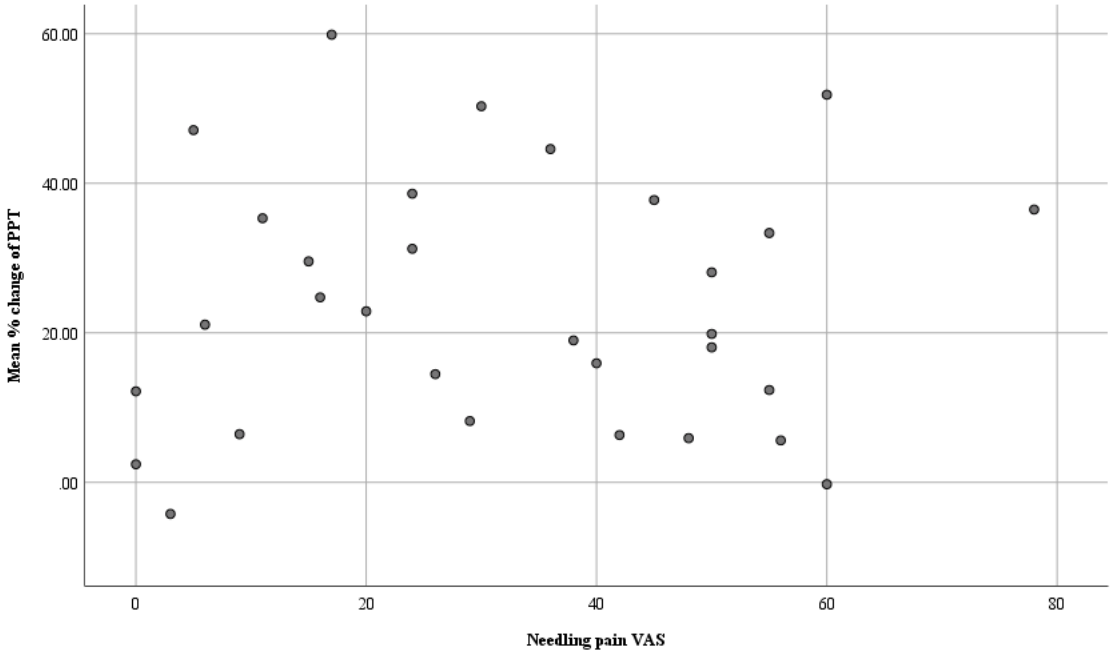


Figure 5.14: Scatterplots of relationship between PPT and needling pain by acupuncture intervention with manipulation

Table 5.30: Correlations between PPT and needling pain by acupuncture intervention with manipulation

		mean % change of PPT	Needling Pain VAS
mean % change of PPT	Pearson Correlation	1	0.050
	Sig. (1-tailed)		0.396
	n	31	31
Needling Pain VAS	Pearson Correlation	0.050	1
	Sig. (1-tailed)	0.396	
	n	31	31

5.6.2 Correlation between PPT and *deqi*

5.6.2.1 Correlation between PPT and *deqi* VAS

The scatterplots in Figure 5.15 shows a linear relationship between PPT and VAS score of *deqi* when both $SI3m^-$ and $SI3m^+$ are combined and examined. Table 5.31 reveals a significant positive relationship exists ($r = 0.384$, $p < 0.05$). Therefore, higher *deqi* scores by VAS are associated with higher mean percentage scores of PPT when both forms of acupuncture are combined. Table 5.35 illustrates the significant positive relationship exists between VAS of *deqi* and mean percentage change of PPT ($r = 0.265$, $p < 0.05$). Therefore, higher *deqi* scores by VAS are associated with higher mean % change of PPT if just two different acupuncture interventions are examined. Given that the mean percentage change of PPT clustered uniformly around the regression line, the assumption of homoscedasticity has not been violated. Table 5.36 interprets the correlation coefficient, which examined the coefficient and its associated significance value (p). The output confirms the results of the scatterplots in that significant positive relationship exists between the scores of *deqi* (VAS) and mean percentage change of PPT ($r = 0.265$, $p < 0.05$). Therefore, higher needling pain scores by VAS are associated with higher mean percentage change of PPT if two acupuncture interventions are examined.

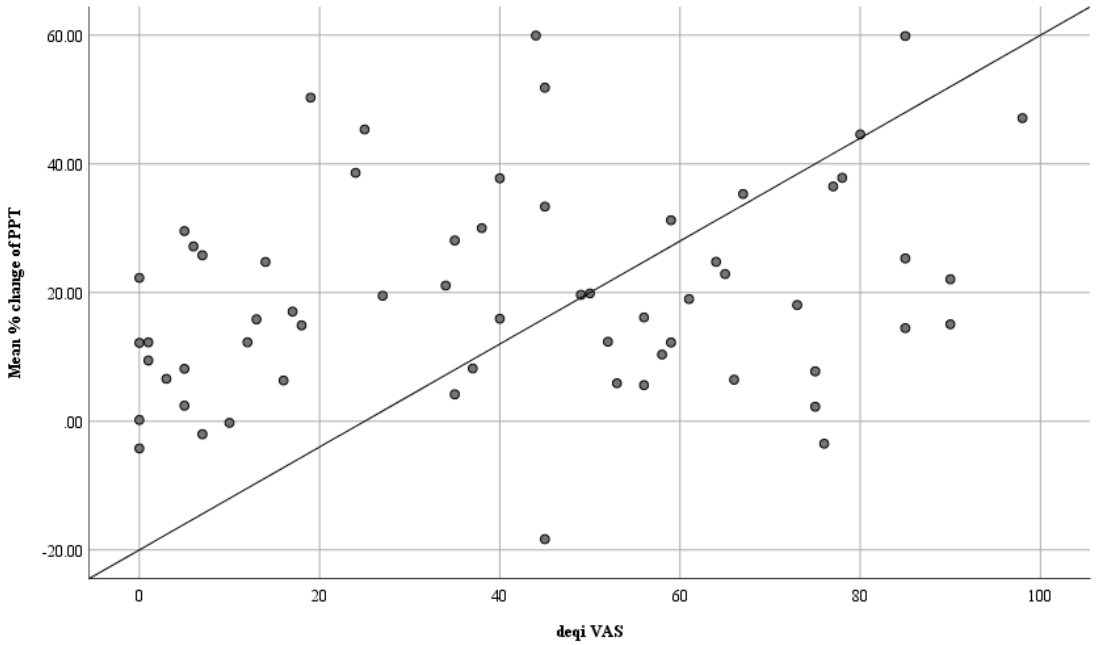


Figure 5.15: Scatterplots of relationship between PPT and *deqi* VAS by SI3m$^-$ and SI3m$^+$

Table 5.31: Correlations between PPT and *deqi* VAS by two acupuncture interventions

		mean % change of PPT	*deqi* VAS
mean % change of PPT	Pearson Correlation	1	0.265*
	Sig. (1-tailed)		**0.018**
	n	63	63
deqi VAS	Pearson Correlation	0.265*	1
	Sig. (1-tailed)	**0.018**	
	n	63	63

*. Correlation is significant at the 0.05 level (1-tailed).

When each of the two needling interventions was examined separately is was observed that there was no linear relationship between PPT and *deqi* score (VAS) for SI3m$^-$ (see Figure 5.16 and Table 5.32) but there was a relationship for SI3m$^+$ ($r = 0.398$, $p < 0.05$) (refer to Figure 5.17 and Table 5.33).

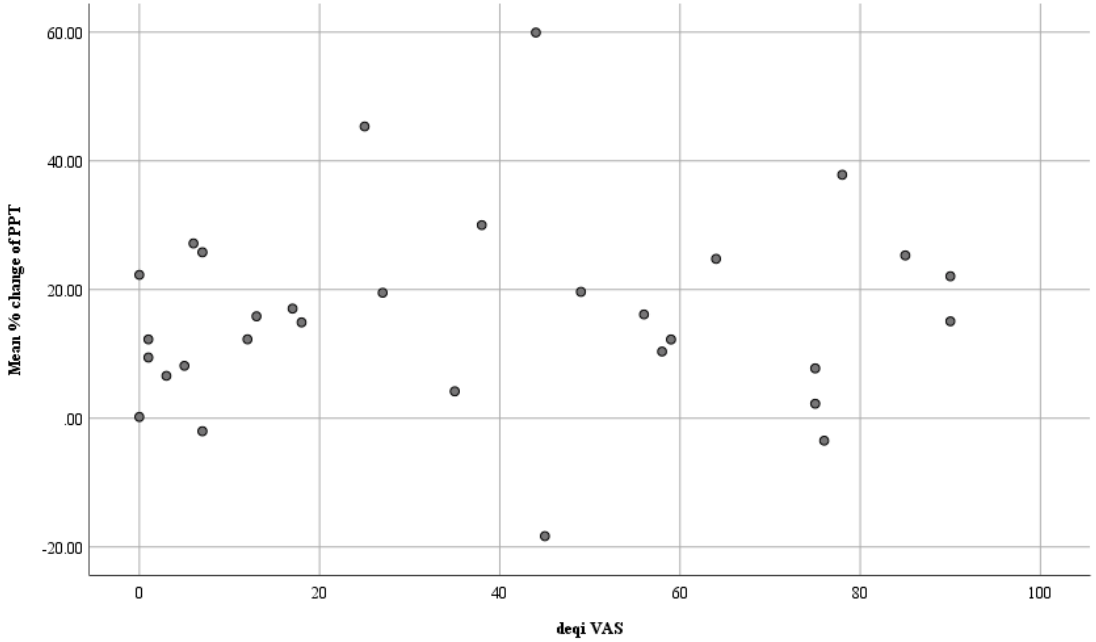


Figure 5.16: Scatterplots of relationship between PPT and *deqi* VAS by SI3m$^-$

Table 5.32: Correlations between PPT and *deqi* VAS by SI3m$^-$

		mean % change of PPT	*deqi* VAS
mean % change of PPT	Pearson Correlation	1	0.077
	Sig. (1-tailed)		0.340
	n	31	31
deqi VAS	Pearson Correlation	0.077	1
	Sig. (1-tailed)	0.340	
	n	31	31

However, when SI3m$^+$ is examined separately, the scatterplots in Figure 5.17 shows a linear relationship between PPT and score of *deqi* (VAS). Table 5.33 also verifies that the significant positive relationship exists between the mean % change of PPT and the scores of *deqi* measured by VAS ($r = 0.398$, $p < 0.05$), when only acupuncture on right SI 3 with manipulation is examined.

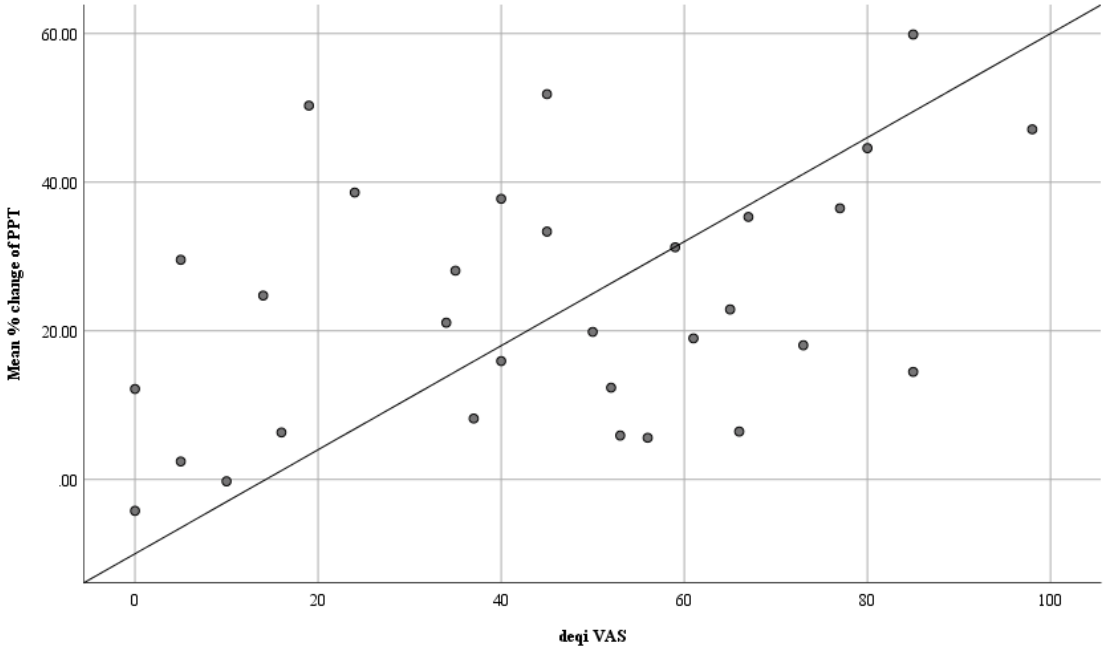


Figure 5.17: Scatterplots of relationship between PPT and *deqi* VAS by SI3m$^+$

Table 5.33: Correlation between PPT and *deqi* VAS by SI3m$^+$

		mean % change of PPT	*deqi* VAS
mean % change of PPT	Pearson Correlation	1	0.398*
	Sig. (1-tailed)		**0.013**
	n	31	31
deqi VAS	Pearson Correlation	0.398*	1
	Sig. (1-tailed)	**0.013**	
	n	31	31

*. Correlation is significant at the 0.05 level (1-tailed).

5.6.2.2 Correlation between PPT and MDI

A relationship was examined for mean% PPT changes and MDI, the scatterplots in Figure 5.18 shows a linear relationship when both SI3m$^-$ and SI3m$^+$ interventions are combined ($r = 0.233$, $p < 0.05$) (see Table 5.34).

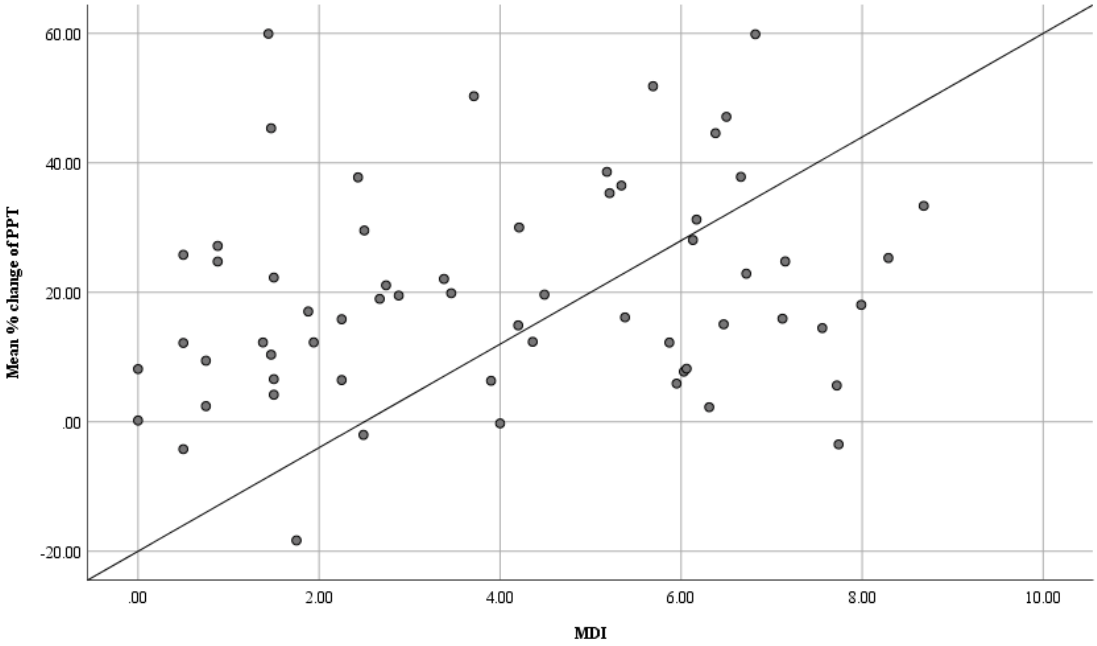


Figure 5.18: Scatterplots of relationship between PPT and *deqi* MDI in two acupuncture interventions

Table 5.34: Correlations between PPT and MDI by two acupuncture interventions

		mean % change of PPT	MASS Index
mean % change of PPT	Pearson Correlation	1	0.233*
	Sig. (1-tailed)		**0.033**
	n	63	63
MASS Index	Pearson Correlation	0.233*	1
	Sig. (1-tailed)	**0.033**	
	n	63	63

*. Correlation is significant at the 0.05 level (1-tailed).

However, the scatterplots assessing the relationship between mean % change of PPT and the MDI scores for the intervention of SI 3 without manipulation (Figure 5.19) does not show a linear relationship between mean % change of PPT and the scores of MDI ($r = 0.024$, $p > 0.05$) when acupuncture to right SI 3 without manipulation is examined separately (see Table 5.35).

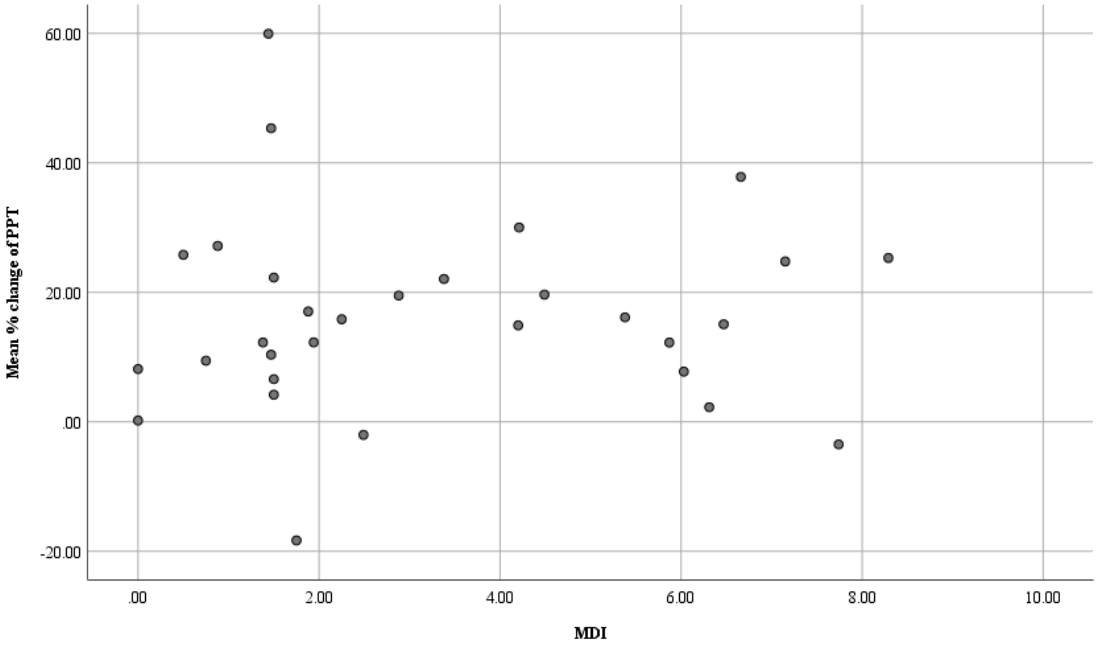


Figure 5.19: Scatterplots of relationship between PPT and MDI by SI3m-

Table 5.35: Correlations between PPT and MDI by SI3m-

		mean % change of PPT	MASS Index
Mean % change of PPT	Pearson Correlation	1	0.024
	Sig. (1-tailed)		0.449
	n	31	31
MASS Index	Pearson Correlation	0.024	1
	Sig. (1-tailed)	0.449	
	n	31	31

For the examination of the intervention of SI 3 with manipulation, the scatterplots (Figure 5.20) did show a linear relationship between mean % change of PPT and MDI. Table 5.36 shows the coefficient (r = 0.307) and the associated p value (0.046). Therefore, higher MID scores are associated with higher mean %PPT scores during acupuncture intervention with manipulation.

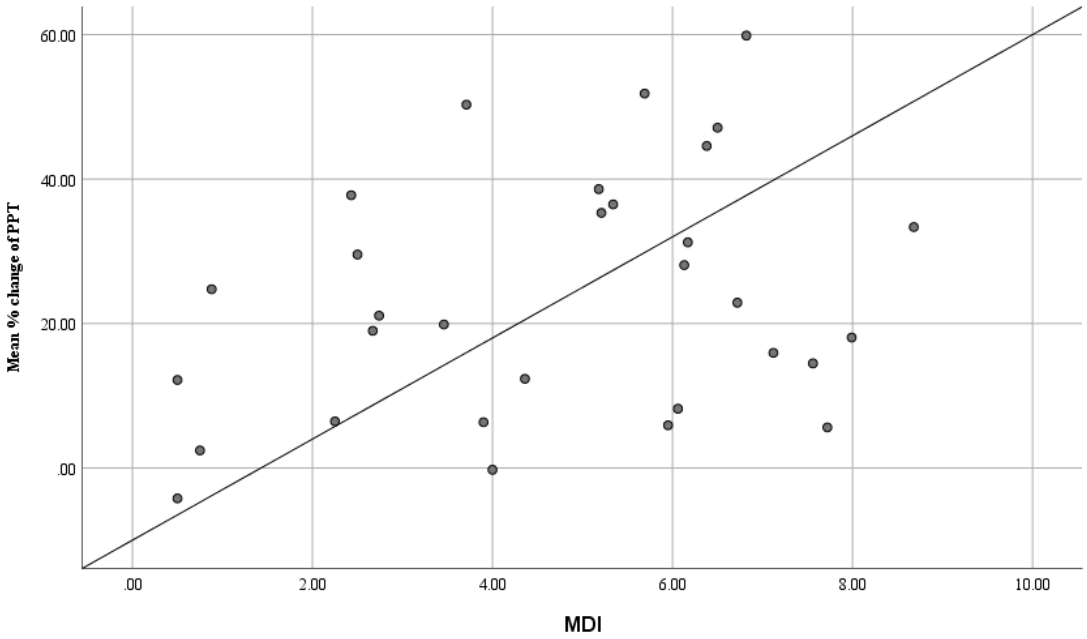


Figure 5.20: Scatterplots of relationship between PPT and MDI by SI3m$^+$

Table 5.36: Correlations between PPT and MDI by SI3m$^+$

		mean % change of PPT	MASS Index
Mean % change of PPT	Pearson Correlation	1	0.307*
	Sig. (1-tailed)		**0.046**
	n	31	31
MASS Index	Pearson Correlation	0.307*	1
	Sig. (1-tailed)	**0.046**	
	n	31	31

*. Correlation is significant at the 0.05 level (1-tailed).

5.6.3 Correlation between needling pain and *deqi*

5.6.3.1 Correlation between needling pain and *deqi* measured by VAS

Figure 5.21 is a scatterplots chart indicating a linear relationship between needling pain and *deqi* scores of VAS when SI3m$^-$, SI3m$^+$ interventions are combined. It can be seen (see Table 5.37 and Figure 5.21) that a significant positive relationship exists between needling pain and *deqi*. ($r = 0.397$, $p < 0.01$).

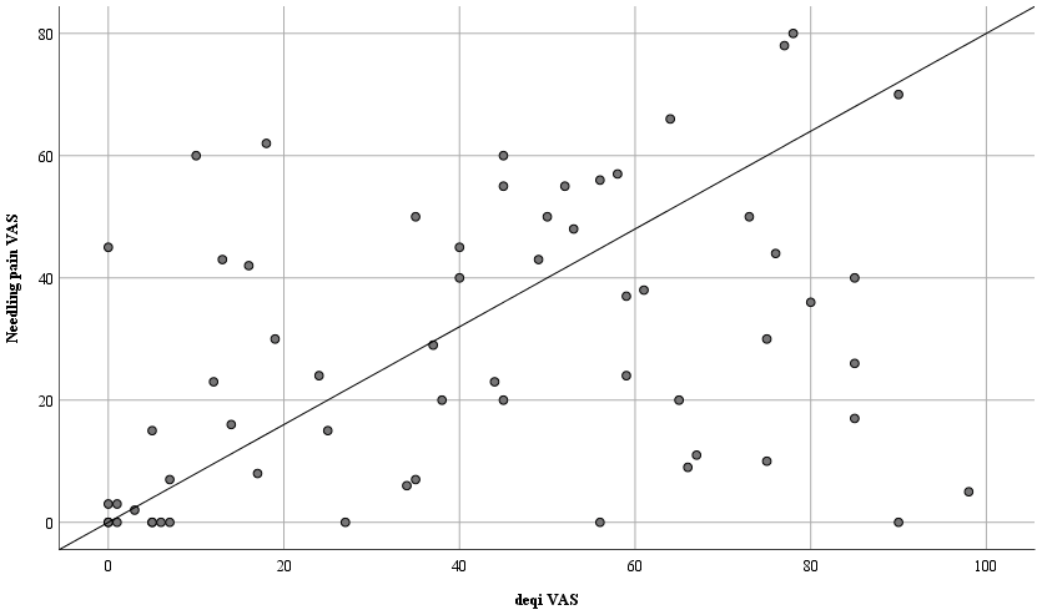


Figure 5.21: Scatterplots of relationship between needling pain and *deqi* VAS by acupuncture interventions – SI3m$^-$, SI3m$^+$

Table 5.37: Correlations between needling pain and *deqi* VAS by two acupuncture interventions – SI3m$^-$, SI3m$^+$

		deqi VAS	Needling pain VAS
deqi VAS	Pearson Correlation	1	0.397**
	Sig. (1-tailed)		**0.001**
	n	63	63
Needling pain VAS	Pearson Correlation	0.397**	1
	Sig. (1-tailed)	**0.001**	
	n	63	63

**. Correlation is significant at the 0.01 level (1-tailed).

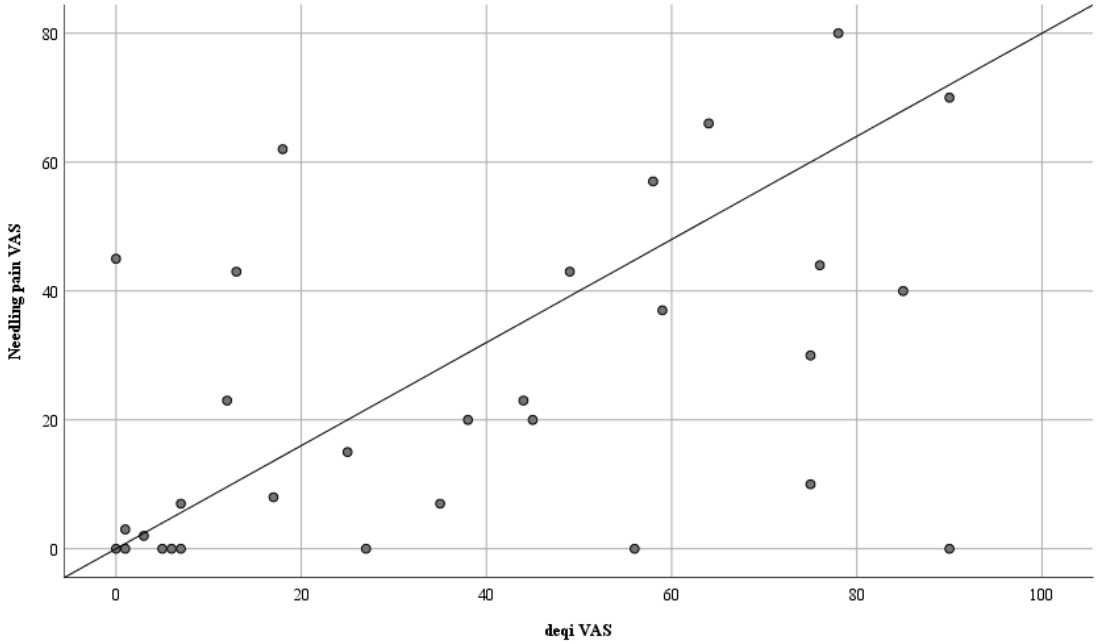


Figure 5.22: Scatterplots of relationship between needling pain and *deqi* VAS by acupuncture intervention – SI3m$^-$

Table 5.38: Correlations between needling pain and *deqi* VAS by acupuncture intervention – SI3m$^-$

		Needling pain VAS	*deqi* VAS
Needling pain VAS	Pearson correlation	1	0.494**
	Sig. (1-tailed)		**0.002**
	n	31	31
deqi VAS	Pearson correlation	0.494**	1
	Sig. (1-tailed)	**0.002**	
	n	31	31

**. Correlation is significant at the 0.01 level (1-tailed).

Similarly, a correlation for VAS of needling pain and *deqi* (see Figure 5.22 and Table 5.38), when only SI3m$^-$ is examined shows that a significant positive relationship exists between these two parameters ($r = 0.494$, $p < 0.05$).

However, for the acupuncture intervention of SI 3 with manipulation, there was no significant positive relationship between *deqi* and needling pain ($r = 0.199$, $p > 0.05$) (see Figure 5.23 and Table 5.39).

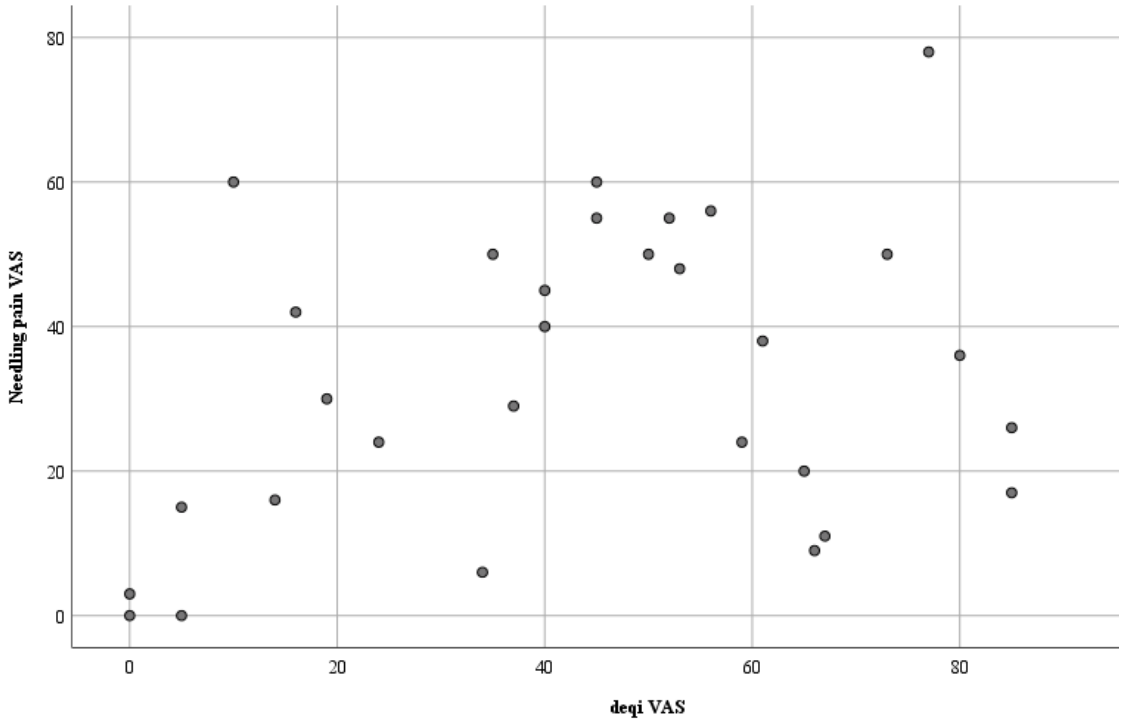


Figure 5.23: Scatterplots of relationship between needling pain and *deqi* VAS by acupuncture intervention – SI3m$^+$

Table 5.39: Correlations between needling pain and *deqi* VAS by acupuncture intervention – SI3m$^+$

		deqi VAS	Needling pain VAS
deqi VAS	Pearson Correlation	1	0.199
	Sig. (1-tailed)		0.142
	n	31	31
Needling pain VAS	Pearson Correlation	0.199	1
	Sig. (1-tailed)	0.142	
	n	31	31

5.6.3.2 Correlation between needling pain VAS and MDI

When SI3m$^-$and SI3m$^+$ are combined to examine if there is a relationship between VAS scores of needling pain and scores of MDI, a significant relationship was found ($r = 0.562$, $p < 0.001$) (see Figure 5.24 and Table 5.40) .

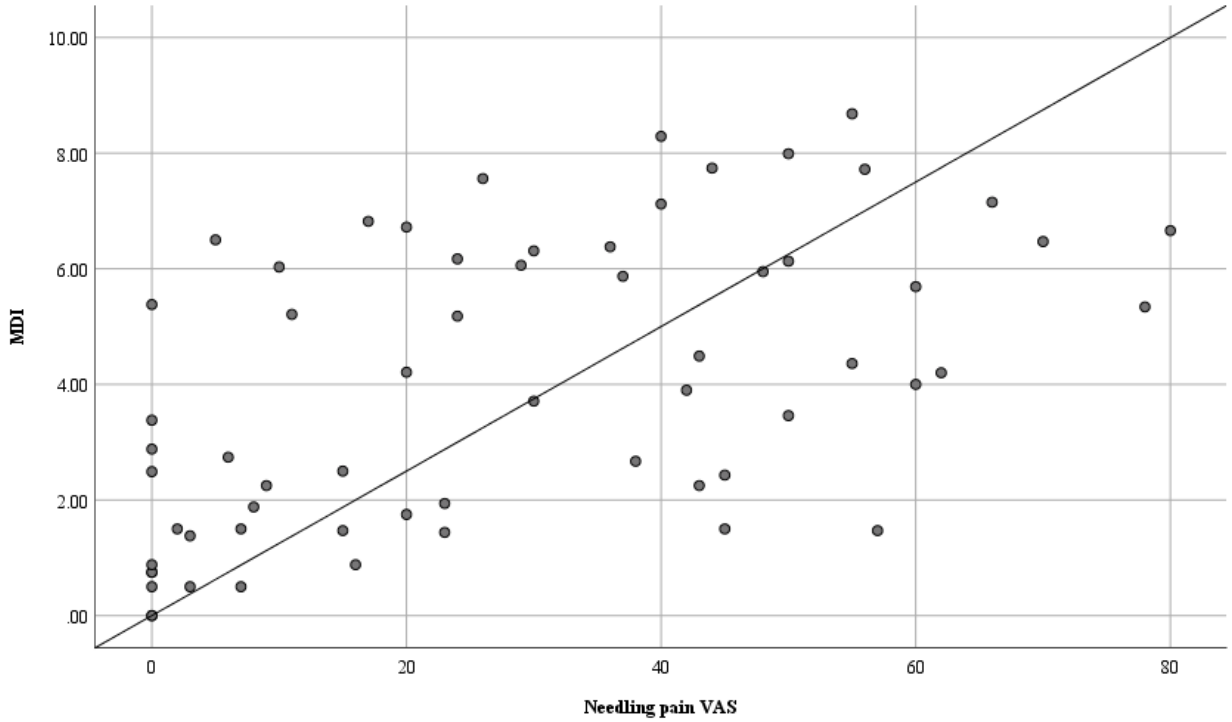


Figure 5.24: Scatterplots of relationship between needling pain and MDI by SI3m$^-$ and SI3m$^+$ interventions

Table 5.40: Correlations between needling pain and MDI by SI3m$^-$ and SI3m$^+$

		MASS Index	Needling Pain VAS
MASS Index	Pearson Correlation	1	0.562**
	Sig. (1-tailed)		**< 0.001**
	n	63	63
Needling Pain VAS	Pearson Correlation	0.562**	1
	Sig. (1-tailed)	**< 0.001**	
	n	63	63

**. Correlation is significant at the 0.01 level (1-tailed).

When only SI3m$^-$ was examined, a bivariate correlation was undertaken between needling pain VAS scores and MDI values (refer to Figure 5.25 and Table 5.41). It was hypothesised that a positive relationship would exist between these two variables. Results of the correlation indicate that higher scores of needling pain VAS were associated with higher MDI scores ($r = 0.585$, $p < 0.001$) for the SI3m$^-$ intervention.

Similarly, the scatterplots was attained for needling pain VAS scores and MDI scores for the SI3m$^+$ intervention indicating that assumptions of linearity and homoscedasticity were not violated (see Figure 5.26 and Table 5.42). A bivariate correlation was undertaken between these two parameters and it was hypothesised that a positive relationship would

exist between these two variables. Results of the correlation indicate that higher needling pain VAS scores were associated with higher MDI scores ($r = 0.464$, $p < 0.005$) for the SI3m^{+}intervention

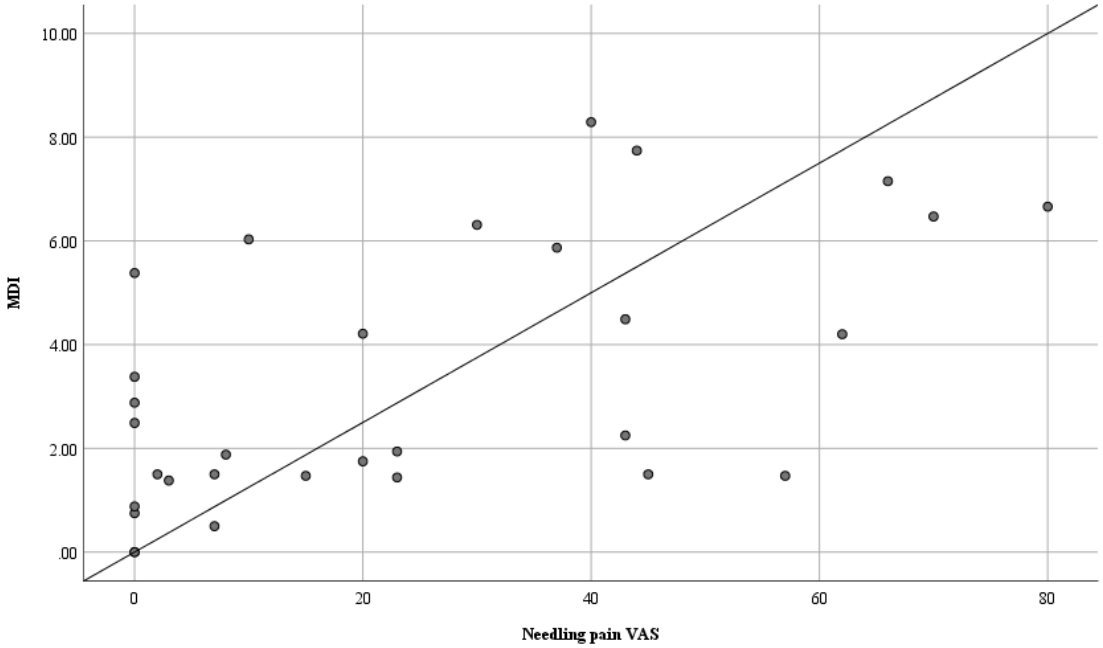


Figure 5.25: Scatterplots of relationship between needling pain and MDI by SI3m^{-} intervention

Table 5.41: Correlations between needling pain and MDI by SI3m^{-}

		Needling pain VAS	MDI
Needling pain VAS	Pearson Correlation	1	0.585**
	Sig. (1-tailed)		**< 0.001**
	n	31	31
MDI	Pearson Correlation	0.585**	1
	Sig. (1-tailed)	**< 0.001**	
	n	31	31

**. Correlation is significant at the 0.01 level (1-tailed).

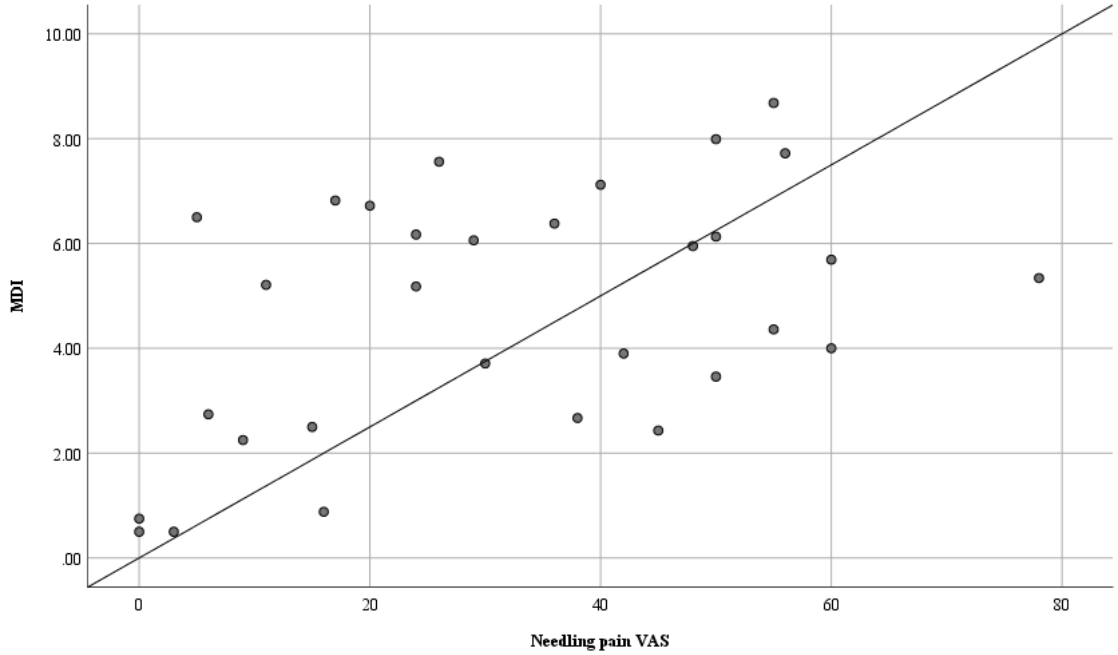


Figure 5.26: Scatterplots of relationship between needling pain and MDI by SI3m$^+$ intervention

Table 5.42: Correlations between needling pain and MDI by SI3m$^+$

		Needling Pain VAS	MDI
Needling pain VAS	Pearson Correlation	1	0.464**
	Sig. (1-tailed)		**0.004**
	n	31	31
MDI	Pearson Correlation	0.464**	1
	Sig. (1-tailed)	**0.004**	
	n	31	31

**. Correlation is significant at the 0.01 level (1-tailed).

5.6.4 Correlation between MDI and *deqi* VAS

First the two needling interventions combined (SI3m$^-$ and SI3m$^+$) were examined regarding potential correlation. As seen from the scatterplots, there was a linear relationship between the two measurements of *deqi* (refer to Figure 5.27). To interpret the correlation coefficient, the coefficient and its associated p value was tested. Table 5.43 shows t that there was a significant positive relationship between the two different measurements of *deqi* – the VAS *deqi* and the MDI.

Following this separate correlations were sought for the two needling interventions (SI3m$^-$ and SI3m$^+$). Both results of these correlation analyses indicate that higher *deqi*

VAS scores are associated with higher MDI scores (refer to Figure 5.28, Table 5.44, Figure 5.29 and Table 5.45).

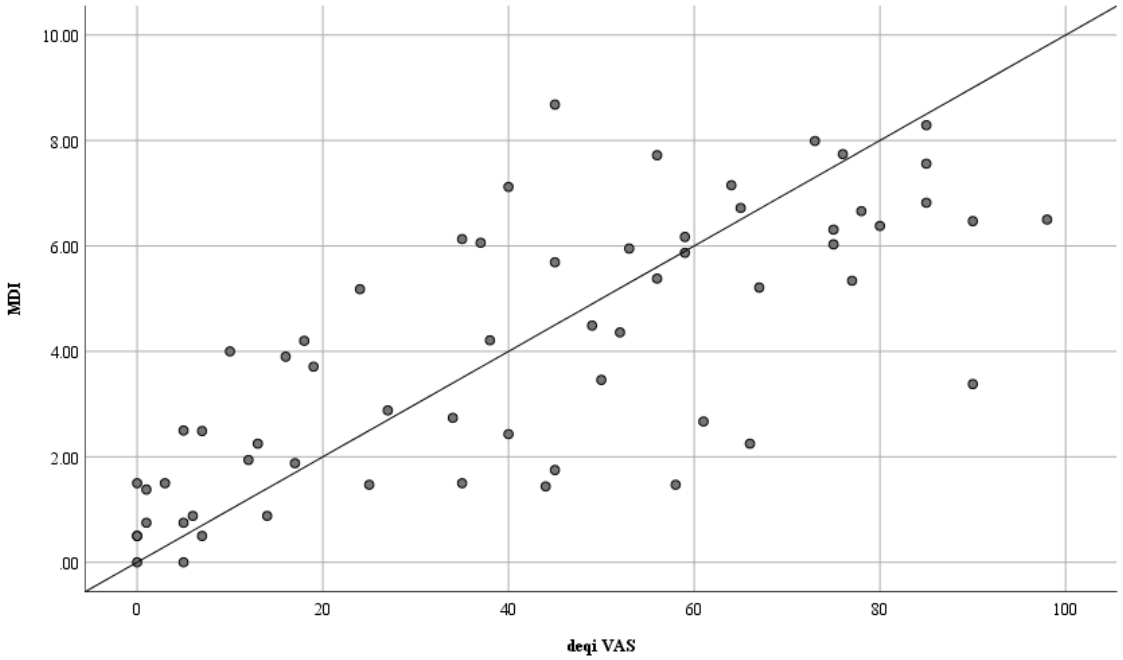


Figure 5.27: Scatterplots of relationship between MDI and *deqi* VAS by SI3m$^-$ and SI3m$^+$ intervention

Table 5.43: Correlations between MDI and *deqi* VAS by SI3m$^-$ and SI3m$^+$

		deqi VAS	MDI
deqi VAS	Pearson Correlation	1	0.747**
	Sig. (1-tailed)		**< 0.001**
	n	62	62
MDI	Pearson Correlation	0. 747**	1
	Sig. (1-tailed)	**< 0.001**	
	n	62	62

**. Correlation is significant at the 0.01 level (1-tailed).

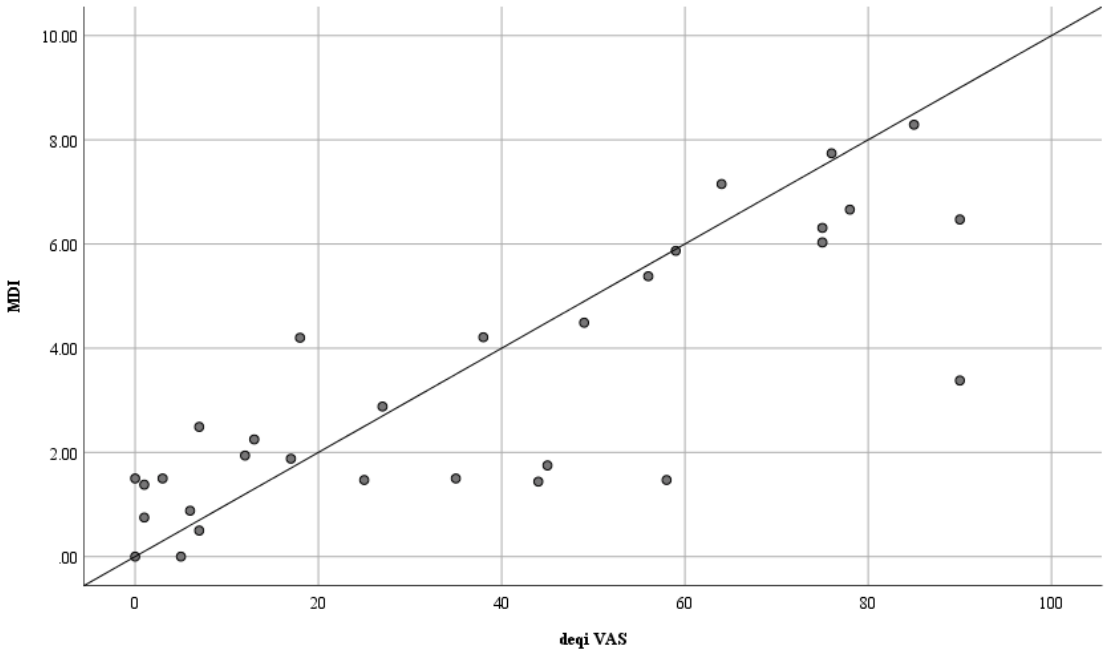


Figure 5.28: Scatterplots of relationship between MDI and *deqi* VAS by SI3m$^-$

Table 5.44: Correlations between MDI and *deqi* VAS by SI3m$^-$

		MDI	*deqi* VAS
MDI	Pearson Correlation	1	0.820**
	Sig. (1-tailed)		< 0.001
	n	31	31
deqi VAS	Pearson Correlation	0.820**	1
	Sig. (1-tailed)	< 0.001	
	n	31	31

**. Correlation is significant at the 0.01 level (1-tailed).

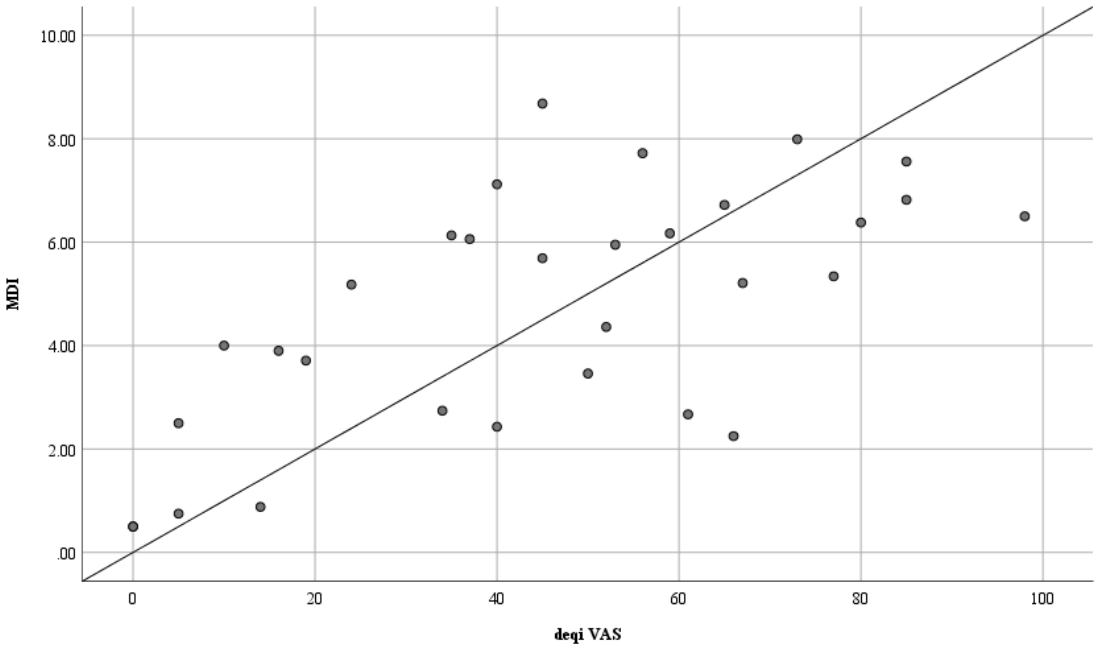


Figure 5.29: Scatterplots of relationship between MDI and *deqi* VAS by SI3m$^+$

Table 5.45: Correlations between MDI and *deqi* VAS by SI3m$^+$

		MDI	*deqi* VAS
MDI	Pearson Correlation	1	0.661**
	Sig. (1-tailed)		< 0.001
	n	31	31
deqi VAS	Pearson Correlation	0.661**	1
	Sig. (1-tailed)	< 0.001	
	n	31	31

**. Correlation is significant at the 0.01 level (1-tailed).

Chapter 6: Discussion and implications

6.1 Introduction

This was the first prospective manual acupuncture PPT study to the SI 3 acupoint, which was randomised, double-blinded, with a crossover controlled trial design conducted on healthy participants. The research objectives were to: (i) examine the role of needling the acupoint SI 3, situated on the right hand, on increasing PPT at ten regional sites (SI 11^{R}, SI 11^{L}, GV 4, GV 14, BL 60^{R}, BL 60^{L}, HT 7^{R}, HT 7^{L}, GB 21^{R}, GB 21^{L}) following three different interventions; (ii) examine the effects of needling the acupoint SI 3, situated on the right hand, on the intensity and quality of needling sensation (*deqi*); (iii) examine the role of needling the acupoint SI 3, situated on the right hand, on the intensity of pain associated with the interventions at the needling site (needling and sham laser). To support this aim two systematic reviews of RCTs in SI 3 and PPT, and a three arms prospective crossover trial were undertaken.

This thesis makes a significant contribution to the body concerning the influence of acupuncture therapy to the pain threshold. The findings from this body of work have shown that acupuncture to SI 3 may influence the regional PPT. The thesis findings demonstrate that:

1) Acupuncture to SI 3 can increase the regional PPT, acupuncture with manipulation could increase PPT more than the intervention without manipulation.
2) Acupuncture to SI 3 may increase the needling pain, while there would be no difference between with manipulation and without manipulation.
3) Acupuncture to SI 3 may induce *deqi* but no difference was found between the two needling interventions with needle manipulation and without needle manipulation.

6.2 Systematic reviews' key findings

The design of this three arms randomised crossover trial was dependent on the two systematic reviews of RCTs in Chapter 3 conducted prior to the development of the protocol for the clinical study.

The first systematic review was the first study to evaluate the clinical evidence of manual acupuncture to the acupoint SI 3 for pain syndromes. Forty-seven out of the 57 RCTs (82.5%) were of rated as high quality and 41 trials (71.9%) showed effective pain relief. The acupoint SI 3 could be an important therapy point in acupuncture pain management according to both ancient and modern Chinese medical texts, treating pain along the Small Intestine channel, Governor Vessel and Bladder channel. However, in all the acupoint prescriptions of the 57 RCTs SI 3 was combined with other acupoints. Moreover, it was unclear which side of the body SI 3 was selected for treatment and none of the studies measured *deqi*, a fundamental characteristic of acupuncture treatment (Hui et al 2007). The current study was designed to investigate the effects on the specific acupuncture point SI 3 solely, and evaluated the *deqi* as well.

The second systematic review identified 25 studies that employed PPT as a measurement following acupuncture treatment. These high quality trial demonstrated the high reliability and validity of algometry in assessing the PPT which can be applied in the investigation of acupuncture effectiveness. However, the relationship between PPT and other parameters of acupuncture treatment, such as *deqi*, is still uncertain.

Therefore, a randomised, crossover trial based on the findings of the two literature reviews were conducted.

6.3 Methodological discussion

First and foremost, this is a high quality RCT on acupuncture. Although it was not possible to blind the participating acupuncturist to the treatment, all important outcome measures were assessed independently being subject and assessor double-blind.

Additionally, PPT as an outcome measure in this study the stability, reliability and validity of the algometer should be of concern as the repeated pressure form PPT may potentially cause a change in the pain threshold. Fortunately, some studies (Gomes et al. 2008; Finocchietti et al. 2015) has showed that dynamic pressure algometry is a reliable equipment for evaluating pain threshold with high temporal and spatial resolution. The algometer can be applied as a simple clinical bed-side examination technique and as a quantitative measurement for research data collection. Furthermore, the following approaches had been adopted to reduce any potential errors of using the mechanical algometer:

1. Employment of a mechanical algometer which has been utilised by most researchers according to the systematic review (see Section 3.2).
2. The acupuncture clinic where the data was collected was a temperature controlled environment.
3. Prior to use, the algometer accuracy was verified with test weights.
4. Prior to each measure, the algometer was returned to zero.
5. The person measuring with the algometer had been well trained and had sufficient practiced to attain consistent pressure loading.

In order to minimize the influence of random errors, the mean of three measurements were obtained during the PPT tests.

6.4 Overview and summary of findings from the trial

This research project revealed the effects of needling the acupuncture point SI 3 on regional PPT, needling pain and *deqi*, using two needling interventions and a control sham intervention. This study also explored relationships between the acupuncture and PPT, and also evaluated needling pain and *deqi* in healthy participants.

The data for the reliability analysis suggests that agreement between observers is generally high, being slightly lower for high PPT values (Chesterton et al 2007). At UTS, Cheah's study (2015) reviewing the available raw PPT data from several studies supported the reliability and reproducibility of PPT in human experimental research. There were no strong or noticeable effects of age or BMI on regional PPT. However, his study result showed that data analysis on PPT should be completed separately by gender and experimental design for PPT between subjects should ensure a matched gender ratio across groups. Therefore, the data analyses of this thesis only considered the intervention approach, the regional body site and the gender due to the limited sample size. Moreover, the limited sample size only allowed the PPT data to be analysed by interventions and regional sites and excluded gender as a variable.

The overall effects on PPT of three interventions ($SI3m^-$, $SI3m^+$ and SL) to the acupoint SI 3 located on the right hand showed that acupuncture can significantly enhance the PPT at all ten selected regional sites. Respectively, for acupuncture without manipulation, site

GV4 obtained the most elevation of PPT while site $SI11^{L}$ attained the second highest PPT increase. On the contrary, for acupuncture with manipulation, the site $SI11^{L}$ obtained the highest increase of PPT, but site GV4 acquired the second highest elevation of PPT. Interestingly, the increase of PPT at site $HT7^{R}$ was the lowest, which is the closest measurement site to the needling area of SI 3. A possible explanation is acupuncture to the right SI 3 can elevate the human body's PPT universally, especially at site GV4 and contralateral site $SI11^{L}$, but has less influence to the close area and homolateral body regional site.

In general, acupuncture to the right SI 3 with manipulation can increase PPT significantly higher than acupuncture without manipulation ($p < 0.001$). However, when comparing the ten measurement sites, only $SI11^{R}$ showed a statistically significant difference between $SI3m^{-}$ and $SI3m^{+}$ ($p < 0.05$). It could be interpreted that acupuncture to SI 3 with manipulation can enhance PPT compared to without manipulation, especially on contralateral shoulder region.

The subjects were aware of significant needling pain when acupuncture needle was inserted to SI 3 on the right hand. Nevertheless, they were not conscious of the different extent of the needling pain between times when needled without manipulation and with manipulation. For males, the mean needling pain scores were similar to the combined gender needling pain scores. However, women did not feel significant difference between acupuncture without manipulation and sham laser regarding pain, which is different from what other studies have reported (Kok et al. 2015; Popescu et al. 2010). But the results should be interpreted with caution. Females might be more receptive to psychological bias. For example, in this study, subject No. 27 described her strong *deqi* sensation during sham laser intervention; and some female participants reported obvious pain during the sham laser intervention. Previous studies have explored whether gender differences in pain occur with the DNIC effects (Popescu et al. 2010) however, no study have investigated the implication of gender and psychological influence in modulating pain.

In the current double-blind experimental study, participants attained more *deqi* than needling pain, which may indicate the influence by DNIC. DNIC might have inhibited the experience of pain marginally compared to other needling sensations that were arising simultaneously. Interestingly this has been found in animal experiments (Murase & Kawakita 2000) but not in the human studies (Schliessbach et al. 2012). The comparison of intensity of *deqi* with needling pain were very similar. Moreover, it was the same

situation with respect to the two different measures of *deqi* – VAS and MASS. Therefore, it may not be necessary to assess *deqi* via MASS as MASS is a complex instrument for the measurement of *deqi*. It could be more practical and easier for participants in human experimental studies to measure *deqi* by using a VAS solely. The participants' experience of feeling tense and anxious were much lower than needling pain and did not differ significantly across the three interventions, which may indicate the safety of acupuncture. Regarding the four bilateral pairs of regional sites PPT measurement sites - $HT7^{R}$ and $HT7^{L}$, $SI11^{R}$ and $SI11^{L}$, $GB21^{R}$ and $GB21^{L}$, $BL60^{L}$ and $BL60^{R}$, it was found that PPT elevations on the left side regional sites were greater than the right side except for the site BL60. It is possible that this measurement site may have obtained higher PPT after repeated pressure measurements (Walton et al. 2011) in consideration of measurement procedures.

Since there was no correlation ($p > 0.05$) observed between PPT and needling pain, the penetration of an acupuncture needle by itself may not be sufficient to induce an analgesic effect mediated by DNIC. That may also mean that somatic pain may not be relieved merely by increasing needling pain. However, no relationship was observed between PPT and *deqi* if just a needle was inserted without manipulation while a significant positive relationship was found between PPT and *deqi* ($p < 0.05$) when the needle was manipulated. This might support the traditional concept of the importance of needle manipulation in acupuncture therapy. The same outcome was obtained for both the *deqi* VAS and *deqi* MDI scores. Regarding the correlation between needling pain and *deqi*, the positive relationship suggest that *deqi* is a somatic sensation that arises with, and is similar to, the sensation of pain. The positive linear relationship between MDI scores and *deqi* VAS scores highlights again that the VAS could substitute MASS in the measurement of *deqi*.

Strictly speaking, non-parametric statistical testing should be used for most of the data analysis reported in this study as the tests of homogeneity were not of equal variances. However, the ANOVA using a General Liner Model (GLM) may, and was, employed due to a sufficient number of participants ($n>30$) in this crossover study reported in this thesis. However at times both ANOVA (GLM) and non-parametric testing were applied in the date analysis of this study, and the results for both testing were similar in statistical testing of significance. Therefore, this decision of using the ANOVA (GLM) as the primary statistical test is supported. Both specificity analysis and sensitivity analysis was

conducted through the use of the ANOVA (GLM) and nonlinear models used in this research study.

6.5 Strengths of the Trial

The current research is unique when compared with previous studies of acupuncture from four aspects. First, this project was the first study concerning SI 3 as a single acupoint. It is surprising to find that no RCTs or pain studies using acupuncture to treat pain used the SI 3 acupoint as a single needling site as SI 3 is a commonly used acupoint in many pain treatment. Second, this trial was a randomised, double-blind (subject and assessor) crossover trial, which has addressed many important design features that could produce bias. The current study also introduces two different measures of *deqi* to determine the relationship between *deqi* and the effect on PPT following acupuncture to SI 3. Finally, the use of a sham laser acupuncture control intervention has minimised the non-specific effects on the study such as time tied effects. The choice of a non-invasive sham laser control also allowed a comparison between an invasive ($SI3m^{-}$) and a non-invasive control technique (SL) to SI 3.

In conclusion, this was the first time that the relationships between two different acupuncture interventions and needling pain and *deqi* have been investigated especially in regard to the acupoint site of SI3. It is hoped that these findings may contribute to further understanding of the mechanism of acupuncture in modulating pain.

6.6 Implications for Chinese medical theory

Although traditional Chinese acupuncture theory is based on philosophical premises and considered controversial, many researchers have been trying to integrate it into the modern medical system. In particular, to determine where needles are applied, what effect they have, and how the effect is achieved.

In the classical *Jingluo* (Ch: channels and collaterals) theory, the channel and collaterals are the pathways through which blood and *qi* flow, and the points are the important nodes on the pathways. Only following the insertion of an acupuncture needle in the specific acupoint can the specific channel be stimulated, thereby having therapeutic effect. However, modern biology has not discerned a reliable anatomical basis for the so-called

channel and acupoint. Since we don't know exactly what acupoints are, the effect of acupoint remains a question of dispute.

The previous research on LI 4 at UTS has found that PPT elevation was associated with needle insertion, needle retention and manipulation. This SI 3 relevant study also found that an increase of PPT was related to the needle penetration. However acupuncture with manipulation can increase PPT to a greater extent than acupuncture without manipulation. It appears that SI 3 is not only a general pain relief site for needling but also a specific effective acupoint for pain in the area around GV 4 (lower lumbar region) and contralateral SI 11 (upper lateral thoracic region), which supports the *Jingluo* theory of CM. Interestingly participant 13 expressed verbally obvious pain reduction when this site was pressed heavily. The primary indications for needling SI 3 should be pain relief along the Small Intestine channel, Governor Vessel and Bladder channel. The trial result looks be consistent with SI 3 being the meeting point of GV, one of the eight extraordinary channels. However, it is hard to confirm unless more PPT measurement sites could be assessed in the same channel.

According to the innervation of the spinal nerves (refer to Table 2.3), only the spinal nerves exiting between cervical vertebra 7 and thoracic vertebra 2 (C8 and T1) are related to the location of SI 3 on the hand. It appears that the effects of needling the acupuncture point *Houxi* (SI 3) on PPT, needling sensation and needling pain are not modulated by these spinal nerves as the PPT scores increased significantly across the body not just for the measurement sites within the dermatomes of the two spinal nerves exiting at C8 and T1.

The Chapter of The Nine Needles and the Twelve Origin" in the *Huang Di Nei Jing Ling Shu* recorded that "When the *qi* arrive, then this shows the effect" (Unschuld 2016, p. 46). It has been commonly understood that *deqi* means the arrival of *qi* at the needling site, although there are still different statements regarding the signs of *deqi* (Hao et al. 2015). In fact, *deqi* was first mentioned in the *Nanjing* (Eng: The Classic of Difficulties) (Bovey, 2006). Moreover, most statements recorded about *deqi* in the classical Chinese medical books over time, believed that the effectiveness of acupuncture will only have a positive benefit when *deqi* is elicited. Therefore, *deqi* became a necessary pursuit when administering acupuncture therapy in clinical practice. However, there remain still a considerable dispute about whether *deqi* is necessary (Bovey 2006). This study examined the 'dose' of *deqi* as one of the acupuncture variables and found a positive linear

correlation with PPT. The results suggest the elicitation of *deqi* is required for obtaining a therapeutic effect, although it could be a psychophysical response, not just a physical response, as *deqi* scores were recorded from participants receiving the sham laser.

6.7 Implications for practice

Acupuncture can be used as a non-pharmaceutical approach to treating for pain (Johnston 2013). Elevation of pain threshold may be one mechanism underlying this effect. This study investigated SI 3 as an important pain relief acupoint. The result of this project indicates that SI 3 can be utilised as a general acupoint to increase the PPT, which can reduce somatic pain across the body. However, the range of PPT scores that were increased at the regional sites across the human body were different. For example because of the specific increased effect demonstrated at the GV4 PPT measurement site (located on the lumbar spine) lower back pain could be specifically indicated rather than general body pain. Furthermore SI 3 had a better effect on increasing PPT at the contralateral measurement site of SI 11 therefore SI 3 may be specifically indicated for treating contralateral shoulder pain.

Furthermore, in order to obtain better pain modulation, needle manipulation is necessary during the acupuncture treatment. Finally, the elicitation of *deqi* is necessary for improving the pain relieving effects following acupuncture.

6.8 Limitations of the current study

Despite of the strengths and potential clinical benefits identified, there is some caution required when interpreting the conclusions drawn from the current study.

Firstly, the literature reviews were limited to those published in English. RCTs published in other languages have not been identified and assessed. These studies could have impacted on the reviews' conclusions.

Secondly, this project is a small sample size trial due to the limited time allocated time for the study. As a result, the validity of some outcomes may be questioned as a small sample size could over-estimate the results (van Der Boon et al. 2012). Moreover, the small number of participants in the study could not investigate the gender difference conclusively for the PPT outcomes.

Thirdly, the generalisation of the result may be limited because of the nature of it being a single centre study.

Furthermore, only 10 human body regional sites were selected for PPT measurement. More sites should be chosen if the traditional meridian theory needs to be further explored and eventually confirmed.

Additionally, because the study used healthy participants only, the findings cannot be extrapolated to a diseased population especially those with chronic pain.

Because of the large individual PPT differences observed, the acquired PPT data may display a degree of high dispersion. In this study, few people presented with very high pain thresholds that could produce bias (refer to Figure 5.1). Setting a standard PPT range to screen participants may solve this issue.

Another limitation relates to the sham laser placebo control. A deactivated laser device represents a suitable placebo intervention. However, placebo laser acupuncture does not mimic acupuncture, and it does not control for non-specific effects of needling. Consequently, it can only provide a partial answer to the question of efficacy. Furthermore, as the study is designed with a washout period of one week between interventions, there is always the possibility of some carry-over effect which cannot be ruled out completely.

Finally, PPT as the outcome measurement tool may not accurately detect a decrease in a participants who have a very low baseline PPT score (Walton et al. 2011). There are few people with very high pain thresholds and that could also produce a confounding effect (refer to Figure 5.1).

6.9 Recommendations for future research

Whereas, all the findings were regarding SI 3 in this study, more pain-related acupuncture points could be explored in the future based on the approach of this study. In particular, pain relevant *shu* points in five transport points system (Ch: *Wu Shu*) should be investigated. Kim et al. (2012) conducted an animal experiment to observe the changes in the expression of neurotransmitters, upon the needle insertion to the sea points (Ch: *he* point), which is one of the five transport points. The effect of needles applied at the *shu*

points of five transport points of the 12 acupuncture channels on the changes of PPT or functions of neurotransmitters could be observed in suggested for future studies.

Since the study shows a significant increase in PPT in the intervention groups compared to the control group, then it encourages researchers to replicate the study with patients with pain-related conditions.

In the future, the underlying mechanism of acupuncture for its pain modulating effects requires further careful and well-designed investigation. Dorsher (2020) claims that the current evidence supports neurologic basis of acupuncture signalling instead of perimuscular fascia, mechanical and paracrine/autocrine mechanisms. The internal world in human body deserves more investigation.

Chapter 7: Conclusion

In concluding this thesis, it may be stated that acupuncture to the acupoint *Houxi* (SI 3) can elevate the PPT and this study has further developed a standard operating procedure for studying regional PPT in future acupuncture human experimental studies.

Both intervention and site of needling were found to be important contributors to the effects on regional PPT in healthy participants. The effects on PPT at GV 4 & SI 11L measurement regions were more obvious. The study found a statistical difference in regional PPT measurement changes among the three interventions. The presence or absence of needle insertion was an important variable to the PPT and *deqi* measurement but did not influence the sensation of needling pain. The presence or absence of needle manipulation was an important variable for increasing PPT measures but had no influence on the intensity of needle sensation and pain experienced by the participants however there was a close relationships between the intensity of needling pain and needling sensation associated with PPT. The intervention of needling was also found to be the important contributor to the reporting of the intensity of *deqi*. However, the intensity of *deqi* reported by the participants was not significantly different between two different interventions ($SI3m^+$ and $SI3m^-$), however there was a significantly difference between genders to some extent.

This study has provided findings that support the common CM assumption or assertion that *deqi* is necessary for eliciting a therapeutic effect especially for pain syndromes. Therefore the measure of *Deqi* should become an important assessment tool in acupuncture RCTs to determine the adequacy of the acupuncture delivered in a study. We also found that the VAS is reliable measure to examine *deqi*, while the more complex and nuanced MASS instrument may not necessary be due to its time consuming completion requirement. In contrast we also reported that needling pain had no positive correlation with PPT changes. The intervention of needling was found to be an important contributor to the needling pain, however, the needling pain was not significantly different between the two different needling interventions, but was significantly different between genders to some extent. It is of interest to note that on several occurrences there were significant differences in needling pain and *deqi* sensation between male and female participants. For example, significant differences of needling pain and *deqi* were found between $SI3m^-$ and SL for male participants. In contrast, no difference was found between $SI3m^-$ and SL for

females. Further research is needed to confirm these observations. Therefore, needle pain is not necessary or essential for eliciting a pain modulating effect.

Finally this study did not find preferential PPT effects based on the segmental nervous system such as dermatomes (an area of skin innervated by a single spinal nerve root) or myotomes (a group of muscles innervated by a single spinal nerve root) regarding PPT, needling sensation and needling pain. The thesis finding also presents *deqi* as not only physiological but also psychological, thereby supporting the concept of *deqi* as a psychophysical response (Razavy et al. 2018). Acupuncture was shown to be safe in this study and no adverse events were reported. Similarly were no significant levels of participant tension or anxiety experienced by the participants. In conclusion, acupuncture therapy guidelines should be established for pain management in order to have a beneficial therapeutic result for both acute and chronic pain syndromes and potentially less financial costs and potentially less adverse side effects.

Clinical Significance

Finally the clinical significance of the current research is that it critically evaluates several key aspects of clinical practice. Firstly it confirms the clinical function of needling the acupoint SI 3 for modulating general body pain. Secondly it supports the role of *deqi* (needling sensation) due to its correlation with an increase in pain threshold. This suggests the attainment of *deqi* is a clinical needling requirement for pain relief. Finally it provides some evidence that there are differential pain modulating effects across body areas in that some areas obtained greater increases in pain threshold which primarily occurred at related channel acupoints on the Small Intestine and Governing Vessel. The ability of acupuncture to modulate pain is especially important as an alternative to opioid medication for pain. Acupuncture as a non-pharmaceutical intervention can have an important role in treating both acute and chronic pain. Just recently the NICE guidelines for chronic pain have recommended acupuncture as one of three interventions for longstanding pain (NICE 2021).

Reference List

Abd-Elsayed, A. & Deer, T.R. 2019, 'Different Types of Pain', in A. Abd-Elsayed (ed.), *Pain A Review Guide*, 1st edn, Springer Nature Switzerland AG, Cham, Switzerland, pp. 15-6.

Ahn, CB., Lee, SJ., Lee, JC., Fossion, J.P.J. & Sant'Ana. A. 2011, 'A clinical pilot study comparing traditional acupuncture to combined acupuncture for treating headache, trigeminal neuralgia and retro-auricular pain in facial palsy', *Journal of Acupuncture and Meridian Studies*, vol. 4, no. 1, pp. 29-43.

Aird, M. 2005, 'Variability in the precision of acupoint location methods', PhD thesis, Faculty of Science, University of Technology, Sydney.

Aird, M. Cobbin, D. & Rogers, C. 2002, 'A study of the comparative precision of traditional and contemporary methods of locating acupoints', *Journal of Alternative and Complementary Therapies*, vol. 8, no. 5, pp. 635-42.

Alam, A. & Juurlink, D.N. 2016, 'The prescription opioid epidemic: an overview for anesthesiologists', *Can J Anaesth*, vol. 63, no. 1, pp. 61-8.

Alecrim-Andrade, J., Maciel-Junior, JA., Cladellas, XC., Correa-Filho, HR. & Machado, HC. 2006, 'Acupuncture in migraine prophylaxis: a randomised sham-controlled trial', *Cephalalgia*, vol. 26, no. 5, pp. 520-9.

Appleyard, I. 2018, 'Use of acupuncture in the management of pain', *Nursing Standard*, vol. 33, no. 9, pp. 24-9.

Auteroche, B., Gervais, G., Auteroche, M., Navailh, P. & Toui-Kan, E. *Acupuncture and moxibustion:* a *guide to clinical practice*. Edinburgh; New York: Churchill Livingstone, 1992.

Bäcker, M., Grossman, P., Schneider, J., Knoblauch, N.T.M., Gareus, I.K., Hammes, M., Linde, K., Melchart, D. & Dobos, G.J. 2003, 'Vegetative reaction to acupuncture in migraineurs depends on the vagal tone before treatment: a randomised, controlled trial', *Focus on Alternative and Complementary Therapies*, vol. 8, no. 4, pp. 477-8.

B cker, M., Hammes, M.G. 2010, *Acupuncture in the treatment of pain : an integrative approach*, trans. D. Gustav, Churchill Livingstone, Edinburgh.Bahrami-Taghanaki, H., Liu, YM., Azizi, H., Khorsand, A., Esmaily, H., Bahrami, A. & Zhao, BX. 2014, 'A

randomised, controlled trial of acupuncture for chronic low-back pain', *Alternative Therapies in Health and Medicine*, vol. 20, no. 3, pp. 13-9.

Bai, L., Qin, W., Tian, J., Dong, M., Pan, X., Chen, P., Dai, J., Yang, W. & Liu, Y. 2009, 'Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks', *Brain Research*, vol. 1279, pp. 37-49.

Bannon, A.W. 2012, '*Pain therapeutics*', in J.E. Barrett, J.T. Coyle & M. Williams (eds), Translational Neuroscience: Applications in Psychiatry, Neurology, and Neurodevelopmental Disorders, Cambridge University Press, New York, pp. 168-77.

Barlas, P., Robinson, J., Allen, J. & Baxter, G.D. 2000, 'Lack of effect of acupuncture upon signs and symptoms of delayed onset muscle soreness', *Clinical Physiology*, vol. 20, no. 6, pp. 449-56.

Bauer, M., Bolash, B., Camardella, L., Koppelman, M.H., McDonald, J., Meade, L. & Miller, D.W. 2017, 'Acupuncture's Role in Solving the Opioid Epidemic: Evidence, Cost-Effectiveness, and Care Availability for Acupuncture as a Primary, Non-Pharmacologic Method for Pain Relief and Management White Paper 2017', The American Society of Acupuncturists, the American Alliance for Professional Acupuncture Safety, the Acupuncture Now Foundation, the American TCM Association, the American TCM Society & National Federation of TCM Organizations, pp. 1.

Bovey, M. 2006, 'Deqi', *the Journal of Chinese Medicine*, no. 81, pp. 18-29.

Brennum, J., Kjeldsen, M., Jensen, K. & Jensen, T. S. 1989, 'Measurements of human pressure-pain thresholds on fingers and toes', *Pain*, vol. 38, no. 2, pp. 211-7.

Brinkhaus, B., Witt, C.M., Jena, S., Linde, K., Streng, A., Irnich, D., Hummelsberger, J., Hammes, M., Pach, D. & Melchart, D. 2006, 'Interventions and physician characteristics in a randomised multicenter trial of acupuncture in patients with low-back pain', *Journal of Alternative & Complementary Medicine*, vol. 12, no. 7, pp. 649-57.

Brinkhaus, B., Witt, C.M., Jena, S., Linde, K., Streng, A., Wagenpfeil, S., Irnich, D., Walther, H.U., Melchart, D. & Willich, S.N. 2006, 'Acupuncture in patients with chronic low back pain: a randomised controlled trial', *Archives of Internal Medicine*, vol. 166, no. 4, pp. 450-7.

Carmichael, AN. Morgan, L. & Fabbro, E.D. 2016, 'Identifying and assessing the risk of opioid abuse in patients with cancer: an integrative review', *Subst Abuse Rehabil*, vol. 7, pp. 71-9.

Ceccherelli, F., Bordin, M., Gagliardi, G. & Caravello, M. 2001, 'Comparison between superficial and deep acupuncture in the treatment of the shoulder's myofascial pain: a randomised and controlled study' *Acupuncture & Electro-therapeutics Research*, vol. 26, no. 4, pp. 229-38.

Ceccherelli, F., Gioioso, L., Casale, R., Gagliardi, G., & Ori, C. 2010, 'Neck pain treatment with acupuncture: does the number of needles matter?' *The Clinical journal of pain*, vol. 26, no. 9, pp. 807-12.

Ceccherelli, F., Marino, E., Caliendo, A., Dezzoni, R., Roveri, A., & Gagliardi, G. 2014, '3,5,11 needles: looking for the perfect number of needles—a randomised and controlled study', *Acupuncture & Electro-therapeutics RES., INT. J.*, vol. 39, pp. 241-58.

Ceccherelli, F., Tortora, P., Nassimbeni, C., Casale, R., Gagliardi, G. & Giron, G. 2006, 'The therapeutic efficacy of somatic acupuncture is not increased by auriculotherapy: a randomised, blind control study in cervical myofascial pain', *Complementary Therapies in Medicine*, vol. 14, no. 1, pp. 47-52.

Chan, AW., Tetzlaff, J.M., Gotzsche, P.C., Altman, D.G., Mann, H., Berlin, J.A., Dickersin, K. Hróbjartsson, A., Schulz, K. F., Parulekar, W.R., Krleža-Jerić, K., Laupacis, A. & Moher, D. 2013, 'SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials', *BMJ: British Medical Journal*, vol. 346, pp. e7586.

Chapple, W. 2013, 'A Proposed Catalog of the Neuroanatomy and Stratified Anatomy for the 361 Acupuncture Points of the 14 Channel, *Journal of Acupuncture and Meridian Studies*, vol. 6, no. 5, pp. 270-4.

Cheah, S.L. 2015, 'An examination of subject variables that influence pressure pain threshold', PhD thesis, University of Technology Sydney.

Chen, XZ., Yang, YK., Yang, J., Yang, MX., Feng, SW., Hu, XJ., Luo, X., Feng, Y., Liang, FR. & Bai, LJ. 2013, 'Acupuncture Deqi intensity and propagated sensation along channels may, respectively, differ due to different body positions of subjects', *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, pp. 897048: 1-6.

Chen, YH., Lee, HJ., Lee, M.T; Wu, YT., Lee, YH., Hwang, LL., Hung, MS., Zimmer, A., Mackie, K. & Chiou, LC. 2018, 'Median nerve stimulation induces analgesia via orexin-initiated endocannabinoid disinhibition in the periaqueductal gray', *Proceedings of the National Academy of Sciences of the United States of America*, vol. 115, no. 45, pp. e10720-9.

Cheng, K.J. 2014, 'Neurobiological Mechanisms of Acupuncture for Some Common Illnesses: A Clinician's Perspective', *Journal of Acupuncture and Meridian Studies*, vol. 7, no. 3, pp. 105-14.

Chesterton, L.S., Barlas, P., Foster, N.E., Baxter, G.D. & Wright, C.C. 2003, 'Gender differences in pressure pain threshold in healthy humans', *Pain*, vol. 101, no. 3, pp. 259-66.

Chesterton, L.S., Sim, J., Wright, C.C. & Foster, N.E. 2007, 'Interrater reliability of algometry in measuring pressure pain thresholds in healthy humans, using multiple raters', *Clin J Pain*, vol. 23, no. 9, pp. 760-6.

Chiu, Y. H., Silman, A. J., Macfarlane, G. J., Ray, D., Gupta, A., Dickens, C., Morriss, R. & McBeth, J. 2005, 'Poor sleep and depression are independently associated with a reduced pain threshold. Results of a population based study', *Pain*, vol. 115, no. 3, pp. 316-21.

Cho, JH., Nam, DH., Kim, KT. & Lee, JH. 2014, 'Acupuncture with non-steroidal anti-inflammatory drugs (NSAIDs) versus acupuncture or NSAIDs alone for the treatment of chronic neck pain: an assessor-blinded randomised controlled pilot study', *Acupuncture in Medicine*, vol. 32, no. 1, pp. 17-23.

Choi, YJ., Lee, JE., Moon, WK. & Cho, SH. 2013, 'Does the effect of acupuncture depend on needling sensation and manipulation?' *Complementary Therapies in Medicine*, vol. 21, pp. 207-14.

Chu, L.S.W., Yeh, S.D.J. & Wood, D.D. 1979, *Acupuncture manual a western approach*, Marcel Dekker, New York, USA, pp. 51.

Coleman, K., Norris, S., Weston, A., Grimmer-Somers, K. & Hillier, S. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines, viewed on 11 May 2020, < https://www.mja.com.au/sites/default/files/NHMRC.levels.of.evidence.2008-09.pdf>.

Corti, R., Binggeli, C., Sudano, I., Spieker, L., Hänseler, E., Ruschitzka, F., Chaplin, W.F., Lüscher, T.F. & Noll, G. 2002, 'Coffee acutely increases sympathetic nerve activity and blood pressure independently of caffeine content. Role of habitual versus nonhabitual drinking', *Circulation: Journal of the American Heart Association*, vol. 106, no. 23, pp. 2935-40.

Coyle, M., Aird, M. Cobbin, D. & Zaslawski, C. 2000, 'The cun measurement system: an investigation into its suitability in current practice', *Acupuncture in Medicine*, vol. 18, no. 1, pp. 10-14.

Crew, K.D., Capodice, J.L., Greenlee, H., Apollo, A., Jacobson, J.S., Raptis, G., Blozie, K., Sierra, A. & Hershman, D.L. 2007, 'Pilot study of acupuncture for the treatment of joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients', *Journal of Cancer Survivorship*, vol. 1, no. 4, pp. 283-91.

Dang, W. & Yang, J. 1998, 'Clinical study on acupuncture treatment of stomach carcinoma pain', *Journal of traditional Chinese medicine*, vol. 18, no. 1, pp. 31-8.

Davis, M.E. & Hung, K. 1975, *Introduction to western acupuncture*, Lansdowne, Melbourne.

De Kooning, M., Tobbackx, Y., Meeus, M., Wauters, L., Ickmans, K., De Vilder, P., Roose, J., Verhaeghe, T. & Nijs, J. 2015, 'Acupuncture-analgesia following a single treatment session in chronic whiplash is unrelated to autonomic nervous system changes: a randomised cross-over trial', *Pain physician*, vol. 18, no. 6, pp. 527-36.

Deganello, A., Battat, N., Muratori, E., Cristofaro, G., Buongiorno, A., Mannelli, G., Picconi, M., Giachetti, R., Borsotti, G. & Gallo, O. 2016, 'Acupuncture in shoulder pain and functional impairment after neck dissection: a prospective randomised pilot study', *The Laryngoscope*, vol. 126, no. 8, pp. 1790-5.

Dohmen, K., Baraona, E., Ishibashi, H., Pozzato, G., Moretti, M., Matsunaga, C., Fujimoto, K. & Lieber, C.S. 1996, 'Ethnic differences in gastric σ-alcohol dehydrogenase activity and ethanol first-pass metabolism', *Alcoholism: Clinical and Experimental Research*, vol. 20, no. 9, pp. 1569-76.

Dorsher, P. 2020, 'Acupuncture signaling; Is it fascial or neurologic?', *Integrative Medicine Research*, vol. 9, no. Supplement 1, pp. 13.

Dulloo, A.G., Duret, C., Rohrer, D., Girardier, L., Mensi, N., Mensi, M., Chantre, P. & Vandermander, J. 1999, 'Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans', *The American Journal of Clinical Nutrition*, vol. 70, no. 6, pp. 1040-5.

Ernst, E. 2006, 'Acupuncture - a critical analysis', *Journal of Internal Medicine*, vol. 259, no. 2, pp. 125-37.

Escalona-Marfil, C., Coda, A., Ruiz-Moreno, J., Riu-Gispert, L.M. & Gironès, X. 2020, 'Validation of an electronic visual analog scale mhealth tool for acute pain assessment: prospective cross-sectional study', *Journal of Medical Internet Research*, vol. 22, no. 2, pp. e13468: 1-12.

Eshkevari, L. 2017, 'Acupuncture and chronic pain management', *Annual Review of Nursing Research*, vol. 35, pp. 117-34.

Finocchietti, S., Graven-Nielsen, T. & Arendt-Nielsen, L., 2015, 'Dynamic mechanical assessment of muscle hyperalgesia in humans: The dynamic algometer', *Pain Research & Management*, vol. 20, no. 1, pp. 29-34.

Fischer, A.A. 1987, 'Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold', *Pain*, vol. 30, no. 1, pp. 115-26.

Schliessbach, J., van der Klift, E., Siegenthaler, A., Arendt-Nielsen, L. Curatolo, M. & Streitberger, K., 2012, 'Does acupuncture needling induce analgesic effects comparable to diffuse noxious inhibitory controls?' Evidence-Based Complementary and Alternative Medicine, vol. 2012, pp. 785613:1-5.

Giesecke, T., Williams, D. A., Harris, R. E., Cupps, T. R., Tian, X., Tian, T. X., Gracely, R. H. & Clauw, D. J. 2003, 'Subgrouping of fibromyalgia patients on the basis of pressure-pain thresholds and psychological factors', *Arthritis & Rheumatism*, vol. 48, no. 10, pp. 2916-22.

Goldberg, D.S. & McGee, S.J., 2011, 'Pain as a global public health priority', *BMC Public Health*, vol. 11, no. 1, pp. 770-4.

Gomes, M.B., Guimarães, J.P., Guimarães, F.C. & Neves, A.C.C., 2008, 'Palpation and pressure pain threshold: reliability and validity in patients with temporomandibular

disorders', *CRANIO: The Journal of Craniomandibular Practice*, vol. 26, no. 3, pp. 202-10.

Goulden, E. A. 1921, 'The treatment of sciatica by galvanic acupuncture', *British Medical Journal*, vol. 1, no. 3145, pp. 523-4.

Goyal, R.N., Bishnoi, S. & Agrawal, B. 2011, 'Electrochemical sensor for the simultaneous determination of caffeine and aspirin in human urine samples', *Journal of Electroanalytical Chemistry*, vol. 655, no. 2, pp. 97-102.

Hao, J., Zhu, J., Zhang, P., Xin, SY., Qi, DD., Hu, NJ., Lin, C., Wang, P., Zhao, MY., Hu, SQ. & Wu, GW. 2015, 'Our viewpoints on Deqi in the later ages after birth of classical works "The Yellow Emperor's Internal Classic" and "Canon of Difficult Medical Problems"', *Acupuncture Research*, vol.40, no. 2, pp. 166-9.

Hawker, G.A., Mian, S., Kendzerska, T. & French, M. 2011, 'Measures of Adult Pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP)', *Arthritis Care & Research*, vol. 63, no. S11, pp. S240-S252.

He, D., Veiersted, K.B., Høstmark, A.T. & Medbø, J.I. 2004, 'Effect of acupuncture treatment on chronic neck and shoulder pain in sedentary female workers: a 6-month and 3-year follow-up', *Pain*, vol. 109, no. 3, pp. 299-07.

He, WJ., Zhao, X., Li, YQ., Xi, Q. & Guo, Y. 2012, 'Adverse Events Following Acupuncture: A Systematic Review of the Chinese Literature for the Years 1956–2010', *The Journal of Alternative and Complementary Medicine*, vol.18, no. 10, pp. 892-01.

Holdcroft, A. & Power, I. 2003, 'Management of pain', *BMJ (Clinical Research Edition)*, vol. 326, no. 7390, pp. 635-9.

Hoseinpour, S., Amanollahi, A., Sobhani, V., Mohseni, A. & Arazi, E. 2015, 'Comparison of neck and shoulder strengthening exercises with weights, traction plus physiotherapy, and acupuncture in the treatment of patients with chronic cervical disk herniation', *International Journal of Scientific Research in Knowledge*, vol. 3, no. 4, pp. 114-20.

Huang, WJ., Pach, D., Napadow, V., Park, K., Long, XY., Neumann, J., Maeda, Y., Nierhaus, T., Liang, FR., Witt, C.M. 2012, 'Characterizing acupuncture stimuli using brain imaging with fMRI - a systematic review and meta-analysis of the literature', *PLoS ONE*, vol. 7, no. 4, pp. e32960.

Huang-fu, M. *1994, Systematic classic of acupuncture and moxibustion (Zhenjiu Jiayi Jing)*, in S. Z. Yang, & C. Chace (trans), Blue Poppy Press, Boulder, CO, USA, pp. 182.

Hübscher, M., Vogt, L., Bernhörster, M., Rosenhagen, A. & Banzer, W. 2008, 'Effects of acupuncture on symptoms and muscle function in delayed-onset muscle soreness', *Journal of Alternative and Complementary Medicine*, vol. 14, no. 8, pp. 10181-16.

Hui, K.K., Nixon, E.E, Vangel, M.G., Liu, J., Marina, O., Napadow, V., Hodge, S.M., Rosen, B.R., Makris, N. & Kennedy, D.N. 2007, 'Characterization of the " *deqi* " response in acupuncture', BMC Complementary and Alternative Medicine, vol. 7, no. 33.

ICD-11 for Mortality and Morbidity Statistics (ICD-11 MMS) 2018 version https://icd.who.int/browse11/l-m/en <January13, 2019>

Ioannidis, J.P.A., Evans, S.J.W., Gøtzsche, P.C., O' Neill, R.T., Altman, D.G., Schulz, K. & Moher, D. 2004, 'Better reporting of harms in randomised trials: An extension of the consort statement', *Annals of Internal Medicine*, vol. 141, no. 10, pp. 781-8.

Irnich, D., Behrens, N., Gleditsch, J.M., Stör, W., Schreiber, M.A., Schöps, P., Vickers, A.J. & Beyer, A. 2002, 'Immediate effects of dry needling and acupuncture at distant points in chronic neck pain: results of a randomised, double-blind, sham-controlled crossover trial', *Pain*, vol. 99, no. 1-2, pp. 83-9.

Irnich, D., Cummings, M., Behrens, N., Molzen, H., König, A., Gleditsch, J., Krauss, M., Natalis, M., Senn, E., Beyer, A. & Schöps, P. 2001, 'Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain', *BMJ: British Medical Journal*, vol. 322. No. 7302, pp. 1574-9.

Itoh, K., Katsumi, Y., Hirota, S. & Kitakoji, H. 2007, 'Randomised trial of trigger point acupuncture compared with other acupuncture for treatment of chronic neck pain', *Complementary Therapies in Medicine*, vol. 15, no. 3, pp. 172-9.

Itoh, K., Minakawa, Y. & Kitakoji, H. 2011, 'Effect of acupuncture depth on muscle pain', *Chinese Medicine*, vol. 6, no. 1, pp. 6-24.

Johnston, S.L. 2013, 'Acupuncture & Pain', Paraplegia News, vol. 67, no. 2, pp. 13.

Johnston, M.F., Hays, R.D., Subramanian, S.K., Elashoff, R.M., Axe, E.K., Li, JJ., Kim, I., Vargas, R.B., Lee, J. & Yang, L. 2011, 'Patient education integrated with acupuncture for relief of cancer-related fatigue randomised controlled feasibility study', *BMC Complementary and Alternative Medicine*, vol. 11, no. 1, pp. 1-9.

Kang, KW., Kim, WY., Kim, TH., Shin, BC., Jung, SY., Kim, AR. & Choi., SM. 2012, 'Adjacent, distal, or combination of point-selective effects of acupuncture on temporomandibular joint disorders: A randomised, single-blind, assessor-blind controlled trial', *Integrative Medicine Research*, vol. 1, no. 1, pp. 36-40.

Kang, SH., Kim, YK., Yeom, M., Lee, H., Jang, H., Park, HJ. & Kim, K. 2018, 'Acupuncture improves symptoms in patients with mild-to-moderate atopic dermatitis: A randomised, sham-controlled preliminary trial', *Complementary Therapies in Medicine*, vol. 41, pp. 90-8.

Kaplan, G. B., Greenblatt, D. J., Ehrenberg, B. L., Goddard, J. E., Cotreau, M. M., Harmatz, J. S. & Shader, R. I. 1997, 'Dose dependent pharmacokinetics and psychomotor effects of caffeine in humans', *The Journal of Clinical Pharmacology*, vol. 37, no. 8, pp. 693-03.

Karsta, M., Rollnikb, J. D., Finkc, M., Reinharda, M. & Piepenbrocka, S. 2000, 'Pressure pain threshold and needle acupuncture in chronic tension-type headache - a double-blind placebo-controlled study', *Pain*, vol. 88, pp. 199-03.

Kim, HJ., Yang, GS., Greenspan, J.D., Downton, K.D., Griffith, K.A., Renn, C.L., Johantgen, M. & Dorsey, S.G. 2017, 'Racial and ethnic differences in experimental pain sensitivity: systematic review and meta-analysis', *Pain (Amsterdam)*, vol. 158, no. 2, pp. 194-211.

Kim, KH., Kim, YR., Baik, SK., Noh, SH., Kim, DH., Lee, SW. & Yang, GY. 2016, 'Acupuncture for patients with lumbar spinal stenosis: a randomised pilot trial', *Acupuncture in Medicine*, vol. 34, no. 4, pp. 267-75.

Kim, YS., Choi, DH., Choi, TJ., Jang, HS., Na, CS., Tae, SH., Lee, KI., Kim, SM., Pyo, BS. & Yoon, DH. 2012, 'Effects of acupuncture at the sea point on the changes of plasma and tissue levels of NO, nNOS, norepinephrine in rats', Korean Journal of Acupuncture, vol. 29, no. 2, pp. 300-14.

Kinser, A.M.,Sands, W.A. & Stone, M.H. 2009, 'Reliability and Validity of a Pressure Algometer', *Journal of Strength and Conditioning Research*, vol. 23, no. 1, pp. 312-4.

Kizhakkeveettil, A., Rose, K.A., Kadar, G.E. & Hurwitz., E.L. 2017, 'Integrative acupuncture and spinal manipulative therapy versus either alone for low back pain: a randomised controlled trial feasibility study', *Journal of Manipulative and Physiological Therapeutics*, vol. 40, no. 3, pp. 201-13.

Kleinhenz, J., Streitberger, K. Windeler, J. Güßbacher, A. Mavridis, G. & Martin, E. 1999, 'Randomised clinical trial comparing the effects of acupuncture and a newly designed placebo needle in rotator cuff tendinitis', *Pain*, vol. 83, no. 2, pp. 235-41.

Kok, M.M., van der Heijden, L.C., Sen, H., Löwik, M.M., Anthonio, R., Louwerenburg, H.W., de Man, F.H., Linssen, G.C., Ijzerman, M.J., Doggen, C.J., Maas, A.H., Mehran, R. & von Birgelen, C. 2015, 'Gender difference in chest pain after implantation of newer generation coronary drug-eluting stents: a patient-level pooled analysis from Twente and Dutch peers', *Journal of the American College of Cardiology*, vol. 66, no. 15, pp. Suppl B242.

Kong, J., Fufa, D.T., Gerber, A.J., Rosman, I.S., Vangel, M.G., Gracely, R.H. & Gollub, R.L. 2005, 'Psychophysical outcomes from a randomised pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain', *The Journal of Pain*, vol. 6, no. 1, pp. 55-64.

Kong, J., Gollub, R., Huang, T., Polich, G., Napadow, V., Hui, K., Vangel, M., Rosen, B. & Kaptchuk, T.J. 2007, 'Acupuncture *de qi*, from qualitative history to quantitative measurement', *The Journal of Alternative and Complementary Medicine*, vol. 13, no. 10, pp. 1059-70.

Kosek, E. & Ekholm, J. 1995, 'Modulation of pressure pain thresholds during and following isometric contraction', *Pain*, vol.61, no. 3, pp. 481-6.

Kumnerddee, W. 2009, 'Effectiveness Comparison between Thai Traditional Massage and Chinese Acupuncture for Myofascial Back Pain in Thai Military Personnel: A Preliminary Report', *J Med Assoc Thai*, vol. 92, suppl. 1, pp.s117-23.

Kvorning, N., Holmberg, C., Grennert, L., Åberg, A. & Åkeson, J. 2004, 'Acupuncture relieves pelvic and low-back pain in late pregnancy', *Acta Obstet Gynecol Scand*, vol. 83, no. 3, pp. 246-50.

Kwak, HY., Kim, JI., Park, JM., Lee, SH., Yu, HS., Lee, JD., Cho, KH., Katai, S., Tsukayam, H., Kimurad, T. & Choi, DY. 2012, 'Acupuncture for whiplash-associated disorder: a randomised, waiting-list controlled, pilot trial' *European Journal of Integrative Medicine*, vol. 4, no. 2, pp. e151-e58.

Lautenbacher, S., Kunz, M., Strate, P., Nielsen, J & Arendt-Nielsen, L. 2005, 'Age effects on pain thresholds, temporal summation and spatial summation of heat and pressure pain', *Pain*, vol. 115, no. 3, pp. 410-8.

Lee, J., Choi, D., Oh, T. & Yune, T. 2013 'Analgesic effect of acupuncture is mediated via inhibition of JNK activation in astrocytes after spinal cord injury', *Plos One*, vol. 8, no. 9, pp. e73948.

Lelo, A., Birkett, D.J., Robson, R.A. & Miners, J.O. 1986, 'Comparative pharmacokinetics of caffeine and its primary demethylated metabolites paraxanthine, theobromine and theophylline in man', *British Journal of Clinical Pharmacology*, vol. 22, no. 2, pp. 177-82.

Lewis, G.N., Luke, H., Rice, D.A., Rome, K. & McNair, P.J. 2012, 'Reliability of the conditioned pain modulation paradigm to assess endogenous inhibitory pain pathways', *Pain Research Manage*, vol. 17, no. 2, pp. 98-102.

Lewis, J., Sim, J. & Barlas, P. 2017, 'Acupuncture and electro-acupuncture for people diagnosed with subacromial pain syndrome: A multicentre randomised trial', *European Journal of Pain*, vol. 21, no. 6, pp. 1007-19.

Li, H., Shang, XJ. & Dong, QR. 2015, 'Effects of transcutaneous electrical nerve stimulation on rats with the third lumbar vertebrae transverse process syndrome', Acupuncture in Medicine, vol. 33, no. 5, pp. 400-5.

Li, SH. 1976, Acupuncture points 2001: a comprehensive textbook/manual of 20th century, M.D. Broffman & S.F. Pei (trans), Hundred Talents Press, Taipei, Taiwan, pp. 421.

Li, WH., Cobbin, D. & Zaslawski, C. 2008, 'A comparison of effects on regional pressure pain threshold produced by deep needling of LI 4 and LI 11, individually and in combination', *Complementary Therapies in Medicine*, vol. 16, no. 5, pp. 278-87.

Li, W. & Zhao, Z. 2016, 'Early meridian theories on unearthed medical bamboo slips from the Han Tomb in Laoguanshan of Chengdu', Chinese Acupuncture & Moxibustion, vol. 36, no. 12, pp. 1314-8.

Li, Z. & Liu, X. (trans.) 2008, 'Chapter 1 Jiuzhen Shi'er Yuan: Nine Needles and Twelve Primary Acupoints' *Yellow Emperor's Cannon of Medicine • Spiritual Pivot I*, vol. 1, 1st edn, World Publishing Corporation Xi'an, Shaanxi, China, pp. 15.

Linde, L.D., Kumbhare, D.A., Joshi, M. & Srbely, J.Z. 2018, 'The Relationship between rate of algometer application and pain pressure threshold in the assessment of myofascial trigger point sensitivity', *Pain Practice*, vol.18, no. 2, pp. 224-9.

Lindsay, N.M. & Scherrer, G.S. 2019, 'Countering opioid side effects', *Science*, vol. 365, no. 6459, pp. 1246-7.

Liu, S., Zhou, W., Ruan, X., Li, R.H., Lee, T., Weng, X.C., Hu, J. & Yang, G.D. 2007, 'Activation of the hypothalamus characterizes the response to acupuncture stimulation in heroin addicts', *Neuroscience Letters*, vol. 421, no. 3, pp. 203-8.

Liu, ZW. & Liu, L. (eds) 2010, 'Volume 2： Clinical Fundamentals in Chinese Medicine', *Essentials of Chinese Medicine*, Springer, London & New York, pp. 53.

Lorusso, L., Salerno, M., Sessa, F., Nicolosi, D., Longhitano, L., Loreto, C., Carotenuto, M., Messina, A., Villano, I., Cibelli, G., Valenzano, A., Monda, M., Murabito, P., Mollica, M.P., Messina, G. & Viggiano, A. 2018, 'Autoalgometry: an important tool for pressure pain threshold evaluation', *Journal of Clinical Medicine*, vol. 7, no. 9, pp. 273-82.

Lou, XF. & Jiang, SH. 2012, 'Anatomical characters and classification of acupoint', *Chineses Acupuncture & Moxibustion*, vol. 32, no. 4, pp. 319-23.

Lou, XF., Shi, Q., Mei, J., Jiang, SH., Zhang, RF. & Tang, ML. 2013, 'Relationship among nutrient vaseular chains, propagated sensation along the meridians (PSM) and visible meridians phenomena in integument tissueof the leg', The 13th Annual Academic Conference of Zhejiang Acupuncture and Moxibustion Society, Wenzhou, pp. 156-61.

Loyeung, B.Y.K. & Cobbin, D.M. 2013, 'Investigating the effects of three needling parameters (manipulation, retention time, and insertion site) on needling sensation and pain profiles: a study of eight deep needling interventions', *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, article ID 136763, 12 pages.

Lu, H. 1992, A comprehensive textbook of theory and points in Chinese acupuncture, Academy of Oriental Heritage, Vancouver, B. C. Canada, pp. 115, 135, 263, 794-5.

Maciocia, G. 2008, The practice of Chinese medicine the treatment of diseases with acupuncture and Chinese herbs, Elsevier, Philadelphia, PA, USA, pp. 987.

MacPherson, H., Thomas, K., Walters, S. & Fitter, M., 2001, 'A prospective survey of adverse events and treatment reactions following 34,000 consultations with professional acupuncturists', *Acupuncture in Medicine*, vol. 19, no. 2, pp. 93-102.

MacPherson, H., Tilbrook, H., Richmond, S., Woodman, J., Ballard, K., Atkin, K., Bland, M., Eldred, J., Essex, H. & Hewitt, C. 2015, 'Alexander technique lessons or acupuncture sessions for persons with chronic neck pain: a randomised trial', *Annals of internal medicine*, vol. 163, no. 9, pp. 653-62.

Maquet, D., Croisier, J, Demoulin, C. & Crielaard, J., 2004, 'Pressure pain thresholds of tender point sites in patients with fibromyalgia and in healthy controls', *European Journal of Pain*, vol. 8, no. 2, pp. 111-7.

Martin, R.M. 2019, 'Influence of biological sex, trait gender, and state gender on pain threshold, pain tolerance, and ratings of pain severity', *Personality and Individual Differences*, vol. 138, pp. 183-7.

Mavrommatis, C.I., Argyra, E., Vadalouka, A. & Vasilakos, D.G. 2012, 'Acupuncture as an adjunctive therapy to pharmacological treatment in patients with chronic pain due to osteoarthritis of the knee: A 3-armed, randomised, placebo-controlled trial', *Pain*, vol. 153, no. 8, pp. 1720-6.

Melchart, D., Streng, A., Hoppe, A., Brinkhaus, B., Witt, C., Wagenpfeil, S., Pfaffenrath, V., Hammes, M., Hummelsberger, J., Irnich, D., Weidenhammer, W., Willich, S.N. & Linde, K. 2005, 'Acupuncture in patients with tension-type headache: randomised controlled trial', *BMJ: British Medical Journa*, vol. 331, no. 7513, pp. 376-82.

Merskey, H. & Bogduk, N. (eds) 1994, *Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms*, 2nd edn, International Association for the Study of Pain, Task Force on Taxonomy, Seattle.

Merskey, H., & Spear, F. G. (1967). *Pain: psychological and psychiatric aspects.* London: Bailliere, Tindall & Cassell.

Min, MH., Choi, YG., Kim, YJ., Park, HJ., Lee, SC., Joo, HN., Han, SM. & Lim, S. 2009, 'The effect of Sa-am acupuncture on knee osteoarthritis', *Korean Journal of Acupuncture*, vol. 26, no. 4, pp. 53-66.

Molsberger, A.F., Boewing, G., Diener, H.C., Endres, H.G., Kraehmer, N., Kronfeld, K. & Zenz, M. 2006, 'Designing an acupuncture study: the nationwide, randomised, controlled, German acupuncture trials on migraine and tension-type headache', *Journal of Alternative & Complementary Medicine*, vol. 12, no. 3, pp. 237-45.

Molsberger, A.F., Schneider, T., Gotthardt, H. & Drabik, A. 2010, 'German randomised acupuncture trial for chronic shoulder pain (GRASP)-a pragmatic, controlled, patient-blinded, multi-centre trial in an outpatient care environment', *Pain*, vol. 151, no. 1, pp. 146-54.

Murase, K & Kawakita, K. 2000, 'Diffuse noxious inhibitory controls in anti-nociception produced by acupuncture and moxibustion on trigeminal caudalis neurons in rats', *The Japanese Journal of Physiology*, vol. 50, no. 1, pp. 133-40.

Nabeta, T. & Kawakita, K. 2002, 'Relief of chronic neck and shoulder pain by manual acupuncture to tender points—a sham-controlled randomised trial', *Complementary Therapies in Medicine*, vol. 10,no. 4, pp. 217-22.

National Health and Medical Research Council 1999, *How to Review the Evidence: Systematic Identification and Review of the Scientific Literature*, Canberra, Australia.

Ni, M. (trans.) 1995, *The Yellow Emperor's Classic of Medicine,* 1st edn, Shambhala, Boston, Mass.

NICE (National Institute for Health and Care Excellence) guideline [NG193] 2021, *Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain*, viewd 3 June 2021, https://www.nice.org.uk/guidance/ng193.

O'Connor, J. & Bensky, D. (ed.) 1992, *Acupuncture: a comprehensive text*, Eastland Press, Seattle, Washington, USA, pp. 240.

Pain Australia n.d. *Painful Facts*, Painaustralian Limited, viewed on 6 May 2020, <www.painaustralia.org.au › about-pain › painful-facts>.

Park, G., Kim, CW., Park, SB., Kim, MJ. & Jang, SH. 2011, 'Reliability and usefulness of the pressure pain threshold measurement in patients with myofascial pain', *Ann Rehabil Med*. vol. 35, no. 3, pp. 412-7.

Pauli, P., Rau, H., Zhuang, P, Brody, S. & Birbaumer, N. 1993, 'Effects of smoking on thermal pain threshold in deprived and minimally-deprived habitual smokers', *Psychopharmacology*, vol. 111, no.4, pp. 472-6.

Pelfort, X., Torres-Claramuntb, R., Sánchez-Soler, J.F., Hinarejos, P., Leal-Blanquet, J., Valverde, D. & Monllau, J.C. 2015, 'Pressure algometry is a useful tool to quantify pain in the medial part of the knee: An intra- and inter-reliability study in healthy subjects', *Orthopaedics & Traumatology: Surgery & Research*, vol. 101, no. 3, pp. 559-63.

Plaster, R., Vieira, W.B., Alencar, F.A.D., Nakano, E.Y. & Liebano, R.E. 2014, 'Immediate effects of electroacupuncture and manual acupuncture on pain, mobility and muscle strength in patients with knee osteoarthritis: a randomised controlled trial', *Acupuncture in medicine*, vol. 32, no. 3, pp. 236-41.

Pohodenko-Chudakova, I. O. 2005, 'Acupuncture analgesia and its application in cranio-maxillofacial surgical procedures', *Journal of Cranio-Maxillofacial Surgery*, vol. 33, no. 2, pp. 118-22.

Popescu, A., Leresche, L., Truelove, E.L. & Drangsholt, M.T. 2010, 'Gender differences in pain modulation by diffuse noxious inhibitory controls: A systematic review', *Pain*, vol.150, no. 2, pp. 309-18.

Porkert, M. & Hempen, C.H. 1995, *Classical acupuncture-the standard textbook*, Phainon Editions & Media GmbH, Dinkelscherben, Germany, pp. 246.

Pukall, C.F., Young, R.A., Roberts, M.J., Sutton, K.S. & Smith, K.B. 2007, 'The vulvalgesiometer as a device to measure genital pressure-pain threshold', *Physiologicl Measurement*, vol. 28, no. 12, pp. 1543-50.

Rampes, H. & James, R. 1995, 'Complications of acupuncture', *Acupuncture in Medicine*, vol. 13, no. 1, pp. 26-33.

Razavy, S., Gadau, M., Zhang, S.P., Wang, F.C., Bangrazi, S., Berle, C., Li, T., Li, W.H. & Zaslawski, C. 2018, 'Anxiety related to De Qi psychophysical responses as measured

by MASS: a sub-study embedded in a multisite randomised clinical trial', *Complementary Therapies in Medicine*, vol. 39, pp. 24-35.

Rebhorn, C., Breimhorst, M., Buniatyan, D., Vogel, C., Birklein, F. & Eberle, T. 2012, 'The efficacy of acupuncture in human pain models: a randomised, controlled, double-blinded study', *Pain*, vol. 153, pp. 1852-62.

Rezvani, M., Yaraghi, A., Mohseni, M. & Fathimoghadam, F. 2014, 'Efficacy of Yamamoto new scalp acupuncture versus Traditional Chinese acupuncture for migraine treatment', *The Journal of Alternative and Complementary Medicine*, vol. 20, no. 5, pp. 371-4.

Ritenbaugh, C., Hammerschlag, R., Calabrese, C., Mist, S., Aickin, M., Sutherland, E., Leben, J., DeBar, L., Elder, C. & Dworkin, S.F. 2008, 'A pilot whole systems clinical trial of traditional Chinese medicine and naturopathic medicine for the treatment of temporomandibular disorders', *The Journal of Alternative and Complementary Medicine*, vol. 14, no. 5, pp. 475-87.

Rogers, C.J. & Rogers, C. 1989, Acupuncture point location and point dynamics manual. Third Edition. Acupuncture Colleges Press: Sydney, Australia.

Rogers, C. & Rogers, C. 1995, *Point location and point dynamics manual*. Acupuncture Colleges, Australia.

Schliessbach, J., van der Klift, E., Arendt-Nielsen, L., Curatolo, M., Streitberger, K. 2011, 'The effect of brief electrical and manual acupuncture stimulation on mechanical experimental pain', *Pain medicine*, vol. 12, no. 2, pp. 268-75.

Schliessbach, J., van der Klift, E., Siegenthaler, A., Arendt-Nielsen, L., Curatolo, M. & Streitberger, K. 2012, 'Does acupuncture needling induce analgesic effects comparable to diffuse noxious inhibitory controls?', *Evidence - Based Complementary and Alternative Medicine*, vol. 2012, pp. 785613: 1-5.

Schmid-Schwap, M., Simma-Kletschka, I., Stockner, A., Sengstbratl, M., Gleditsch, J., Kundi, M. & Piehslinger, E. 2006, 'Oral acupuncture in the therapy of craniomandibular dysfunction syndrome – a randomised controlled trial (RCT)', *The Middle-European Journal of Medicine*, vol. 118, no. 1-2, pp. 36-42.

Schoth, D.E., Blankenburg, M., Wager, J., Broadbent, P., Zhang, J., Zernikow, B. & Liossi, C. 2019, 'The association between quantitative sensory testing and pain or disability in paediatric and young adult chronic pain: Protocol for a systematic review and meta-analysis', *BMJ Open*, vol. 9, no. 10, pp. e031861: 1-5.

Scott, J. & Huskisson, E. C. 1976, 'Graphic representation of pain', *Pain*, vol. 2, no. 2, pp. 175-84.

Shanghai College of Traditional Medicine 1992, *Acupuncture: a comprehensive text*, trans. J. O'Connor & D. Bensky (eds), Eastland Press, Seattle, Washington, USA. pp. 582.

Shaw, V., Diogo, R. & Winder, I.C. 2020, 'Hiding in plain sight-ancient Chinese anatomy', Anatomical Record, vol. 303, no. 9, pp. 1-14.

Shen, Y.F. & Goddard, G. 2007, 'The short-term effects of acupuncture on myofascial pain patients after clenching', *Pain Practice*, vol. 7, no. 3, pp. 256-64.

Sherman, K.J., Hogeboom, C.J. Cherkin, D.C. & Deyo, R.A. 2002, 'Description and validation of a noninvasive placebo acupuncture procedure', *The Journal of Alternative & Complementary Medicine*, vol. 8, no. 1, pp. 11-9.

Shi, XM. & Zhou, JZ. 2007, *Shi Xue-min's comprehensive textbook of acupuncture and moxibustion*, People's Medical Publishing House, Beijing, pp. 74, 89, 94, 113, 118, 130, 149, 151, 156, 162, 163.

Simma, I., Gleditsch, J.M., Simma, L. & Piehslinger, E. 2009, 'Immediate effects of microsystem acupuncture in patients with oromyofacial pain and craniomandibular disorders (CMD): a double-blind, placebo-controlled trial', *British Dental Journal*, vol. 207, no. 12, pp. 4.

Sivin, N. 1993, '*Huang ti nei ching* 黃帝內經' in M. Loewe (ed.), In Early Chinese Texts: A Bibliographical Guide, University of California Press, Berkeley and Los Angeles, pp. 199-201.

Sjölund, B.H. & Persson, A.L. 2007, 'Pressure pain threshold changes after repeated mechano-nociceptive stimulation of the trapezius muscle: possible influence of previous pain experience', *The Journal of Pain*, vol. 8, no. 4, pp. 355-62.

Sprott, H. 1998, 'Efficiency of acupuncture in patients with fibromyalgia', *Clinical Bulletin of Myofascial Therapy*, vol. 3, no. 1, pp. 37-43.

Stanke, K. M. & Ivanec, D. 2016, 'Pain threshold – Measure of pain sensitivity or social behavior?', *Psihologija*, vol. 49, no. 1, pp. 37-50.

State Insurance Regulatory Authority: Guidelines for the management of acute whiplash-associated disorders – for health professionals. Sydney: third edition, 2014. P.43. viewed 13 January 2018, https://www.sira.nsw.gov.au/resources-library/motor-accident-resources/publications/for-professionals/whiplash-resources/SIRA08110-1117-396462.pdf

Streitberger, K., Eichenberger, U., Schneider, A., Witte, S. & Greher, M. 2007, 'Ultrasound measurements of the distance between acupuncture needle tip at P6 and the median nerve', *The Journal of Alternative and Complementary Medicine*, vol. 13, pp. 585-92.

Strudwick, M.W., Hinks, R.C. & Choy, S.T. B. 2007, 'Point injection as an alternative acupuncture technique--an exploratory study of responses in healthy subjects', *Acupuncture in Medicine*, vol. 25, no. 4, pp.166-74.

Stux, G. & Pomeranz, B. 1988, *Basics of acupuncture*, Springer-Verlag, Berlin, Heidelberg, New York, London, Paris, Tokyo, Hong Kong, Barcelona, pp. 118.

Sun, MY., Hsieh, CL., Cheng, YY., Hung, HC., Li, TC., Yen, SM. & Huang, IS. 2010, 'The therapeutic effects of acupuncture on patients with chronic neck myofascial pain syndrome: a single-blind randomised controlled trial', *The American journal of Chinese medicine*, vol. 38, no. 05, 849-59.

Sun, YZ., Wang, YJ. & Wang, W. 2012, 'Effect of acupuncture plus rehabilitation training on shoulder-hand syndrome due to ischemic stroke', *Journal of Acupuncture and Tuina Science*, vol. 10, no. 2, pp. 109-13.

Szabo, S. 2007, 'Comparison of the effects of manual acupuncture, electroacupuncture and TENS on regional pressure pain threshold readings'. PhD thesis, Faculty of Science, University of Technology, Sydney.

Sze, F.KH., Wong, E. Yi, X. & Woo, J. 2002, 'Does acupuncture have additional value to standard poststroke motor rehabilitation?', *Stroke*, vol. 33, no. 1, pp. 186-94.

Tai, D. 1997, *Acupuncture*, David Tai, Sydney, NSW, Australia, pp. 135.

Targino, R.A., Imamura, M., Kaziyama, H.H.S., Souza, L.P.M., Hsing, W.T., Furlan, A.D., Imamura, S.T. & Neto, R.S.A. 2008, 'A randomised controlled trial of acupuncture added to usual treatment for fbromyalgia', *Journal of Rehabilitation Medicine*, vol. 40, no. 7, pp. 582-8.

To, M. & Alexander, C. 2015, 'The effects of Park sham needles: a pilot study', *Journal of Integrative Medicine*, vol. 13, no. 1, pp. 20-4.

Tobbackx, Y., Meeus, M., Wauters, L., De Vilder, P., Roose, J., Verhaeghe, T. & Nijs, J. 2013, 'Does acupuncture activate endogenous analgesia in chronic whiplash-associated disorders? A randomised crossover trial', *European Journal of Pain*, vol. 17, no. 2, 279-89.

Tsang, A., Von Korff, M., Lee, S., Alonso, J., Karam, E., Angermeyer, M.C., Borges, G.L., Bromet, E.J., Demytteneare, K., de Girolamo, G., de Graaf, R., Gureje, O., Lepine, J.P., Haro, J.M., Levinson, D., Oakley Browne, M.A., Posada-Villa, J., Seedat, S. & Watanabe, M. 2008, 'Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders', *Journal of Pain*, vol. 9, no. 10, pp. 883-91.

Uğurlu, F.G., Sezer, N., Aktekin, L., Fidan, F., Tok, F. & Akkuş, S. 2017, 'The effects of acupuncture versus sham acupuncture in the treatment of fibromyalgia: a randomised controlled clinical trial', *Acta reumatologica portuguesa*, vol. 42, no. 1, pp. 32-7.

Unschuld, P.U. 2016, *Huang Di Nei Jing Ling Shu: The Ancient Classic on Needle Therapy*, University of California Press, Oakland, California, USA, pp. 46, 67.

van Der Boon, R.M., de Jaegere, P.P., & van Domburg, R.T. 2012, 'Multivariate analysis in a small sample size, a matter of concern', The American Journal of Cardiology, vol.109, no. 3, pp. 450.

Vas, J., Perea-Milla, E., Méndez, C., Navarro, C.S., Rubio, J.M.L., Brioso, M. & Obrero, I.G. 2006, 'Efficacy and safety of acupuncture for chronic uncomplicated neck pain: a randomised controlled study', *Pain*, vol. 126, no. 1, 245-55.

Vincent, C. 2001, 'The safety of acupuncture: acupuncture is safe in the hands of competent practitioners', *British Medical Journal*, vol. 323, no.7311, pp. 467-8.

Wallasch, T. M., Weinschuetz, T., Mueller, B. & Kropp, P. 2012, 'Cerebrovascular response in migraineurs during prophylactic treatment with acupuncture: A randomised controlled trial', *The Journal of Alternative andComplementary Medicine*, vol. 18, no. 8, pp. 777‐83.

Walton, D., Macdermid, J., Nielson, W., Teasell, R., Chiasson, M. & Brown, L. 2011, 'Reliability, standard error, and minimum detectable change of clinical pressure pain threshold testing in people with and without acute neck pain', *Journal of Orthopaedic & Sports Physical Therapy*, vol. 41, no. 9, pp. 644-50.

Wang, JY. 2003 'Treatment of Acute Lumbar Sprain by Acupuncture plus Cupping', *Journal of Acupuncture and Tuina Science*, vol. 1, no. 6, pp. 37-8.

Wang, JY. & Robertson, J.D. 2008, *Applied channel theory in Chinese medicine*, Eastland Press, Seattle, Washington, USA, pp. 174, , 572-3.

Wang, LP., Zhang, XZ., Guo, J., Liu, HL., Zhang, Y., Liu, CZ., Yi, JH., Wang, LP., Zhao, JP. & Li, SS. 2011, 'Efficacy of acupuncture for migraine prophylaxis: a single-blinded, double-dummy, randomised controlled trial', *Pain*, vol. 152, no. 8, pp. 1864-71.

Wang, LP., Zhang, XZ., Guo, J., Liu, HL., Zhang, Y., Liu, CZ., Yi, JH., Wang, L.P., Zhao, J.P. & Li, S.S. 2012, 'Efficacy of acupuncture for acute migraine attack: a multicentre single blinded, randomised controlled trial', *Pain Medicine*, vol. 13, no. 5, 623-30.

Wang, SH. 1997, *The pulse classic (Mai jing*), in SZ. Yang (trans.), Blue Poppy Press, Bouler, CO, USA, PP. 32.

Wang, YI., Xue, C.CL., Helme, R., Costa, C.D. & Zheng, Z. 2015, 'Acupuncture for Frequent Migraine: A Randomised, Patient/Assessor Blinded, Controlled Trial with One-Year Follow-Up', *Evidence - Based Complementary and Alternative Medicine*, vol. 2015, pp. 920353: 1-14.

Wayne, P.M., Krebs, D.E., Macklin, E.A., Schnyer, R., Kaptchuk, T.J., Parker, S.W., Scarborough, D.M., McGibbon, C.A., Schaechter, J.D. & Stein, J. 2005, 'Acupuncture for upper-extremity rehabilitation in chronic stroke: a randomized sham-controlled study', *Archives of Physical Medicine and Rehabilitation*, vol. 86, no. 12, pp. 2248-55.

Wen, Q., Zhao, Y., Wang, C., Xing, D., Lv, J., Pan, H., Yang, Y., Li, J. & Li, N. 2014, 'Effects of acupuncture intervention on omalgia incidence rate of ischemic stroke in acute stage', *World Journal of Acupuncture-Moxibustion*, vol. 24, no. 1, pp. 19-25.

Wilke, J., Vogt, L., Niederer, D., Hübscher, M., Rothmayr, J., Ivkovic, D., Rickert, M. & Banzer, W. 2014, 'Short-term effects of acupuncture and stretching on myofascial trigger point pain of the neck: A blinded, placebo-controlled RCT', *Complementary Therapies in Medicine*, vol. 22, no. 5, pp. 835-41.

Wolff, H. G., Hardy, J. D. & Goodell, H. 1941, 'Measurement of the effect on the pain threshold of acetylsalicylic acid, acetanilide, acetophenetidin, aminopyrine, ethyl alcohol, trichloroethylene, a barbiturate, quinine, ergotamine tartrate and caffeine: an analysis of their relation to the pain experience', *The Journal of Clinica Investigation*, vol. 20, no. 1, pp. 63-80.

World Health Organisation, 2009, *WHO Standard acupuncture point locations*, in the Western Pacific Region, pp. 89.

Yu, LL., Wang, W., Li, L., Qin, QG., Yu, YT., Liu, K., Zhao, YF., Rong, P. & Zhu, B. 2019, 'Inhibition of electroacupuncture on nociceptive responses of dorsal horn neurons evoked by noxious colorectal distention in an intensity-dependent manner', *Journal of Pain Research*, vol. 12, pp. 231-42.

Yuan, J., Purepong, N., Hunter, R.F., Kerr, D.P., Park, J., Bradbury, I. & McDonough, S. 2009, 'Different frequencies of acupuncture treatment for chronic low back pain: an assessor-blinded pilot randomised controlled trial', *Complementary Therapies in Medicine*, vol. 17, no. 3, pp. 131-40.

Yuan, XY. 2002 A study into the effects of deep manual acupuncture on pain pressure threshold MSc Thesis, Faculty of Science, University of Technology, Sydney.

Yuan, YQ., Wang, ZT. & Peng, JM. 2005, 'Investigation to the academic achievements of Hanqing Dou's acupuncture technique', *Shanghai Journal of Acupuncture and Moxibustion*, vol, 24, no. 1, pp. 29-30.

Yüksel, M., Ayaş, Ş., Cabıoğlu, M.T., Yılmaz, D. & Cabıoğlu, C. 2019, 'Quantitative data for transcutaneous electrical nerve stimulation and acupuncture effectiveness in treatment of fibromyalgia syndrome', *Evidence - Based Complementary and Alternative Medicine*, vol. 2019, Article ID 9684649, 12 pages https://doi.org/10.1155/2019/9684649.

Zaslawski, C.J. 2006, 'The relevance of needling parameters and participant experience for acupuncture research', PhD Thesis: University of Technology, Sydney.

Zaslawski, C.J. Cobbin, D. Lidums, E. & Petocz, P. 2003, 'The impact of site specificity and needle manipulation on changes to pain pressure threshold following manual acupuncture: a controlled study', *Complementary Therapies in Medicine*, vol. 11, no.1, pp. 11-21.

Zhang, HL., Sun, JG., Wang, C., Yu, CC., Wang, WW., Zhang, M., Lao, LX. Yi, M., Wan, Y. 2016, 'Randomised controlled trial of contralateral manual acupuncture for the relief of chronic shoulder pain', *Acupuncture in Medicine*, vol. 34, no. 3, 164-70.

Zhang, SP., Yip, TP. & Li, QS. 2011, 'Acupuncture treatment for plantar fasciitis: a randomised controlled trial with six months follow-up', *Evidence - Based Complementary and Alternative Medicine*, vol. 2011, pp. 154108: 1-10.

Zhao, MY., Zhang, P., Li, J., Wang, LP., Zhou, W., Wang, YX., She, YF., Ma, LX., Wang, P., Hu, NJ., Lin, C., Hu, SQ. Wu, GW. Wang, YF., Sun, JJ., Jiang, SZ. & Zhu, J. 2017, 'Influence of *de qi* on the immediate analgesic effect of SP6 acupuncture in patients with primary dysmenorrhoea and cold and dampness stagnation: a multicentre randomised controlled trial', *Acupuncture in Medicine*, vol. 35, no. 5, pp. 332-8.

Zucker, N.A., Tsodikov, A., Mist, S.D., Cina, S., Napadow, V. & Harris, R.E. 2017, 'Evoked pressure pain sensitivity is associated with differential analgesic response to verum and sham acupuncture in fibromyalgia', *Pain Medicine*, vol. 18, no. 8, pp. 1582-92.

Appendices

Information sheet, Consent form, Questionnaire,

Declarations, and supporting information

Appendix 1. Criteria for the PEDro Scale

1 eligibility criteria were specified

2 subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)

3 allocation was concealed

4 the groups were similar at baseline regarding the most important prognostic indicators

5 there was blinding of all subjects

6 there was blinding of all therapists who administered the therapy

7 there was blinding of all assessors who measured at least one key outcome

8 measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups

9 all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"

10 the results of between-group statistical comparisons are reported for at least one key outcome

11 the study provides both point measures and measures of variability for at least one key outcome

Notes on administration of the PEDro scale:

All criteria Points are only awarded when a criterion is clearly satisfied. If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.

Criterion 1 This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.

Criterion 2 A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.

Criterion 3 *Concealed allocation* means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".

Criterion 4 At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis

of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.

Criteria 4, 7-11 *Key outcomes* are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.

Criterion 5-7 *Blinding* means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.

Criterion 8 This criterion is only satisfied if the report explicitly states *both* the number of subjects initially allocated to groups *and* the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.

Criterion 9 An *intention to treat* analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.

Criterion 10 A *between-group* statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group $\times$ time interaction). The comparison may be in the form hypothesis testing (which provides a *p* value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.

Criterion 11 A *point measure* is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. *Measures of variability* include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges) and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.

Appendix 2. SPIRIT 2013 Checklist: Recommended Items to Address in a Clinical Trial Protocol and Related Documents

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Line 2-4, Page 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Line 8-9, Page 4
	2b	All items from the World Health Organization Trial Registration Data Set	Line 8, Page 4
Protocol version	3	Date and version identifier	Line 12-13, Page 20 (protocol version: F2.0)
Funding	4	Sources and types of financial, material, and other support	Line 4-7, Page 22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 1-2, 22
	5b	Name and contact information for the trial sponsor	Line 1-9, Page 2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Line 5, Page 22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Line 17-19, Page 15
Introduction			

1

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 4-6
	6b	Explanation for choice of comparators	Page 4-6
Objectives	7	Specific objectives or hypotheses	Page 6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Line 17, Page 6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Line 13-15, Page7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 10-12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Line 3-4, Page12
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Line 19-20, Page 11 Line 1-2, Page 12
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Line 5-8, Page 12
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 13-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure1,2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page 8-9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Line 12-18, Page 7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Line12-14, Page 9
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Line 7-17, Page 9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Line 7-17, Page 9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Line 18-21, Page 9 Line 1-4, Page 10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Not applicable
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Line 9-14, Page 15 Figure 1
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Not applicable

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Line 15-19, Page 15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 15-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Not applicable
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Line 8-10, Page 12 Line 22-23, Page 15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Line 17-19, Page 15
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Line 17-19, Page 15
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Line 4-9, Page 17
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Line 17-19, Page 15
Ethics and dissemination			

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	This trial has been approved by the Institutional Review Boards and Ethics Committees of the First Teaching Hospital of CDUTCM. See Line 11-16, Page 21
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	See ethics approval document
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Institutional Review Boards and Ethics Committees of the First Teaching Hospital of CDUTCM.
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Line 16-17, Page 21
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Line 2-3, Page 22
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Line 16-17, Page 15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Line 4-9, Page 17

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Follow the SPIRIT Statement
	31b	Authorship eligibility guidelines and any intended use of professional writers	Follow the SPIRIT Statement
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Follow the SPIRIT Statement
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Have been approved by the institutional review boards and ethics committees of the 1st Teaching Hospital of CDUTCM
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Appendix 3. Research Team Roles and Responsibilities

1. Names, affiliations, and roles of protocol co-contributors

Institution	Co-contributors	Role / Responsibilities	
UTS	A/P Chris Zaslawski	Chief Investigator / Principal Supervisor Contributor to refinement of the study protocol and approval of the final manuscript	All authors will contribute to the refinement of the study protocol and approval of the final manuscript.
UTS	Dr Yew Kian Bertrand Loyeung	Co-Supervisor Contributor to refinement of the study protocol and approval of the final manuscript	
UTS	Prof Chi Eung Danforn Lim	Co-Supervisor Contributor to refinement of the study protocol and approval of the final manuscript	
UTS	Ms Xiaoqin Wu	Higher Degree Research Student: PhD Sc (Research) Candidate Main Design of Study Protocol Participants Recruitment Participants Communications HREC Application Data Collection & Data Management Budget Administration Risk Analysis SUSAR (Serious unexpected adverse events report) procedures Management of Protocol Compliance	

2. Trial Sponsor

The sponsor was the UTS and partial funding was supplied by the Australian Government Research Training Program Scholarship.

3. Role of study sponsor and funders

The funding sources had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

4. Composition and responsibilities of committees are as follows:

Committee	Membership	Responsibilities
Trial management committee (TMC)	There will be one Chief investigator (Principal Supervisor - CZ) Co-Investigator (BL) Co-Investigator (DL) Research Student (XW)	Study planning and documentation
		Organisation of steering committee meetings
		Provide risk, ethics committee and SUSAR (Serious unexpected suspected adverse events) reports to appropriate bodies
		Budget administration and contractual issues
		Data collection
		Management of protocol compliance
		Development of Trial Design
		Assistance with board /independent ethics committee applications
		Data verification
		Randomisation
		Recruitment, along with the follow up of study participants and adherence to study protocol
Steering committee (SC)	Co-Investigator (BL) Research Student (XW)	Design and conduct IE-SI3-PPT-*deqi*-NP project
		Preparation of the protocol and revisions
		Preparation of investigators brochure (IB) and CRFs (case report forms)
		Recruitment of patients and liaising with other co-contributors
		Organise steering committee meetings
		Agreement of final protocol
		Publication of study reports
		Reviewing progress of study and if necessary agreeing changes to the protocol and/or investigators brochure to facilitate the smooth running of the study
Data manager	Nominated Data manager to be confirmed	Maintenance of trial IT system and data entry
		Data verification

Appendix 4. Participant Information Sheet and Consent Form

UNIVERSITY OF TECHNOLOGY SYDNEY

Acupuncture Pain Threshold Study

Participant Information Sheet

Title: Investigating the effects of the acupoint SI3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain

Short Title: IE-SI3-PPT-DEQI-NP

Principal Investigator: A/P Christopher Zaslawski

Co-investigator: Dr Yew Kian Bertrand Loyeung

Co-investigator/ Research Student: Ms Xiaoqin Wu (Margaret)

Site Location: UTS Chinese Medicine Clinic
CB04, Level 2 (Street level, Harris Street), UTS City Campus
Corner of Harris and Thomas Streets (opposite ABC Ultimo Centre on Harris St)

Protocol: UTS HREC Application ID： ETH18-2294

Part I – What does my participation in the study involve?

You are invited to take part in "Investigating the effects of the acupoint SI3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain", which may be suitable for you. Before you decide if you wish to participate in this study, we would like you to understand why the study is being done, what it will involve and how your information will be used. Please take the time to read the following information carefully and discuss it with others if you wish. One or more of our team will go through the information sheet with you and answer any questions you have. Please ask questions about anything that you do not understand or want to know more about.

1. **What is the purpose of this study?**

   The aim of this study is to evaluate: 1) The effect of acupuncture on pressure pain threshold (PPT); 2) The strength and quality of needling sensation (*deqi*) reported; and 3) The strength of pain at the needling site.

2. **Why have I been invited to participate in this study?**

   You are eligible to participate in this study because: 1) You are 18-70 years old; 2) You are right-handedness; 3) You have no medical history of chronic musculoskeletal disorder; and 4) You have no diagnosis of pain caused by any diseases in the recent seven days; 5) You are non-smoker.

3. **Do I have to take part in the research?**

   Participation in this study is voluntary. It is completely up to you to decide whether to take part in this study. If you do decide to take part, you will be given this Participant Information Sheet and Consent Form to sign and you will be given a copy to keep also. If you decide to take part, you can change your mind and withdraw from the study at any stages, for any reasons. Your decision not to take part, or take part and then withdraw from the study will not affect your relationship with the UTS or researchers.

4. **What does participation in this study involve?**

   If you agree to participate in this study, you will then be asked to give permission to the researcher to contact you, so that the researcher will let you know about the details of our project.

Please abstain from alcohol for 18 hours, caffeine for 4 hours, eating or exercise for 24 hours prior to any of your appointment times. You will be required to attend for three sessions each taking approximately one hour. Moreover, you will be take prone position during the session. There are three interventions to the trial including the needling insertion on SI3 (SI3 is an acupoint. When the hand is slightly flexed, SI3 is located at the ulnar end of the distal transverse skin crease of the palm, at the border between the red and white flesh) of the right hand with manipulation, the needling insertion on SI3 of right hand without manipulation and the laser treatment on SI3 of the right hand. A qualified acupuncturist will provide the acupuncture. You will be participating in a study where you will be randomly allocated into a sequence of three different interventions. Each intervention session will take approximately 3-21 minutes with an extra 20 minutes needed for data collection. You will be asked to sign a consent form before any assessment is conducted. There is at least one-week washout period between each intervention session.

We would like to know how you would describe the sensations of your acupuncture intervention both when the needles are inserted and afterwards. This will show us exactly how dull or sharp your sensations are. We realise that individual acupuncture points may feel different but we would like you to give us an overall impression.

Before needling and at different time intervals, an algometer will be applied to a number of regions on your body (see figure below) to measure the pressure pain threshold. Pressure pain threshold refers to discomfort produced by pressing on your skin or muscles (see photograph below). It does not puncture the skin.

You will be asked to expose some areas of the body during algometric measurement and these are only located on your back, wrists and ankles.

Part II – How is the study being conducted?

5. What if you don't want to take part in this study, or if you want to withdraw later?

Participation in this study is voluntary. It is completely up to you whether you participate. If you decide not to participate, it will not affect the medical treatment you will receive in the future. Whatever your decision, it will not affect your relationship with the researchers or the University of Technology Sydney.

If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason, by contacting Ms Xiaoqin Wu (Margaret) on her mobile 0424 633 146 or email: Xiaoqin.Wu@student.uts.edu.au. You can stop the experiment or withdraw your responses before we deal with data analysis. However, it may not be

possible to remove your data from the study results if your identifying details have already been used in the analysis.

6. **How will this study be paid? Will you benefit from the study? Will taking part in this study cost you anything, and will you be paid?**

   This research is supported by an Australian Government Research Training Program Scholarship. To thank you for your participation a pecuniary of $15 will be given to you for each of you clinic visit, which covers your travel cost.

7. **Are there any risks/inconvenience to you in taking part in this study?**

   There are some minor risks associated with acupuncture, for example possible bruising at the needling site, local bleeding or oedema resulting from bleeding, redness, itching, and dizziness or fainting. All care will be taken by the acupuncturist to minimise such possibilities.

8. **How will your confidentiality be protected?**

   Your identity will be confidential since all data will be identified by a code and not by name. Any identifiable information that is collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named above and the Human Research Ethics Committees (HRECs) will have access to your details.

9. **What will happen to the results?**

   If you give us permission by signing the consent form, the study results will be used in following ways:

   • Published in the book.

   • Published for future references in a peer reviewed academic journal.

   • Presented in conferences, forums, media, or workshops.

   • Electronic publication.

   • Reported to the HREC for research ethics monitoring purposes.

   • Used to the research student's thesis.

   In any publications/report, research information will be provided in such a way that you cannot be identified.

10. **What should you do if you want to discuss this study further before you decide to participate?**

    After you have read this information sheet and consent form, the research student, Ms Xiaoqin Wu (Margaret), can discuss with you on any queries you may have. If you would like to know more at any stage, please do not hesitate to contact her on her mobile [redacted] or email: Xiaoqin.Wu@student.uts.edu.au. Alternatively, you may contact Dr Yew Kian Bertrand Loyeung via his email (YewKian.Loyeung-1@uts.edu.au) or his contact number (02 9514-7850).

11. **Whom would you contact if you have any concerns or a complaint about the conduct of this study?**

    If you have concerns about the research that you think researchers can help you with, please feel free to contact Ms Xiaoqin Wu (Margaret) ([redacted] or email: Xiaoqin.Wu@student.uts.edu.au, Dr Yew Kian Bertrand Loyeung (ph.: +61 2 9514 7850 or email YewKian.Loyeung-1@uts.edu.au).

This study has been approved by the University of Technology Sydney Human Research Ethics Committee [ETH182294]. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat on ph.: +61 2 9514 2478 or email: Research.Ethics@uts.edu.au], and quote the UTS HREC reference number. Any matter raised will be treated confidentially, investigated and you will be informed of the outcome.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

PARTICIPANT CONSENT FORM - STUDENT RESEARCH

[To be used in conjunction with the Participant Information Sheet]

Title: Investigating the effects of the acupoint SI 3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain

Short Title: IE-SI3-PPT-DEQI-NP

Principal Investigator: A/P Christopher Zaslawski

Co-investigator: Dr Yew Kian Bertrand Loyeung

Co-investigator/ Research Student: Ms Xiaoqin Wu (Margaret)

Site Location: UTS Chinese Medicine Clinic
CB04, Level 2 (Street level, Harris Street), UTS City Campus
Corner of Harris and Thomas Streets (opposite ABC Ultimo Centre on Harris St)

Protocol: UTS HREC Application ID： ETH18-2294

1. I have read the attached Participant Information Sheet outlining the nature and purpose of the research study and I understand what I am being asked to do.

2. I have discussed my participation in this study with the member of the study team named below. I have had the opportunity to ask questions and I am satisfied with the answers I have received.

3. I have been informed about the possible risks of taking part in this study.

4. I freely consent to participate in the research project as described in the attached Participant Information Sheet.

5. I understand that my participation is voluntary and that I am free to withdraw at any time during the study without affecting my future health care.

6. I understand that if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, the investigator/sponsor will request my permission to access my medical records for collection of follow-up information for research and analysis.

Signature of participant (Please PRINT name and sign)

_____	_____	_____
PRINT name of participant	Signature of participant	Date
_____	_____	_____
PRINT name of witness	Signature of witness	Date
_____	_____	_____
PRINT name of investigator	Signature of investigator	Date

ALL WITNESSES MUST BE OVER 18 YEARS OF AGE

UNIVERSITY OF TECHNOLOGY SYDNEY

WITHDRAWAL OF PARTICIPATION

Title: Investigating the effects of the acupoint SI3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain

Short Title: IE-SI3-PPT-DEQI-NP

Principal Investigator: A/P Christopher Zaslawski

Co-investigator: Dr Yew Kian Bertrand Loyeung

Co-investigator/ Research Student: Ms Xiaoqin Wu (Margaret)

Site Location: UTS Chinese Medicine Clinic
CB04, Level 2 (Street level, Harris Street), UTS City Campus
Corner of Harris and Thomas Streets (opposite ABC Ultimo Centre on Harris St)

Protocol: UTS HREC Application ID： ETH18-2294

I hereby wish to WITHDRAW my intent to participate further in the above research project and understand that such withdrawal will not jeopardise my future health care.

Participant's Name (printed)

_____

Signature

_____

Date

_____

In the event the participant decided to withdraw verbally, please give a description of the circumstances. Coordinating Investigator to provide further information here:

Coordinating Investigator to sign the withdrawal of consent form on behalf of a participant if verbal withdrawal has been given:

Participant's Name (printed)

_____

Signature of Investigator _____

Date

_____

The section for revocation of consent should be forwarded to Principal investigator: Name: A/P Christopher Zaslawski.

Address: University of Technology Sydney CB04.06.
15 Broadway, Ultimo, NSW, 2007
TEL: + 61 2 9514 7856
Email: Chris.Zaslawski@uts.edu.au

Appendix 5. Script for Subjects' Recruitment

UNIVERSITY OF TECHNOLOGY SYDNEY

Script for subjects' recruitment

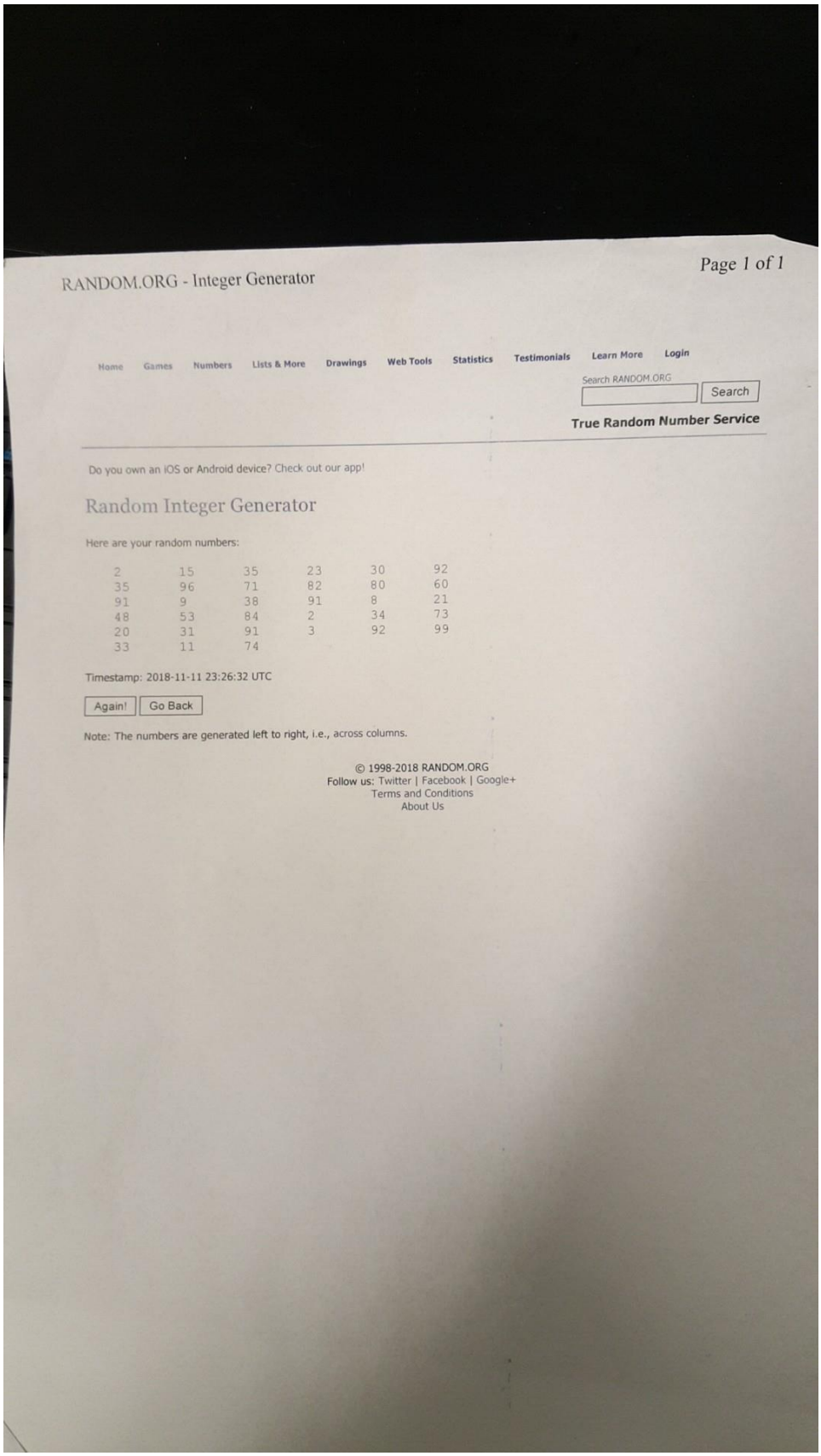
Hello, my name is Margaret. I am a Ph. D student at Life Science School in the Science Faculty. I am conducting research on acupuncture pain threshold among healthy human, and I am inviting you to participate because: 1) You are 18-70 years old; 2) You are right-handedness; 3) You have no medical history of chronic musculoskeletal disorder; and 4) You have no diagnosis of pain caused by any diseases in the recent seven days; 5) You are non-smoker.

Participation in this research will be required to attend for three acupuncture intervention sessions each taking approximately one hour. Participation in this research will be required to abstain from alcohol for 18 hours, caffeine for 4 hours, eating or exercise for 24 hours prior to any of the three sessions. There is at least one-week washout period between each intervention session. Only one acupoint on your hand will be applied. I would like to know how you would describe the sensations of your acupuncture intervention both when the needles are inserted and afterwards through some scales and questionnaires. I will use an algometer to measure pressure pain threshold on ten sites of your body. It does not puncture the skin. Participants will receive a pecuniary of $15 for each of the clinic visit, which covers the travel cost.

If you have any questions or would like to participate in the research, I can be reached at [redacted] or *Xiaoqin.wu@student.uts.edu.au*.

I advocate that anyone, who is interested in this study and eligible, become a volunteer participant for this research project.

Appendix 6. Random Number



RANDOM.ORG - Integer Generator

Page 1 of 1

Home Games Numbers Lists & More Drawings Web Tools Statistics Testimonials Learn More Login

Search RANDOM.ORG Search

True Random Number Service

Do you own an iOS or Android device? Check out our app!

Random Integer Generator

Here are your random numbers:

2	15	35	23	30	92
35	96	71	82	80	60
91	9	38	91	8	21
48	53	84	2	34	73
20	31	91	3	92	99
33	11	74			

Timestamp: 2018-11-11 23:26:32 UTC

Again! Go Back

Note: The numbers are generated left to right, i.e., across columns.

Appendix 7. Incident Adverse Reaction Harms Reporting Form

UNIVERSITY OF TECHNOLOGY SYDNEY

Incident / Adverse Reaction / Harms Reporting Form

Please tick any suitable items:

☐ Incident

☐ Adverse Reaction

☐ Harms

Participant's Name: _____ Participant ID: _____

Incident Date (DD/MM/YYYY): _____ Incident Time (HH:MM): _____

Participant's age: _____

Participant current and relevant diagnosis/problems:

Treating:

Participant care status:

Incident / Adverse Reaction / Harms Description:

Participant impact:

☐ Serious harm/Death ☐ Moderate harm ☐ Minor/No harm ☐ Near miss

Participant outcome:

☐ Death ☐ Serious harm ☐ Moderate harm ☐ Minor harm ☐ No harm

Causal relationship to acupuncture: _____

Rapporteur: _____

Date: _____

Appendix 8. Questionnaires & Data Collection Forms

UNIVERSITY OF TECHNOLOGY SYDNEY

Participant No.: _____ Intervention No.: _____ Date: _____

Initial Health Information Form

This is your health history questionnaire and initial evaluation form for your participation in Acupuncture Pain Threshold Study. We will use this information to help evaluate your health and decide whether you are eligible to participate this research project. Please make it as accurate and complete as possible.

1. Are you a healthy pain-free volunteer? ☐ Yes ☐ No
2. Are you right-handedness? ☐ Yes ☐ No
3. Do you have chronic musculoskeletal disorder? ☐ Yes ☐ No
4. Do you smoke? ☐ Yes ☐ No
5. Do you have depression or sleep disorders? ☐ Yes ☐ No
6. Do you have complications of severe systemic diseases, such as cardio or cerebrovascular diseases, diabetes, kidney diseases, central or peripheral nervous system or digestive system diseases? ☐ Yes ☐ No
7. Do you use of analgesic or sedatives regularly? ☐ Yes ☐ No
8. Do you have haemophilia and use of anticoagulant medication? ☐ Yes ☐ No
9. Are you pregnant or planning to become pregnant in the next 3 months? ☐ Yes ☐ No
10. Are you alcohol abuse and/or drug abuse? ☐ Yes ☐ No
11. Do you have a phobia of needles? ☐ Yes ☐ No
12. Are you allergy to metal? ☐ Yes ☐ No
13. Are you having acupuncture treatment recently? ☐ Yes ☐ No
14. Are you enrolled in other investigational studies? ☐ Yes ☐ No

---

THANK YOU!

Participant No.: _____ Intervention No.: _____ Date: _____

Data Collection Form

Participant number: _____

Intervention number: _____

Date (DD/MM/YEAR): _____

1. PPT measurement.

Order	Site	PPT Measurement (kgf)						
		pre				post		
1	$HT7^{R}$							
2	$SI11^{R}$							
3	$GB21^{R}$							
4	GV14							
5	$GB21^{L}$							
6	$SI11^{L}$							
7	GV4							
8	$HT7^{L}$							
9	$BL60^{L}$							
10	$BL60^{R}$							

Participant No.: _____ Intervention No.: _____ Date: _____

2. Visual Analogue Scale (VAS) for needling pain. Place a mark (×) on the line below to indicate your current level of pain.

0 10

|_____|

No pain Very severe pain

3. Visual Analogue Scale (VAS) for *deqi*. Place a mark (×) on the line below to indicate your current level of deqi.

0 10

|_____|

No *deqi* Intensive *deqi*

4. Place a mark (×) on the line below to indicate your current level of perceptions.

PLEASE INDICATE BY MARKING ON THE LINE YOUR ANSWER TO THE FOLLOWING QUESTIONS

1. How did you feel during the treatment?

_____

Completely calm and relaxed Extremely tense

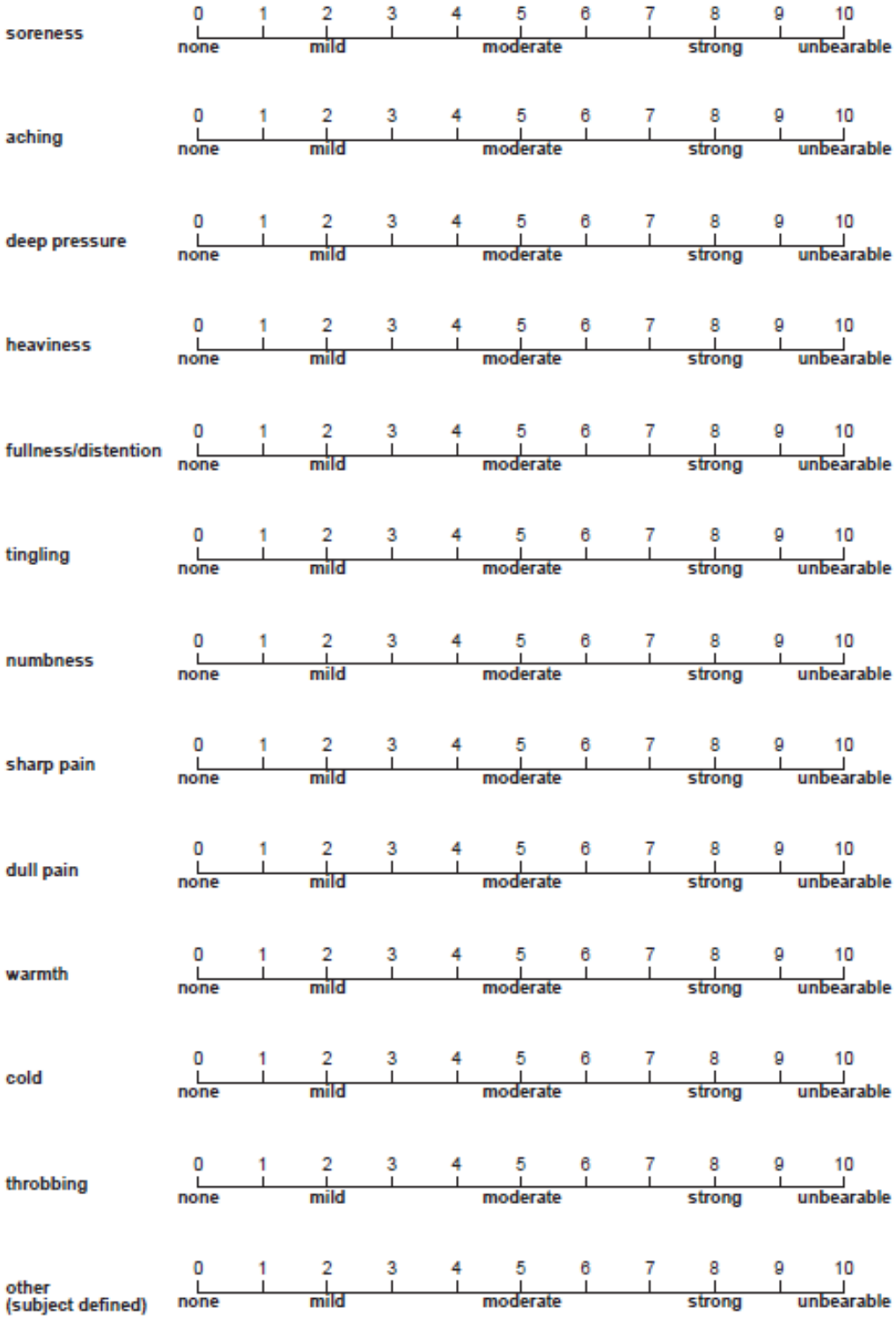
2. Were you anxious about feeling pain from the intervention today?

_____

No, not anxious at all Yes, extremely anxious

Participant No.: _____ Intervention No.: _____ Date: _____

5. MASS for *deq*i. Place a mark (×) on the line below to indicate your current level of *deqi*.



Participant No.: _____ Intervention No.: _____ Date: _____

6. Tick form for acupuncturist

Time	Manipulation	Tick
	t=0 min	
	t=3 min	
	t=6 min	
	t=9 min	
	t=12 min	
	t=15 min	
	t=18 min	
	t=21 min	

Appendix 9. Data Management Plan

Data management planning toolkit

Data management plan

Project overview

Project Name (*):	Investigating the effects of the acupoint SI3 (Houxi) on pressure pain threshold, needling sensation (deqi) and needling pain in healthy participants
Project ID (*):	12808198
Project website:	
Start date:	2018-06-01
End date:	2019-12-01
Funding source	
Grant number(s)	
Activity type:	Strategic basic research
FoR Codes	110404 - Traditional Chinese Medicine and Treatments
SEO Codes	920116 - Skeletal System and Disorders (incl. Arthritis),

Description (*)

The primary aims of this study are to investigate the effects of the acupoint SI3 on: 1. Regional Pressure Pain Threshold (PPT) at ten regional sites; 2. The strength and quality of needling sensation (deqi) reported; and 3. The strength of pain at the needling site in healthy participants.

People

First-named chief investigator (*)	Discipline Leader Christopher Zaslawski <Chris.Zaslawski@uts.edu.au>
Data manager (*)	Ms Xiaoqin Wu <Xiaoqin.Wu@student.uts.edu.au>
Collaborators	1. Professor Chi Eung Danforn Lim <Celim@ unswalumni.com>
Co-supervisor	Mr Yew Kian Loyeung <YewKian.Loyeung-1@uts.edu.au>

Data collection and analysis

Please provide a brief description of your data collection methodology(*)

I will use quantitative data collection methods. For example, I will use algometer to measure pressure pain threshold and will use VAS, MASS and some questionnairs to evaluate needling sensation and needling pain. All methods follow a repeatable process.

Predominant file format(s), e.g. xls, txt (*)
docx and xls.

Software/equipment used to create/collect the data
Software: EXCEL. Equipment: Wagner FPK Algometer (source: www.wagnerinstruments.com).

Software/equipment used to manipulate/analyse the data
Software: IBM SPSS Statistics 24.0 for Windows version 7. Equipment: DELL lap-top computer, a 15 GB USB flash disk.

Data storage

Expected size of the data collected(*) Less than 100GB

Storage Location during project(*) UTS provided collaboration space (e.g. CloudStor, OneDrive, etc)

If other, please provide further details: *Not provided*

Location of the master version Personal equipment (e.g. external drive, own laptop, etc)

Backup and version control procedures: 1. Data locations and forms will be stored securely by password UTS computer and will backup uploading to CloudStor daily, only accessible to the research student, principal supervisor and co-investigator. 2. Paper based data will be stored in key lockable cabinets, within locked room in Chinese medicine clinic at UTS, only accessible to the research student, principal supervisor and co-supervisor. 3. Backup data to a 7.5 GB USB flash disk once a week, only accessible to the research student, principal supervisor and co-supervisor.

Data retention and disposal

Applicable minimum retention period (*) 15 years (clinical research on human subjects)

Do any reasons for extending the minimum retention period apply to your data? *Not provided*

Access and rights

Copyright and intellectual property owners(*) My University

Other owners *Not provided*

Information about contractual obligations or third party licenses that apply to this data *Not provided*

In which country will your data be collected Australia

Access after the project will be managed by(*): permission from the data manager

The data manager is recorded as: Ms Xiaoqin Wu

Ethics and sensitivities

Ethics approval number *Not provided*

Type of sensitivity

Information about privacy, confidentiality or sensitivity to the data and how it will be managed

1. A research data management plan has been created in accordance with the Australian National Data Service (ANDS). ANDS is supported by the Australian Government through the National Collaborative

Research Infrastructure Strategy Program and the Education Investment Fund (EIF) Super Science Initiative. 2. The research data management plan has been recorded on the UTS Research Data Catalogue, STASH. 3. Data locations and forms will be stored securely by password UTS computer, an external drive and CloudStor, only accessible to the research student, principal supervisor and co-supervisor. 4.Paper based data will be stored in key lockable cabinets, within locked room in Chinese medicine clinic at UTS, only accessible to the research student, principal supervisor and co-supervisor.

Appendix 10. Registration Form

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Acupuncture Pain Threshold Study

Registration Form

Current Name:

Family Name: _____ Given Name: _____

Sex: Male☐ Female☐

Weight: _____ kg **Height:** _____ m

Date of Birth (DD/MM/YEAR)**:** _____ **Age:** _____

Residential Address: _____

Postal Address: (only complete this section if you want correspondence forwarded to an address different to your residential address) _____

_____

Contact Details:

Telephone (Home): _____

(Mobile): _____

(Work): _____

E-mail: _____

Known Allergies and Alerts to Adverse Reactions:

_____

Know Chronic Diseases:

_____

Inclusion/exclusion criteria check list. Please tick all options suit you:

☐ Healthy pain-free volunteers.

☐ Right-handedness.

☐ No medical history of chronic musculoskeletal disorder.

☐ No diagnosis of pain caused by any diseases in the seven days before study entry.

☐ Non-smoker.

☐ Willingness to give written informed consent and willingness to participate and comply with the study.

☐ Depression or sleep disorders, complications of severe systemic diseases, such as cardio or cerebrovascular diseases, diabetes, kidney diseases, central or peripheral nervous system or digestive system diseases.

☐ Regular use of analgesic or other drugs (that may dampen pain perception).

☐ Haemophilia and use of anticoagulant medication (that may interfere with blood clotting).

☐ Chronic consumers of sedatives, especially benzodiazepine or antidepressants (inhibiting the reuptake of serotonin, will not be enrolled in the study for the possible interference of the drugs on acupuncture action mechanisms).

☐ Pregnancy.

☐ Alcohol abuse and/or drug abuse.

☐ People highly dependent on medical care.

☐ People with a cognitive impairment, an intellectual disability or a mental illness.

☐ Needle phobia.

☐ Allergy to metal.

☐ Any type of acupuncture intervention used in the seven days before study entry.

☐ Enrolled in other investigational studies.

☐ Recent injury / illness/ medicine.

Participant Signature: _____

Name of Witness: _____

Signature of Witness: _____

Date (DD/MM/YEAR): _____

Appendix 11. Procedure of Participation

1. Pre-Intervention, enrolment and allocation

Prior to clinic visits where the interventions will be administered and data collected, these steps will be completed:

- An extensive explanation of the trial is to be given which includes the extent of the participant's involvement (interventions, measurements / samples taken, and questionnaires).
- If the applicant remains enthusiastic to participate in the study, written consent is sought for study participation and for photos to be taken.
- When signed consent was obtained the "Personal Detail, Initial Health and Participant Code Number" (Appendix 3 & 7) was completed. This form has the participants' identifying features including name, date of birth and contact details. An identification number (ID) was allocated to this form (a numerical number following the previous participant's number). The Participant Details and Code Number Identification Form and Consent Forms were to be stored separate to all other data gathering forms (which will only display the participants ID code so as to de-identify participants).
- Then participants were assigned to six sequences groups as per the process outlined in section 4.13.1.
- Participants were then scheduled for all three clinic visits in advance and notified by email or SMS of the allotted dates and times.

2. Data Collection

- The first time visit clinic, the participant completed a Registration Form (Appendix 9). On arrival at any of the clinic visits, the participant was asked to tell the investigator any changes of his or her health.
- PPT Readings and self-report assessment were entered directly into the Data Collection Form (Appendix 8). This form was sorted by participant number (no personally identifying information).
- Information was duplicated into the Excel Worksheet on a password secured computer.

3. Plans to promote participant retention and complete follow up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

- To encourage retention, participants will be offered a small financial remuneration for their participation the study. It will be $15 transportation fee for each intervention session.
- In the event of withdrawal from the study, any data collected for that participant will be kept and noted as 'incomplete' as part of the findings. Participants will be notified that even with withdrawal from the study; data collected to date will be retained and used as part of the study findings.

In the event of withdrawal from the study, there will be a one-week follow up for that participant to offer opportunities to report adverse events and harms.

Appendix 12. Criteria for Discontinuing or Modifying Allocated Interventions for a Given Trial Participant

1. Discontinuing:

Inclusion within the study may cease on any of the following:

- If participants withdraw their consent.
- Identification of new exclusion criteria on the clinic visit.
- If there are any types of adverse reaction to the intervention.
- If there is a fainting on acupuncture or an allergic reaction (e.g to metal).
- Excessive bleeding.
- The patient cannot cope with the treatment procedure.

2. Modification (Rescheduling)

Attendance at acupuncture point SI 3 Intervention visit may be rescheduled on any of the following:

- If the participant withdraws participation for the scheduled day however wishes to remain active in the study, and there are no new exclusion criteria identified.
- Identification of health status which may lead to adverse effects even though the participant wishes to remain active in the study (e.g. general feeling of unwell, recent musculoskeletal injuries)
- Non-adherence to visit preparation instructions (e.g. consumption of alcohol, caffeine, eating or exercise) though the participant wishes to remain active in the study, and there are no new exclusion criteria identified.

Appendix 13. Strategies to Improve Adherence to Intervention Protocols, and Any Procedures for Monitoring Adherence

- For successful admission to the study participants will be the given the Acupuncture Pain Threshold Study Project Information Sheet (Appendix 4) which outlines requirements of the study and instruction on how to remain in the study and will sign the Participant Consent Form (Appendix 4).
- Prior to each clinic visit, patients will be asked to complete the Registration Form (Appendix 10) to identify any new risks or exclusion criteria
- Participants will be asked to refrain from alcohol (Wolff , Hardy & Goodell 1940) for 3.5 hours (Dohmen et al. 1996), caffeine for 32 hours (Kaplan et al. 1997; Lelo et al. 1986), vigorous exercise for 24 hours (Walton et al. 2011), eating for 30 minutes prior to visiting the clinic.
- Participants will be encouraged to ask questions of the investigator at any time before or during the study period.
- It is crucial that there is high adherence to protocol as low adherence can reduce the contrast between the study groups. Participants will be scheduled well in advance and sent scheduling reminders 1 day before their appointments.

Appendix 14. Relevant Concomitant Care and Interventions that Are Permitted or Prohibited during the Trial

- If the participant receives medical advice during the study period to begin taking any of the medications noted in the exclusion criteria, the participant must advise the chief investigator immediately for withdrawal from the study.
- Participants will be requested to refrain from any other acupuncture interventions for the duration of the study.

Participants will be requested to refrain from any concomitant therapies including massage therapy, acupuncture, cupping, moxibustion and guasha for the duration of the study.

Appendix 15. Monitoring & Harms

1. The roles of the data monitoring included:

- Review of the study protocol prior to implementation
- Review cumulative study data to evaluate safety of the participants
- Review of cumulative data for evidence of study-related adverse events
- Review data quality, completeness and timeliness
- Review adherence to protocol
- Report all the above to the Chief Investigator (CZ)

No interim analyses have been planned. However, all adverse events should be reported to the Chief Investigator and the UTS HREC.

2. Harms: Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct.

The CONSORT reporting extension "Better Reporting of Harms in Randomised Trials: An Extension of the CONSORT Statement" (Ioannidis et al. 2004) encourages the use of priming participants on possible adverse events in order to increase reporting rate. This is done by explicitly listing possible adverse events and harms within the Participant Information Sheet (Appendix 3) and participants explicitly agree they understand the risks by signing the Participant Consent form (Appendix 3). Rampes and James found 395 cases of complications after searching all English language case reports from 1966 to 1993 (Rampes & James 1995). Although Rampes and James summarised 29 complications of acupuncture, most of complications will not occur in this study, as only one acupoint was applied on the right hand with the disposable needle by a competent acupuncturist in this study. The potential harms should be minor, such as bruising or fainting. Actually, acupuncture is safe when operated by competent practitioners (Vincent 2001).

Passive harm reporting, whereby a harms report is triggered by the participant, should be encouraged. Additionally, active harm reporting should be implemented whereby the investigator asked the participants about specific adverse events during intervention application (in clinic). Incidents occurring on UTS campus should be reported per protocol in the Hazard and Incident Reporting Online (HIRO) system. Follow up phone interviews at the one week should give participants opportunity to report ongoing adverse reactions or harms. Any adverse events (expected or unexpected) related to acupuncture interventions should be reported to the investigator by participants and recorded by the

investigator at every visit. Possible adverse events related to acupuncture could be local bleeding or oedema resulting from bleeding, redness, itching, and dizziness or fainting, throughout this experiment and the follow up period. Subjects should receive appropriate intervention if any adverse events occur. Serious adverse events should be reported to the primary investigator immediately, and participants would be withdrawn from the study. The following details on adverse events should be documented: date of occurrence; time lost; measures taken related to the acupuncture; causal relationship to acupuncture; treatment for adverse event.

Additionally, the following action plans should be in place:

- All investigators should be briefed on the procedure for reporting adverse effects and harms
- Researchers should hold a current Australian Senior First Aid certification (HLTAID003)
- Participants should be advised to make known to the investigator immediately any observation of adverse reaction during the application of intervention or at any time during the study period, including the close-out and follow up weeks.
- In the event of an emergency, UTS Emergency Protocols is:
  - Dial 6 for UTS Security (all security staff are First Aid trained); Or free call 1800 249 559
  - Dial 000 if life threatening
  - Apply immediate First Aid
  - Royal Prince Alfred Hospital: Dial 9515 6111
  - St. Vincent's Hospital: Dial 8832 1111
- All incidents and adverse events, regardless if reported onsite, or remotely by the participant (e.g. a phone call to the research student or Principal Supervisor/Chief Investigator) will be recorded by completing the Incident / Adverse Reaction / Harms Reporting form (Appendix 7).

Appendix 16. Ethics and Dissemination

1. Protocol amendments: Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g., investigators, REC/IRBs, trial participants, trial registries, journals, regulators)

Any changes to protocols, intervention procedures, and data collection methods should be approved in writing by each of the Investigators listed by completing a Project Change Management Form (Appendix 17), noting the need for the change, impact to the project and participants. This form should accompany re-submission for Ethics approval.

2. Consent or assent:

The research student (XW) introduced the trial to potential trial participants who were shown the main aspects of the trial. Participants also received information sheets. The research student (XW) discussed the trial with participants in light of the information provided in the information sheet. All participants had been given a minimum 7-day window period to decide whether to accept or decline this invitation to participate. The research student (XW) obtained written consent from participants willing to participate in the trial.

Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable.

3. Confidentiality: How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial

Refer to the Research Data Management plan as noted in Section 4.12.4.

4. Declaration of interests: Financial and other competing interests for principal investigators for the overall trial and each study site

Declaration of Financial support:

Country	Institution	Co-contributors	Financial support
Australia	University of Technology, Sydney (UTS)	A/P Chris Zaslawski Dr Yew Kian Bertrand Loyeung Ms Xiaoqin Wu	• This research is supported by an Australian Government Research Training Program Scholarship • 2019 Vice-Chancellor's Graduate Research Student Conference Fund

5. Access to data: Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators

Refer to the Research Data Management plan as noted in section 4.12.4.

6. Ancillary and post-trial care: Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation

As outlined in Sections 4.15 and Appendix 11, participants should be contacted at two weeks after the trial period to give opportunity to report late adverse reactions or other concerns.

7. Dissemination policy:

- Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions
- It was planned for Trial results to be published in a relevant health related journal.
- Authorship eligibility guidelines and any intended use of professional writers
- Authorship will be granted to each of the investigators listed.
- Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code
- It was intended to submit the full protocol as a manuscript for publication.

Appendix 17. Project Change Management Form

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Project Change Management Form

1. PROJECT DETAILS

Name of Project	File references
Investigating the effects of the acupoint SI3 (*Houxi*) on pressure pain threshold, needling sensation (*deqi*) and needling pain	

2. REQUEST DETAILS

Date of Request	Request No.	Name of Requestor	Project Position

3. CHANGE DETAILS

Project Category	Proposed Change	Reason for Variance
Scope		
Time		
Risk Management		
Other		

4. CHANGE JUSTIFICATION

Priority	***Immediate***	***Essential***	***Urgent***	***High***	***Medium***	***Low***
Intended outcome(s)						
Expected benefit(s)						

5. IMPACT OF CHANGE

List any important impact of the change(s) on the Project deliverables

6. SUPPORTING DOCUMENTATION

Appendix 18. Explanations of Technical Terms Used

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Technical Terms

The following definitions are about this research project.

- **PPT**: Pressure pain threshold (PPT) is defined as the minimum force applied, which produced when press hard on something and could induce pain. PPT is the force from comfortable pressure to slightly unpleasant pain, which has been used in evaluating tenderness symptom generally. (Maquet et al. 2004; Walton et al. 2011)
- ***deqi***: *Deqi* is a Chinese word, which means grasp the *qi* and is also known as needling sensation. *Deqi* is the technique of producing the meridional induction in the acupoint, which is assumed by many acupuncturists to be associated with a therapeutic effect and for this reason is often sought during needling (MacPherson et al. 2001). The perceptions of needle sensation originated from the Yellow Emperor's Cannon of Medicine • Suwen - "When manipulating the needle to grasp the *qi*, also have the patient inhale."(Ni 1995, p. 107). In Yellow Emperor's Cannon of Medicine • Spiritual Pivot stated, "Needling[should be done when *qi* has arrived. If] Qi has not arrived, [doctors must wait till it has arrived and] should not stick to the time [of using the needling techniques]." (Li & Liu 2008, p. 15). "*Qi* has arrived" is the same meaning of "grasp the *qi*", which means needling sensation.
- **MASS**: MASS is the abbreviation of Massachusetts General Hospital (MGH) Acupuncture Sensation Scale. To monitor needling sensations, Kong et al. (2007) adapted to measure sensations evoked by acupuncture stimulation as perceived by the patient alone.
- **VAS**: A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. Operationally the VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimetres from the left hand end of the line to the point that the patient marks. (Scott & Huskisson 1976). The VAS score in this research project is to measure the amount of both pain and *deqi* sensations that a patient feels ranges across a continuum from none to an extreme amount.

Appendix 19. Standard Operating Procedures

Standard Operating Procedure

Dept	Faculty of Science	**Bldg/Rm**	UTS Chinese Medicine Clinic CB04.02	**Supervisor**	Christopher Zaslawski, Yew Kian Loyeung

PURPOSE: To schedule the work flow so that the research team can conduct this project accurately.

MISSION: INVESTIGATING THE EFFECTS OF THE ACUPOINT SI3 (*HOUXI*) ON PRESSURE PAIN THRESHOLD, NEEDLING SENSATION (*deqi*) AND NEEDLING PAIN

PILOT STUDY

Recruitment

Advertising for participants will occur through flyers around the university and possibly through staff notices and social media. Individuals (not necessarily UTS students) known to the PhD student may be approached on occasions. An A4 UTS Science poster based on the information sheet will be posted on noticeboards throughout the University. Information sheets will available at the UTS Chinese Medicine Clinic.

Pre-interview

1. Those interested can contact the research student by email or telephone.
2. The Project Information Sheet and the Consent Form will be sent to each inquirer if they still express interest after the initial contact.
3. A face-to-face interview will be arranged in UTS Chinese Medicine Clinic in seven days after the potential participant received the Information Sheet and Consent Form.

Interview

1. There will be more explanations and answering the questions in detail for the potential participant during the interview.
2. Initial Health Information Form filling for the eligibility screen.
3. The eligible participant will sign the consent form, the registration form and retain all the documents copies.
4. Arrange the first clinic visit time.
5. Establish a confidential file of the participant. Put the sealed envelope to the file, which can only be opened by the acupuncturist. The intervention number of the participant will be attained from a sealed envelope.

Experiment Sequence Instruction

1. Information to the participant re intervention.
2. Provide explanation for *deqi* and needling pain. Request that the participant remember his/her sensation of needling pain and *deqi*.

Request that the participant change into a disposable gown. Participants will be taken to a treatment area and lie prone (face down) on a treatment couch (Figure 1). A curtain will be drawn between the participant's body and right arm. The acupuncturist will be positioned on the side where the arm is exposed while the assessor will be on the other side. In this way, both the assessor and the participants will be blinded to the type of needling intervention (with or without manipulation).

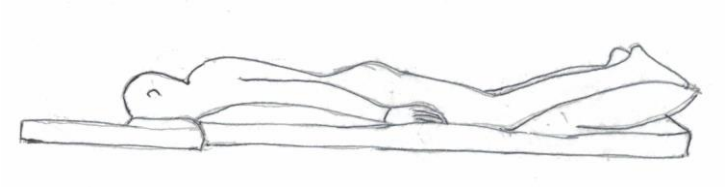

Figure 1: Lie prone position

3. Mark 10 points on the subject's body with a skin marker pen (1.0 mm, Regular tip, Multigate Medical Devices Pty Ltd). The order of site measurement will be $HT7^{R}$, $SI11^{R}$, $GB21^{R}$, GV14, $GB21^{L}$, $SI11^{L}$, GV4, $HT7^{L}$, $BL60^{L}$, and $BL60^{R}$.
4. Pre-intervention PPT measure.
5. Intervention. The acupuncturist will conduct the intervention following the sequence arrangement in the sealed envelope and use the tick form during the intervention procedure.
6. Post-intervention PPT measure.
7. The participant will sit up to finish Needling pain VAS, *deqi* VAS, MASS and a questionnaire.

It takes 30 min to accomplish procedure 4-7 and round 30 min to finish procedure 8.
All PPT measure will operated by the Ph. D student and co-investigator will read and write the record of the algometer.

8. Verification and record keeping: Researchers must sign after writing on the data collection form.

Potential Hazards/Toxicity

There are some minor risks associated with acupuncture, for example possible bruising at the needling site, local bleeding or oedema resulting from bleeding, redness, itching, and dizziness or fainting.
An Incident/Adverse Reaction/Harms Reporting Form is ready for recording in each participant's file.

Accident & First Aid Procedures

- All investigators will be briefed on the procedure for reporting adverse effects and harms
- Researchers should hold a current Australian Senior First Aid certification (HLTAID003)
- Participants will be advised to make known to the investigator immediately any observation of adverse reaction during the application of intervention or at any time during the study period, including the close-out and follow up weeks.
- In the event of an emergency, UTS Emergency Protocols will be

- Dial 6 for UTS Security (all security staff are First Aid trained); Or free call 1800 249 559
- Dial 000 if life threatening
- Apply immediate First Aid
- Royal Prince Alfred Hospital: Dial 9515 6111
- St. Vincent's Hospital: Dial 8832 1111

All incidents and adverse events, regardless if reported onsite, or remotely by the participant (e.g. a phone call to the research student or Principal Supervisor/Chief Investigator) will be recorded by completing the
Incident / Adverse Reaction / Harms Reporting form.

Table Log

Instructions: Researchers enter the study site for interview or experiment should read the SOP and sign in the following table.

Date and Time		Item	Corrective Action Taken	Initials	Verified By/ Date

Material Safety Data Sheet (MSDS) Location

Data locations and forms will be stored in a locked cabin in UTS Chinese Medicine Clinic, only accessible to the research student, principal supervisor and co-investigator.

Waste Disposal and Clean Up Procedures

- General waste disposal: place in general waste bin for removal.
- Single-use sharps should be placed (by the user) into a sharps container that meets the Australian and New Zealand Standards AS 4031:1992 and AS/NZS 4261:1994.

Principal Investigator: Christopher Zaslawski
Contact: Margaret [redacted]
Date when SOP was written: _____ **BY:** _____
Date when SOP was approved by the supervisor: _____ **BY:** _____

TRAINING RECORD

Use the following table to record the training associated with this Standard Operating Procedure.
(Signature of all users is required)
I have read and understand the content of this SOP:

Print Name	Signature	Trained By	Date

Appendix 20. Examine Variable of Mean Percentage Change of PPT by Intervention

```
EXAMINE VARIABLES=Mean change BY Intervention
  /PLOT BOXPLOT STEMLEAF
  /COMPARE GROUPS
  /STATISTICS DESCRIPTIVES
  /CINTERVAL 95
  /MISSING LISTWISE
  /NOTOTAL.
```

Explore
Intervention

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	Intervention	N	Percent	N	Percent	N	Percent
Mean% change	SI3m-	310	100.0%	0	0.0%	310	100.0%
	SI3m+	310	100.0%	0	0.0%	310	100.0%
	SL	310	100.0%	0	0.0%	310	100.0%

Descriptives

	Intervention			Statistic	Std. Error
Mean% change	SI3m-	Mean		16.1456	1.10562
		95% Confidence Interval for Mean	Lower Bound	13.9701	
			Upper Bound	18.3211	
		5% Trimmed Mean		15.6457	
		Median		15.2000	
		Variance		378.944	
		Std. Deviation		19.46649	
		Minimum		-25.00	
		Maximum		83.60	
		Range		108.60	
		Interquartile Range		23.58	
		Skewness		.458	.138
		Kurtosis		.497	.276
	SI3m+	Mean		23.7138	1.19980
		95% Confidence Interval for Mean	Lower Bound	21.3530	
			Upper Bound	26.0747	
		5% Trimmed Mean		22.8559	
		Median		22.1000	
		Variance		446.253	
		Std. Deviation		21.12471	

		Minimum		-19.40	
		Maximum		123.10	
		Range		142.50	
		Interquartile Range		30.95	
		Skewness		.757	.138
		Kurtosis		1.342	.276
	SL	Mean		.2476	.69161
		95% Confidence Interval for Mean	Lower Bound	-1.1133	
			Upper Bound	1.6084	
		5% Trimmed Mean		-.0111	
		Median		.0000	
		Variance		148.281	
		Std. Deviation		12.17709	
		Minimum		-37.00	
		Maximum		43.80	
		Range		80.80	
		Interquartile Range		16.35	
		Skewness		.336	.138
		Kurtosis		.880	.276

Mean% change

Stem-and-Leaf Plots

```
Mean% change Stem-and-Leaf Plot for
Intervention= SI3m-

 Frequency    Stem &  Leaf

     1.00       -2 .  5
     6.00       -2 .  012234
    10.00       -1 .  5677777789
     6.00       -1 .  122333
    17.00       -0 .  55666667778888999
    21.00       -0 .  000011222223333334444
    26.00        0 .  00000001112222223333333444
    35.00        0 .  55555666666677788888888899999999999
    30.00        1 .  000111112222223333333333334444
    40.00        1 .  55555555556666667777777888888888888999999
    27.00        2 .  000000000111222223334444444
    26.00        2 .  55555556666666677788888899
    15.00        3 .  011223333334444
    15.00        3 .  555666666777789
    10.00        4 .  0001234444
     8.00        4 .  56777889
     7.00        5 .  0001222
     3.00        5 .  668
```

```
     2.00        6 .  00
     5.00 Extremes    (>=63)

 Stem width:  10.00
 Each leaf:        1 case(s)
Mean% change Stem-and-Leaf Plot for
Intervention= SI3m+

 Frequency    Stem &  Leaf

     9.00       -1 .  113556899
    24.00       -0 .  000111123333344444566799
    55.00        0 .
001112222233333344445555555556666666666677777788888999
    59.00        1 .
000000011112222222233333344445556666666677777777778889999
    53.00        2 .
00000112222222222333333344444555556666677778888899999
    41.00        3 .  000000112222344444444555555566778889999999
    35.00        4 .  00000000000011112222333445556677777
    17.00        5 .  00011222344455688
     9.00        6 .  112233667
     4.00        7 .  0146
     1.00        8 .  1
     3.00 Extremes    (>=88)

 Stem width:  10.00
 Each leaf:        1 case(s)



Mean% change Stem-and-Leaf Plot for
Intervention= SL

 Frequency    Stem &  Leaf

     2.00 Extremes    (=<-33)
    11.00       -2 .  00011233444
    20.00       -1 .  55555555666666677789
    26.00       -1 .  000000011122233333333444444
    50.00       -0 .
55555555555556666666677777777788888888888999999999
    39.00       -0 .  011111111111222222222223333333344444444
    54.00        0 .
000000000011111111112222222222222222222223333333344444
    48.00        0 .  555555555556666666667777777778888888999999999999
    33.00        1 .  000000001111111222223333333444444
    12.00        1 .  555556669999
     7.00        2 .  0001222
     2.00        2 .  88
     1.00        3 .  0
     5.00 Extremes    (>=35)

 Stem width:  10.00
 Each leaf:        1 case(s)
```

Appendix 21: Tests of Between-subjects Effects

Dependent Variable: Mean% change

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[b]
Corrected Model	100024.866[a]	11	9093.170	28.813	.000	.257	316.938	1.000
Intercept	166219.317	1	166219.317	526.682	.000	.365	526.682	1.000
Intervention	88938.043	2	44469.022	140.904	.000	.235	281.809	1.000
Site	11086.823	9	1231.869	3.903	.000	.037	35.130	.995
Error	289718.263	918	315.597					
Total	555962.446	930						
Corrected Total	389743.129	929						

a. R Squared = .257 (Adjusted R Squared = .248)

b. Computed using alpha = .05

Appendix 22. Multiple Comparisons

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
SI3M-	SI3M+	-7.5682*	1.42692	.000	-10.9180	-4.2185
	SL	15.8980*	1.42692	.000	12.5483	19.2478
SI3M+	SI3M-	7.5682*	1.42692	.000	4.2185	10.9180
	SL	23.4663*	1.42692	.000	20.1165	26.8160
SL	SI3M-	-15.8980*	1.42692	.000	-19.2478	-12.5483
	SI3M+	-23.4663*	1.42692	.000	-26.8160	-20.1165

Based on observed means.

The error term is Mean Square (Error) = 315.597.

*. The mean difference is significant at the .05 level.

Appendix 23. Examine Variable of Mean Percentage Change of PPT by Site

Post Hoc Tests

Intervention

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-9.4484	4.29042	.076	-19.6729	.7761
	SL	7.2387	4.29042	.216	-2.9858	17.4632
SI3M+	SI3M-	9.4484	4.29042	.076	-.7761	19.6729
	SL	16.6871*	4.29042	.001	6.4626	26.9116
SL	SI3M-	-7.2387	4.29042	.216	-17.4632	2.9858
	SI3M+	-16.6871*	4.29042	.001	-26.9116	-6.4626

Based on observed means.

The error term is Mean Square(Error) = 285.320.

*. The mean difference is significant at the .05 level.

a. Site = HT7R

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-10.9000*	4.37041	.038	-21.3151	-.4849
	SL	10.8968*	4.37041	.038	.4816	21.3119
SI3M+	SI3M-	10.9000*	4.37041	.038	.4849	21.3151
	SL	21.7968*	4.37041	.000	11.3816	32.2119
SL	SI3M-	-10.8968*	4.37041	.038	-21.3119	-.4816
	SI3M+	-21.7968*	4.37041	.000	-32.2119	-11.3816

Based on observed means.

The error term is Mean Square(Error) = 296.058.

*. The mean difference is significant at the .05 level.

a. Site = SI11R

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-9.5742	4.39435	.080	-20.0464	.8980
	SL	13.9968*	4.39435	.006	3.5246	24.4690
SI3M+	SI3M-	9.5742	4.39435	.080	-.8980	20.0464
	SL	23.5710*	4.39435	.000	13.0988	34.0432
SL	SI3M-	-13.9968*	4.39435	.006	-24.4690	-3.5246
	SI3M+	-23.5710*	4.39435	.000	-34.0432	-13.0988

Based on observed means.

The error term is Mean Square(Error) = 299.310.

*. The mean difference is significant at the .05 level.

a. Site = GB21R

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-7.0065	4.71824	.303	-18.2505	4.2376
	SL	16.2661*	4.71824	.002	5.0221	27.5102
SI3M+	SI3M-	7.0065	4.71824	.303	-4.2376	18.2505
	SL	23.2726*	4.71824	.000	12.0285	34.5166
SL	SI3M-	-16.2661*	4.71824	.002	-27.5102	-5.0221
	SI3M+	-23.2726*	4.71824	.000	-34.5166	-12.0285

Based on observed means.

The error term is Mean Square(Error) = 345.058.

*. The mean difference is significant at the .05 level.

a. Site = GV14

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-3.1213	4.13007	.731	-12.9637	6.7211
	SL	16.1206*	4.13007	.001	6.2783	25.9630
SI3M+	SI3M-	3.1213	4.13007	.731	-6.7211	12.9637
	SL	19.2419*	4.13007	.000	9.3996	29.0843
SL	SI3M-	-16.1206*	4.13007	.001	-25.9630	-6.2783
	SI3M+	-19.2419*	4.13007	.000	-29.0843	-9.3996

Based on observed means.

The error term is Mean Square(Error) = 264.390.

*. The mean difference is significant at the .05 level.

a. Site = GB21L

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-10.1032	4.78415	.093	-21.5043	1.2979
	SL	21.7194*	4.78415	.000	10.3182	33.1205
SI3M+	SI3M-	10.1032	4.78415	.093	-1.2979	21.5043
	SL	31.8226*	4.78415	.000	20.4215	43.2237
SL	SI3M-	-21.7194*	4.78415	.000	-33.1205	-10.3182
	SI3M+	-31.8226*	4.78415	.000	-43.2237	-20.4215

Based on observed means.

The error term is Mean Square(Error) = 354.765.

*. The mean difference is significant at the .05 level.

a. Site = SI11L

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-7.1161	5.53766	.407	-20.3129	6.0807
	SL	24.4097*	5.53766	.000	11.2129	37.6065
SI3M+	SI3M-	7.1161	5.53766	.407	-6.0807	20.3129
	SL	31.5258*	5.53766	.000	18.3290	44.7226
SL	SI3M-	-24.4097*	5.53766	.000	-37.6065	-11.2129
	SI3M+	-31.5258*	5.53766	.000	-44.7226	-18.3290

Based on observed means.

The error term is Mean Square(Error) = 475.318.

*. The mean difference is significant at the .05 level.

a. Site = GV4

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-6.0452	3.91777	.276	-15.3816	3.2913
	SL	17.4774*	3.91777	.000	8.1410	26.8139
SI3M+	SI3M-	6.0452	3.91777	.276	-3.2913	15.3816
	SL	23.5226*	3.91777	.000	14.1861	32.8590
SL	SI3M-	-17.4774*	3.91777	.000	-26.8139	-8.1410
	SI3M+	-23.5226*	3.91777	.000	-32.8590	-14.1861

Based on observed means.

The error term is Mean Square(Error) = 237.908.

*. The mean difference is significant at the .05 level.

a. Site = HT7L

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-7.5097	4.51983	.226	-18.2809	3.2615
	SL	14.4355*	4.51983	.005	3.6643	25.2067
SI3M+	SI3M-	7.5097	4.51983	.226	-3.2615	18.2809
	SL	21.9452*	4.51983	.000	11.1739	32.7164
SL	SI3M-	-14.4355*	4.51983	.005	-25.2067	-3.6643
	SI3M+	-21.9452*	4.51983	.000	-32.7164	-11.1739

Based on observed means.

The error term is Mean Square(Error) = 316.647.

*. The mean difference is significant at the .05 level.

a. Site = BL60L

Multiple Comparisons[a]

Dependent Variable: Mean% change

Tukey HSD

(I) Intervention	(J) Intervention	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
SI3M-	SI3M+	-4.8577	4.32073	.502	-15.1545	5.4390
	SL	16.4194*	4.32073	.001	6.1226	26.7161
SI3M+	SI3M-	4.8577	4.32073	.502	-5.4390	15.1545
	SL	21.2771*	4.32073	.000	10.9804	31.5738
SL	SI3M-	-16.4194*	4.32073	.001	-26.7161	-6.1226
	SI3M+	-21.2771*	4.32073	.000	-31.5738	-10.9804

Based on observed means.

The error term is Mean Square(Error) = 289.364.

*. The mean difference is significant at the .05 level.

a. Site = BL60R

Appendix 24. Nonparametric Tests

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distributions of HT7R , SI11R, GB21R, GV14, GB21L, SI11L, GV4, HT7L, BL60L and BL60R are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.000	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .050.

Related-Samples Friedman's Two-Way Analysis of Variance by Ranks

HT7R , SI11R, GB21R, GV14, GB21L, SI11L, GV4, HT7L, BL60L, BL60R

Related-Samples Friedman's Two-Way Analysis of Variance by Ranks Summary

Total N	93
Test Statistic	59.718
Degree Of Freedom	9
Asymptotic Sig.(2-sided test)	.000

Pairwise Comparisons

Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.[a]
HT7R -GB21R	-.559	.444	-1.259	.208	1.000
HT7R -HT7L	-1.586	.444	-3.572	.000	.016
HT7R -BL60L	-1.602	.444	-3.608	.000	.014
HT7R -SI11R	-1.661	.444	-3.742	.000	.008
HT7R -GV14	-1.726	.444	-3.887	.000	.005
HT7R -GB21L	-1.726	.444	-3.887	.000	.005
HT7R -BL60R	-1.978	.444	-4.456	.000	.000
HT7R -GV4	-2.376	.444	-5.352	.000	.000
HT7R -SI11L	-2.806	.444	-6.321	.000	.000
GB21R-HT7L	-1.027	.444	-2.313	.021	.933

GB21R-BL60L	-1.043	.444	-2.349	.019	.847
GB21R-SI11R	1.102	.444	2.482	.013	.587
GB21R-GV14	-1.167	.444	-2.628	.009	.387
GB21R-GB21L	-1.167	.444	-2.628	.009	.387
GB21R-BL60R	-1.419	.444	-3.197	.001	.063
GB21R-GV4	-1.817	.444	-4.093	.000	.002
GB21R-SI11L	-2.247	.444	-5.062	.000	.000
HT7L-BL60L	-.016	.444	-.036	.971	1.000
HT7L-SI11R	.075	.444	.170	.865	1.000
HT7L-GV14	.140	.444	.315	.753	1.000
HT7L-GB21L	.140	.444	.315	.753	1.000
HT7L-BL60R	-.392	.444	-.884	.377	1.000
HT7L-GV4	.790	.444	1.780	.075	1.000
HT7L-SI11L	1.220	.444	2.749	.006	.269
BL60L-SI11R	.059	.444	.133	.894	1.000
BL60L-GV14	.124	.444	.279	.781	1.000
BL60L-GB21L	.124	.444	.279	.781	1.000
BL60L-BL60R	-.376	.444	-.848	.397	1.000
BL60L-GV4	.774	.444	1.744	.081	1.000
BL60L-SI11L	1.204	.444	2.712	.007	.301
SI11R-GV14	-.065	.444	-.145	.884	1.000
SI11R-GB21L	-.065	.444	-.145	.884	1.000
SI11R-BL60R	-.317	.444	-.714	.475	1.000
SI11R-GV4	-.715	.444	-1.610	.107	1.000
SI11R-SI11L	-1.145	.444	-2.579	.010	.446
GV14-GB21L	.000	.444	.000	1.000	1.000
GV14-BL60R	-.253	.444	-.569	.569	1.000
GV14-GV4	-.651	.444	-1.465	.143	1.000
GV14-SI11L	-1.081	.444	-2.434	.015	.672
GB21L-BL60R	-.253	.444	-.569	.569	1.000
GB21L-GV4	-.651	.444	-1.465	.143	1.000
GB21L-SI11L	-1.081	.444	-2.434	.015	.672
BL60R-GV4	.398	.444	.896	.370	1.000
BL60R-SI11L	.828	.444	1.865	.062	1.000
GV4-SI11L	.430	.444	.969	.333	1.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.

Asymptotic significances (2-sided tests) are displayed. The significance level is .05.

a. Significance values have been adjusted by the Bonferroni correction for multiple tests.

Appendix 25. Tests of Between-subjects Effects of Needling Pain VAS

Tests of Between-Subjects Effects

Dependent Variable: Needling Pain VAS

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	8999.603[a]	3	2999.868	6.506	.000	.180
Intercept	43710.808	1	43710.808	94.792	.000	.516
Intervention	8993.957	2	4496.978	9.752	**.000**	.180
Gender	5.646	1	5.646	.012	.912	.000
Error	41039.967	89	461.123			
Total	93828.000	93				
Corrected Total	50039.570	92				

a. R Squared = .180 (Adjusted R Squared = .152)

Appendix 26. Nonparametric Test of Needling Pain VAS

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum
SI3m-	31	24.35	24.662	0	80
SI3m+	31	32.19	21.043	0	78
SL	31	8.55	17.808	0	70

Friedman Test

Ranks

	Mean Rank
SI3m-	2.00
SI3m+	2.63
SL	1.37

Test Statistics[a]

N	31
Chi-Square	26.920
df	2
Asymp. Sig.	.000

a. Friedman Test