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Short term sensory and vascular responses to physical agent modalities and exercise in healthy volunteers and patients with distal radius fracture.

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A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy  
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SHORT TERM SENSORY AND VASCULAR RESPONSES TO PHYSICAL AGENT MODALITIES AND EXERCISE IN HEALTHY VOLUNTEERS AND PATIENTS WITH DISTAL RADIUS FRACTURE

(Thesis format: Integrated-Article)

By

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Graduate Program in Health and Rehabilitation Science (Physical Therapy)

A thesis submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

The School of Graduate and Postdoctoral Studies

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Thesis Abstract

Currently, there is weak evidence on the effectiveness of different rehabilitation regimens following distal radius fracture (DRF). This thesis evaluated sensory and vascular effects of exercise, thermal and ultrasound interventions that can be used in the mobilization phase (cast removal) after DRF.

Methods

- This thesis includes 3 studies. The first study compared responses to Immersion in Cold water Evaluation (ICE) in the DRF and uninjured hands. Skin blood flow (Sbf), skin temperature (temp.) and sensory perception thresholds (sPT) at 2000Hz for A–beta fibres and at 5 Hz for C fibres were obtained before, immediately after ICE and 10 min later.

- The second study assessed Sbf, temp., and sPT before and after 3 conditions: control, 1 MHz continuous and 3 MHz pulsed US in healthy subjects.

- The third study assessed Sbf and sPT before and after 3 conditions: control, 5 min of high intensity and low intensity hand exercises in healthy subjects.

- Differences in these were analyzed using General Linear Models.

Results

- In the DRF hand, Sbf increased (Mean Difference (MD) = -42.2 A.U.) immediately, at 1 min (MD= -35 A.U.), and 10 min after ICE (MD= -1 A.U.). There was a decrease in temp. for the index and little fingers immediately after ICE (MD=9. 9 & 9.1 °C) and these did not return to baseline by 10 min (MD= 4.4 & 4 °C). ICE had no effect on sPT at 5 Hz (p>0.05). There was no difference between the DRF and uninjured hand on all measures(p>0.05) except for the sPT at 2000Hz, which remained high on the DRF side for up to 10 min( MD= -1.8 m. A.).
Both pulsed and continuous US caused small to moderate reductions in Sbf (MD= 2.8 A.U. & 3.9 A.U.), temp. (MD = 2.5 °C & 1.1 °C) and sPT at 5 Hz (MD=1.3 m. A. & 1 m. A.). US had no effect on sPT at 2000Hz (p>0.05).

Both type of exercises were insufficient to alter Sbf and sPT at 2000Hz and 5 Hz (p>0.05).

Conclusions

Normal thermo-physiological responses were observed after ICE in both hands. A-beta fibres on the DRF side became less sensitive after ICE.

Minor changes can occur in Sbf, temp., and sPT at 5 Hz following 3 to 5 min exposure to US in healthy subjects.

Hand grip exercises had minimal impact on Sbf or sPT in healthy subjects.

The changes seen with ICE and US are presumed to help with tissue healing and pain modulation which needs further investigation.

Keywords

Distal radius fracture, cold, ultrasound, exercise, skin, sensory, vascular, forearm, hand, cross over trial, repeated measures
CO-AUTHORSHIP STATEMENT

Each of the five chapters in this thesis were designed, performed, analyzed, interpreted, and written by me with the valuable input, guidance, and advice from my supervisor Dr. Joy C. MacDermid. Members of the advisory committee provided regular input in the form of guidance and feedback. Primarily Shaguftha Shaik authored all studies with editing provided by Dr. Joy C. MacDermid.

Other collaborators:

Apart from the advisory committee members, other important collaborators must be recognized because of their roles in various aspects of this thesis.

Dr. Ruby Grewal, Ms. Lynn Stewart and the hand therapists at St Joseph’s Health Care, London, Ontario, helped me during the data collection process for chapter 2. In particular, therapists Shrikanth Chinchalkar, Shanley Pitts, Joey, Leslie, Chelsea, and Emily helped to recruit appropriate patients to complete the required sample size.

Ms. Lynn Stewart and hand therapist Shrikanth Chinchalkar helped and provided support during the completion of chapter 3. Ms. Lynn Stewart gave permission to access hand therapy unit. Shrikanth Chinchalkar arranged for the ultrasound machine to complete the data collection process for the study.
EPIGRAPH

In the Name of Allah (Lord), the Most Gracious, the Most Merciful. All praise and thanks be to Allah, the Lord of all that exists, the Most Gracious, the Most Merciful. The Owner of the Day of Recompense. (Quran, Chapter 1: verse 1-3)

Allah says in Quran,

‘O mankind! Be dutiful to your Lord, Who created you from a single person (Adam), and from him (Adam) He created his wife [Hawwa (Eve)], and from them both He created many men and women... (Quran, Ch. 4: v-1)

(...and made you into nations and tribes that you may know one another, not that you may despise each other)... (Quran, Ch. 49: v-13)

...and fear Allah through Whom you demand (your mutual rights), and (do not cut the relations of) the wombs (kinship). Surely, Allah is Ever an All-Watcher over you.’ (Quran, Ch. 4: v-1)

‘All bounties are in the hands of Allah. He grants them to whom He pleases, And Allah cares for all, and He knows all things.’ (Quran, Ch. 3: v - 73)

‘And verily, the home of the Hereafter is the best for those who fear Allah and obey Him (by abstaining from sins and evil deeds, and by performing righteous good deeds).’ (Quran, Ch. 12: v-109)
DEDICATION

I dedicate this thesis to my beloved parents, grandparents (late), and brother and family members.
ACKNOWLEDGEMENTS

All praises and thanks are due to Allah for His help, blessings and mercy, without Whom this thesis would not have been possible from the initial to the final level. The last and final prophet, Mohammed (peace be upon him) said:

"Whoever is not grateful to the people, he is not grateful to Allah."
(Sahih Bukhari)

Hence, I would like to show my gratitude to all those several individuals who in one way or another contributed and extended their valuable assistance in the preparation and completion of this thesis.

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Lastly, I offer my regards to all those who supported me in any respect during the completion of this project.

I would like to wrap up with a best dua or supplication, narrated by the last and final prophet, Mohammed (peace be upon him):

"He who is favoured by another and says to his benefactor: `Jazak-Allah khairan (may Allah reward you well)’ indeed praised (the benefactor) satisfactorily." (At-Tirmidhi).

Jazak-Allah khairan to all !!
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CHAPTER 1

Introduction and Background
Preamble to chapter

This thesis is a manuscript style thesis that addresses short term effects of thermal, ultrasound and exercise interventions on skin blood flow, skin temperature and sensory perception thresholds in the hands with reference to a distal radius fracture patient population. This chapter outlines background relevant to that topic.

1.1 Background:

Distal radius fracture (DRF) is one of the most common upper-extremity fractures encountered in emergency orthopaedic care.\textsuperscript{1,2} DRF can result in short and long-term impairments and disability that can lead to loss of day to day function.\textsuperscript{5,6} Surgeon or physician, therapist and patient have a specific responsibility in achieving an ultimate goal.\textsuperscript{3,5} After the physician has stabilized the fracture and provided for the acute management, patients are often referred to physiotherapy for rehabilitation.\textsuperscript{3,5} The therapist's responsibility is directed towards oedema and pain reduction, restoration of the range at forearm, wrist, and digital motion; and progressive strengthening, to improve range of motion (ROM) and strength, thus regaining function.\textsuperscript{4,5}

Physical agents or electrotherapeutic modalities and exercise are included in the plan of care for DRF.\textsuperscript{7,8,9,34,43,44} Physical agents may serve as useful adjunctive modalities to decrease pain, increase muscle strength, and facilitate tissue healing or to enhance the effectiveness of other elements in therapy geared towards resolution of movement impairments and restoration of physical function.\textsuperscript{12,17-20} Similarly, exercise has also been shown to improve hand function after DRF.\textsuperscript{8} Even though the aims of physiotherapy are clear, therapeutic interventions used during rehabilitation phase can vary greatly. These interventions can include thermal modalities, ultrasound, electrical stimulation, continuous passive movement, electromyographic
biofeedback, and soft tissue mobilization, mobilising and strengthening exercises, application of resting or dynamic splints, advice, and education.\textsuperscript{9, 12, 17, 19}

A survey of 242 therapists\textsuperscript{9} in the United States showed that exercise program (90\%) and the use of heat or cold modalities (90\%) were the most frequent interventions provided by therapists, while more than 50\% of therapists used compressive wraps, dexterity exercises, ultrasound and soft tissue and joint mobilization during DRF rehabilitation. Even after a course of rehabilitation some patients report residual difficulties in work, sport and leisure activities.\textsuperscript{7,11} Moreover, recent systematic reviews of trials on DRF management have shown that there is weak evidence to support the use of different rehabilitation interventions in both immobilization and mobilization phase after DRF.\textsuperscript{4,8,34,43,44} These reviews and survey results identify the effectiveness of cold, ultrasound and exercise in DRF management but strong evidence is still lacking. There are currently no fixed guidelines for choosing the best dosage for ultrasound therapy or hand grip exercises in healthy subjects as well as patients with DRF. Other clinically important impairments like cold intolerance and impaired neurovascular function may exist following DRF, but for which there is a lack of information. Of particular importance are the complications like reflex sympathetic dystrophy (RSD) and median and radial nerve injuries, which are important due to their influence on day to day activities and functional tasks.\textsuperscript{14} Injury to the peripheral vasculature, defective vasoregulation, and nerve lesions have been suggested as possible routes to cold intolerance.\textsuperscript{23,24} Cold intolerance or cold sensitivity is commonly reported by patients after hand fractures,\textsuperscript{29} which may arise within the initial months or may have a delayed manifestation, depending on the seasonal nature of the injury.\textsuperscript{22, 26-31} The pathophysiology of cold intolerance is still unclear.\textsuperscript{26} However, it is postulated that post-traumatic cold intolerance has both a vascular and neural
etiology among other contributing causes. Smits et al., reported cold intolerance in 38% of patients with hand fractures and Pullock et al., reported half their study participants with confirmed diagnosis of RSD developed cold intolerance after exposing them to an Isolated Cold Stress Test (ICST). Similarly, Ruijs et al., demonstrated 56% of patients with an isolated ulnar or median nerve injury and 70% with a combined ulnar and median nerve injury reporting cold intolerance after an ICST and Cold Intolerance Symptom Severity (CISS) questionnaire.

Physiotherapists need evidence about the effectiveness of treatment techniques to help them make informed decisions about patient care. When neurovascular dysfunction exists in hands, cutaneous thermoregulation, nutritional blood flow, and autonomic functions may get impaired. A sensitive, reliable, and quantitative test for blood flow (e.g. TiVi, thermometer) and sensation (e.g. Neurometer CPT/C) may be extremely useful in diagnosing abnormalities (if any) and monitoring therapeutic outcomes. These objective evaluations may be required at different stages of DRF management to provide a comprehensive view of recovery, identify complications during the course of rehabilitation and thereby assist clinicians and therapists in planning or modifying the treatment goals.

Cryotherapy or ice therapy helps to reduce pain and swelling in DRF. Controlling pain and swelling in the early stage can restore maximal function with minimal complications in the later stages of DRF rehabilitation. There is little evidence to suggest a preference between different methods of pain and edema management, although treatment has been shown to be effective than control. While Cheng et al., found the beneficial effects of ice packs on the 3rd and 5th day of cast removal in patients with DRF, Stockle et al., proposed that continuous cold water treatment is preferable to cool packs for reducing posttraumatic edema in injured tissues. Cold water immersion is thought to cause the least skin temperature reduction, possibly due to the fact
that a greater area receives the treatment, leading to a faster activation of the
thermoregulatory responses that protect the body from abrupt temperature
changes 48 and consequently, the skin temperature is quickly stabilized and
does not adequately reflect the effects of cooling on subcutaneous tissues. 48, 49
However, the impact of cold exposure on sensory and vascular functions
in patients with DRF is incomplete.

One of the major complications after DRF is RSD and it has been reported
previously that in the early stages it can be difficult to distinguish RSD from
the normal pain and swelling associated with the fracture. 6 Serious cases of
RSD may require many months of therapy to alleviate symptoms (pain,
tenderness, impairment of joint mobility, swelling, dystrophy, vasomotor
instability). 50 In addition to this, cold intolerance has been reported in
patients with confirmed diagnosis of RSD, 25 median and ulnar nerve injuries,
24 and in patients with hand fractures. 29 Hence, presence of such
complications can be severely disabling for the patients. 29 Previous survey
reports have shown therapist’s preference for cold to reduce pain and
swelling after DRF, 9,46 but if an underlying neurovascular dysfunction
exists, then it is detrimental for patients to continue treatments with cold
modalities. Given that cold sensitivity is related to functional impairment,
23,28 and quality of life, 28 but not to sensibility, quantitative measurements
like the cold stress test, 21,24, 31 may be important in detecting cold
intolerance in the hand after injury. 21,29, 31 Testing techniques that reflect
fluctuations of both thermoregulatory and nutritional blood flow may be
required for the accurate quantitation of how and where in the
microcirculation derangements of function occur. 32

Therapeutic ultrasound is used to increase tissue extensibility, decrease pain,
and improve healing in wounds, tendons, and bone; and for a number of other
hand conditions. 51 Ultrasound is thought to affect tissue thermodynamics
and as such might result in changes in the peripheral circulatory and sensorial
systems. The effects of US are thought to vary with type of tissue, site and the dosage used. Presently, there is a scarcity of information regarding the effects of ultrasound on hemodynamics resulting from altered treatment times, intensities, and frequencies in human subjects and in patients with DRF. Presently, there is a scarcity of information regarding the effects of ultrasound on hemodynamics resulting from altered treatment times, intensities, and frequencies in human subjects and in patients with DRF.  

Therapeutic exercise is shown to benefit healthy individuals and improve patient outcomes for many health conditions that are treated by physiotherapists. Hand exercises are initiated in DRF after immobilization phase, to improve hand strength and to regain finger, wrist and hand movements to their premorbid activity levels. These authors relate that patients managed conservatively after DRF might benefit from the exercises, but the use of co-interventions in majority of the trials make it difficult to provide a definite conclusion about the actual impact of exercise on hand function. Physiological responses to exercise are also believed to be influenced by the frequency (how often exercise is performed), intensity (resistance), and duration (number of repetitions or time the exercise is performed), muscle contraction type, range of motion (ROM), speed of movement, and mode of exercise. Currently, there is a scarcity of published trials that have investigated the impact of low intensity and high intensity hand grip exercises in the hands of injured and uninjured individuals. Dynamic physical exercise induces an increase in the production of heat in active muscles and increases core body temperature. Skin blood flow plays an important role in temperature control via thermoregulation. Non-thermal factors associated with exercise such as the sympathetic stimulation, baroreflex and exercise pressor reflex also affects the cutaneous circulation. Hence, monitoring sensory and vascular responses in skin during and after exercise provides an important indication of changes in the neurovascular functions in the hand.
Given these considerations, the overall objective of this thesis was to determine the short term sensory and vascular responses to thermal, ultrasound and exercise interventions in the injured and uninjured hands with a focus on the mobilization phase after DRF.

1.2 Brief historical overview (literature review):

This literature review contains six sections. The first section outlines the causes, epidemiology and prevalence of DRF. The second section briefly outlines some of the outcome measures used in the upper extremity rehabilitation, followed by blood flow to the hand and methods used to measure. The third section reviews literature on the hand sensation and how it is measured. This is followed by a discussion regarding rehabilitation after DRF and a brief review of studies that used physical agents/therapeutic modalities and exercise after DRF (with particular attention to cold and ultrasound). This is followed by a review on the basics of cryotherapy, ultrasound therapy and how they are used in hand therapy. The last section covers exercise principles in the rehabilitation of upper extremity fractures in brief. Then we will briefly summarize the limitations in current literature, and an overview of the objectives for this thesis.

1.2.1 Epidemiology of Distal Radius Fracture:

Fracture of the distal radius occurs because of trauma. The injury is defined as a displaced fracture of the lower end of radius within 1.5 inches of wrist joint. These fractures are generally closed and usually involve displacement of fracture fragments. They may be either extra-articular (leaving the articular or joint surface of the distal radius intact) or intra-articular (the articular or joint surface is disrupted). Numerous classifications have been devised to define and group different fracture patterns. Simple
classifications based on clinical appearance, and often named after those who described them, remain in common use (Colles fracture). There is a bimodal distribution of distal radius fractures (DRF) where high-energy fractures (approx. 13%) occur in younger persons (predominately male) during sports activities and through high-energy trauma such as accidents. Whereas, high and low-energy fractures (approx. 75%) occur in older persons, (predominately female) due to falls from standing height or less.

DRF is estimated to be more than one-sixth of all fractures treated in emergency departments. It is one of the most common fractures seen by orthopaedic surgeons with an incidence of 195.2/100,000 persons per year. It is also one of the most common fractures in the females and elderly populations. It has been estimated that a 50-year-old white woman in the USA or Northern Europe has a 15% lifetime risk of a DRF; whereas a white man of the same age has a lifetime risk of a little over 2%. Risk factors for DRF in the elderly have been studied extensively. Decreased bone mineral density, postural instability, gender, ethnicity, heredity, and early menopause have all been demonstrated to be risk factors for this injury. The prevalence of DRF has recently increased in younger people, since they engage more often in high-energy sport activities.

DRF leads to physical and emotional burdens along with financial burden. Acute DRF results in pain, tenderness, swelling, and potential deformity. Patients may be faced with substantial morbidity if fracture healing is delayed or results in clinically significant deformity. Additionally, there are known complications in the treatment of distal radius fracture. Non-union in DRF is uncommon, but many immediate or late complications may occur following this fracture. The rate of reported complications after distal radius fracture varies from 6% to 80%. The recovery period for distal radius fracture can be substantial and the impact of the method of fixation on activities and daily living can be significant. It also results in significant
financial burden. Costs related to DRF are mostly service related and at least $164,000,000 was spent on hospitalizations related to distal radius fracture in the year 2007.\textsuperscript{34, 58, 59}

\section*{1.2.2 Hand or upper extremity assessment instruments:}

Assessment instruments may be divided into groups according to five basic domains: extremity condition, motion, sensibility, function, and patient satisfaction.\textsuperscript{165} (1) Condition involves the neurovascular system as it pertains to tissue viability; nutrition; vessel patency; and arterial, venous, and lymphatic flow. Noninvasive monitoring of extremity volume, skin color, and temperature, and arterial pulses provides important information about the status of skin and subcutaneous tissue and neurovascular function. (2) Measurement of motion depends on muscle-tendon continuity, contractile and gliding capacity, neuromuscular function, and volitional control. Goniometric measurements and isolated muscle strength testing are commonly used methods for evaluating upper extremity motion. (3) Relying on neural continuity, impulse transmission, receptor acuity, and cortical perception, sensibility assessment may be divided into sudomotor or sympathetic response and the ability to detect, discriminate, quantify, and identify stimuli.\textsuperscript{63, 165} (4) Reflecting the integration of all systems, hand function is evaluated through measurements of grip and pinch; coordination and dexterity; and vocational, avocational, and AD L activities. (5) Patient satisfaction tests assess patients’ endorsement/approval of the therapeutic intervention they received.\textsuperscript{165} The outcome assessments used in this research mainly focus on the extremity condition and sensibility in the hand using blood flow, skin temperature and sensory perception threshold measures. The following sections describe the basic concepts and brief review about these measures.

\subsection*{1.2.3 Blood flow to the forearm and hand and how it is measured}
1.2.3.1 Anatomy of blood flow to the hand:

In the hand, the ulnar artery continues as the superficial palmar arch, and the radial artery continues as the deep palmar arch. In approximately 5% of patients, an interosseous median artery is a major contributing vessel. If the arch connects with a branch from another independent artery, that arch is defined as complete. In approximately 78.5% of extremities, the superficial palmar arch is complete, whereas the deep palmar arch is complete in 97% of extremities. Although the patterns of collateral flow may vary tremendously, the presence of three palmar common digital arteries at the level of the metacarpophalangeal joints is a consistent finding. Common digital vessels branch into radial and ulnar proper digital arteries. Either the radial artery or superficial or deep arches, through the princeps pollicis artery (the first palmar metacarpal artery), variably supply the thumb. Distally, within the digital pulp, a large number of vessels cluster with most of the interconnections located superficially near the skin surface. The superficial vessels of less than 100 µm in diameter comprise the microvascular nutritional and thermoregulatory (non-nutritional) vessels (beds). Total blood flow equals nutritional flow (providing material for cellular metabolism) and thermoregulatory flow (does not support cellular metabolism). Under normal conditions, 80% to 95% of the total flow is thermoregulatory, whereas 5% to 20% is nutritional. The relative contributions of each are controlled by complex factors regulating arteriovenous shunting. In cases of decreased total flow and/or inappropriately decreased flow into nutritional beds, cellular ischemia may occur leading to symptoms and/or permanent injury.

1.2.3.2 Anatomical variation in cutaneous circulation:

Cutaneous microcirculation differs according to the location in human body and has few anatomical variations. Most of the body surface is covered with
"hairy" or non-acral (also called non-glabrous) skin, whereas the fingers, lips, ears, forehead, palms, and plantar aspects of the feet are covered with acral or non-hairy (also called glabrous) skin. In the non-glabrous skin, the cutaneous microcirculation is organized as two horizontal plexuses: a lower horizontal plexus composed of large arterioles and venules positioned at the dermal subcutaneous interface, and an upper horizontal network of smaller arterioles and venules in the papillary dermis (1-1.5 mm below the skin surface) from which the capillary loops of the dermal papillae arise. The two plexuses are connected by ascending arterioles that are paired with descending venules and spaced at intervals of 1.5-7 mm. In addition to these two plexuses, glabrous skin also contains a high proportion of arteriovenous anastomoses (direct vascular connections between arterioles and venules). Arterioles in glabrous skin are innervated solely by noradrenergic sympathetic nerves, whereas arterioles in non-glabrous skin are innervated by both noradrenergic and cholinergic sympathetic nerves.

1.2.3.3 Control of skin blood flow:

The control of skin blood flow in humans involves several mechanisms. The forearm (non-glabrous) and palmar skin (glabrous) is innervated by sensory nerves and sympathetic vasoconstrictor and/or sympathetic vasodilator nerves, which respond to thermal, chemical, and mechanical stimuli to provide feedback to the central nervous system and influence cutaneous arteriolar tone (vasoconstriction or vasodilation) via the release of neuropeptides and other vasoactive agents. Reflex control occurs through a vasoconstrictor pathway and through an independent active vasodilator system. These systems are both known to be sympathetic in origin. In the case of the vasoconstrictor system, the transmitters appear to be norepinephrine and one or more co-transmitters. The active vasodilator mechanism is less well defined but appears to be cholinergic and also to involve a co-transmitter, perhaps vasoactive intestinal polypeptide.
Local thermal control of skin blood flow has also been the subject of considerable attention. Direct local warming of the skin leads to a vasodilation that involves nitric oxide and sensory nerves. With respect to direct local cooling, several lines of evidence point to an involvement of the sympathetic vasoconstrictor system in the reduction of skin blood flow. Immediate cutaneous vasoconstrictor response to mild cooling thus requires both intact sensory function and intact sympathetic function whereas the longer-term vasoconstriction appears to have non-neuronal mechanisms. Non-neuronal mechanisms also generate an initial vasodilation, which is manifest when either sensory or sympathetic nerves are blocked. Thus the relatively simple vascular response to direct local cooling of the skin is manifest through a complex combination of sensory, autonomic, and direct effects, involving effects on receptor translocation, transmitter secretion and vascular smooth muscle contractile function. Similarly, the skin vascular responses to exercise have also been shown to differ between glabrous regions such as the palm and sole and non-glabrous regions such as the dorsal hand and forearm. Hence, the blood flow responses obtained through an outcome measure may be prone to variability according to the anatomy of underlying vasculature.

1.2.3. 4 Outcome measures to assess cutaneous circulation:

Adequate microcirculation is a prerequisite for tissue nutrition and oxygen supply. Due to the essential link between microcirculation function and adequate tissue oxygen delivery, the tissue blood supply has been noted as a crucial indicator of injury and disease. Skin is the only readily accessible organ for which blood flow can be measured noninvasively through noncontact imaging. Hence, skin is sometimes used as a model of generalized microvascular function.
Skin blood flow in the hands is typically obtained with laser-Doppler flowmetry (LDF) or laser-Doppler imaging using a single-point LDF (probe) either from the forearm or the finger pad.\textsuperscript{77, 78} Doppler scanners are used to map arterial flow through audible ultrasonic response to arterial pulsing. Although inconsistencies continue to plague attempts to quantify Doppler readings, to date these scanners are accepted as important noninvasive assessment tools. With the larger measurement depth of laser Doppler flowmetry compared to other techniques, it proves to be inefficient for very superficial measurements. The relatively long acquisition time of a single image, the temporal changes in perfusion may often be misinterpreted as spatial heterogeneity.\textsuperscript{78, 81} The observations using laser Doppler are based mainly on dynamic flow velocity changes in the relatively large vessels and hence, the effect of interventions in previous trials were measured from a single artery distal to the treatment area instead of the tissues most directly affected by the treatment.\textsuperscript{77, 151} There is a higher vessel density and high proportion of arteriovenous anastomoses in the palms (glabrous) and finger pads than in the forearms (nonglabrous). Hence, LDF responses obtained through the single point LDF is prone to variability according to the anatomy of underlying vasculature.\textsuperscript{75, 77, 88}

An index of skin blood flow can also be obtained using a novel technique called Tissue Viability Imager (TiVi) which has the capability to measure the red blood concentration in upper dermal tissue (skin depth of 400 to 500 µm).\textsuperscript{78, 84} The TiVi responses can be explained by physiology and can be analyzed directly without any equation as in LDF (LDF flux/MAP). Unlike the LDF which uses a small single-point LDF probe (which is very small compared to the treatment area) to capture the red blood cell flux in finger pad, a TiVi imager directly captures the red blood cell concentration over the whole treatment area. TiVi imager is not affected by the velocity or
movement of blood flow in circulation as in LDF, because it only captures the amount of red blood concentration in the area at that time point.\textsuperscript{78}

1.2.3.5 TiVi (Tissue Viability Imager) 600-polarization spectroscopy camera (version 7.4 Wheels Bridge AB, Linköping, Sweden):

The TiVi is a small and portable device for high-resolution instantaneous imaging of RBC concentration in upper human dermal tissue. Using a digital camera (Canon Rebel EOS model 450D, Japan) with a polarization lens, it is possible to capture images of skin measuring an area of 15X 10 cm and a minimum area of 4 X 3 cm at a device-tissue distance of 5 cm. The system utilizes a high-resolution charge-coupled device (CCD), offering instantaneous image acquisition (1/60 of a sec) with a refresh rate of one image every five seconds at a resolution of 400x400 pixels. A white xenon flash lamp provides illumination over the 450- to 750-nm wavelength region, and a wide area CCD detects the backscattered light from the tissue. The camera has a light penetration depth between 400 to 500 micrometer,\textsuperscript{84} and this light contains information about the main chromophores in the epidermis (melanin) and dermis (hemoglobin), while the surface reflections contain information about the surface topography, such as texture and wrinkles. Once the images are captured, the TiVi images are processed using the TiVi software and then transferred to Excel for statistical analysis. The technique has shown many uses in drug development, burn investigations, pressure studies, and general research maneuvers due to the ease of use, portability, and low cost.\textsuperscript{77, 84} The TiVi has been validated for construct validity to measure superficial RBC concentrations with in vitro fluid models and computer simulations. These in vitro models demonstrated that the TiVi software was able to accurately calculate the oxygen saturation level of 91.5%, which is within the physiological range of oxygen saturation within blood.\textsuperscript{84, 85} It has been shown to be sensitive to change during blood
occlusion testing,\textsuperscript{84} and drug testing on skin,\textsuperscript{86} and has also demonstrated good inter-laboratory reliability.\textsuperscript{87}

Skin temperature is also a valuable indicator of tissue viability which is directly related to digital vessel patency. It is important to report any decrease in temperature after injury or repair. Normal digital temperature ranges between 30° and 35° C and the critical temperature is reported to be 30° C, with lower readings indicating possible vascular compromise.\textsuperscript{83, 165} Infrared thermometers have been shown to have high reliability in measuring surface skin temperatures with little difference in the reliability of the five measurement sites tested for different nerve innervations and vascular supply in the hands of normal individuals and patients with complex regional pain syndrome.\textsuperscript{74}

1.2.4 Sensation in the hand and how it is measured

1.2.4.1 Anatomy of sensory nerve supply to the hand:

The hand is richly innervated and vascularized by a complex network of nerves and blood vessels. The skin contains an abundance of sensory receptors that respond to mechanical, thermal, and noxious stimuli. Most of these receptors are located on the volar surface, especially the fingertips. It is important to consider the integrity of these receptors when applying thermal agents. The digital nerves are branches from the median and ulnar nerves.\textsuperscript{105, 106} Sometimes an anastomosis is found between the median nerve and ulnar nerve in the hands of some individuals, although an anastomosis in the forearm is extremely rare. Knowledge of the neural connection between these two nerves is vital, as patients might present with symptoms of pain, paresthesias or motor weakness that could have been due to an injury to the median nerve or ulnar nerve.\textsuperscript{104} Thus, hand neural responses should be studied on both median and ulnar nerves. There is also a communication
between the digital arteries and digital nerves which is provided by the ‘nervi vasorum’ and the ‘vasa nervosum.’ This connection controls smooth muscle activity within the digital artery to allow for vasodilation or vasoconstriction. It commonly is accepted that sensory and sympathetic fibers course together within nerve trunks, ultimately to supply a common province of skin. Sympathetic fibers provide control of adrenergic neurotransmitters by peripheral nerves and vasculature. And thus the forearm (non-glabrous) and palmar skin (glabrous) innervated by sensory nerves and sympathetic vasoconstrictor and/or vasodilator nerves, respond to different stimuli to provide feedback to the central nervous system and influence cutaneous arteriolar tone (vasoconstriction or vasodilation). When the innervation to the hand is interrupted, the communication within the neurovascular bundle is compromised. In this situation, thermal agents or therapeutic modalities would be contraindicated due to the loss of vasomotor control. A nerve injury will also impair physiological functioning of the hand muscles (strength, coordination), and has a direct impact on sensibility, cold sensitivity, and pain. Thus, measurement of these physical impairments has been a primary focus of evaluating outcomes in hand surgery and hand therapy.

Sterling Bunnell conveyed this succinctly: “Without sensation, a worker can scarcely pick up a small object, and he constantly drops things from his grasp. The so-called eyes of his fingers are blind. He cannot find or distinguish an object with his hand without looking at it. His joint sense also suffers, and he is awkward and fumbles.”

1.2.4.2 Assessment of hand sensation:

Hand sensibility is a complex area where hand therapists have been leaders in the development and application of new knowledge. Sensibility tests include different modalities, e.g., touch, temperature, and proprioception.
Test methods include tests of threshold and innervation density. Selection of appropriate tests requires knowledge of the potential limitations in different techniques and devices. Interpretation of the findings requires knowledge on nerve pathways or distributions, mechanisms of recovery, and measurement properties of the tests involved. Although a number of tests are useful in diagnosis or describing the location of nerve injury, quantitative tests are more appropriate as outcome measures.  

Touch threshold is a primary indicator of sensory nerve function, which is measured using a variety of devices such as Semmes-Weinstein Monofilaments (SWMF), Weinstein Enhanced Sensory Test (WEST), the Pressure-Specified Sensory device (PSSD). Light moving touch can be subjectively measured using the Ten Test (1-10 scale for perception). Tactile discrimination and object identification are used to assess functional sensibility using two-point discrimination (2PD), stereognosis, object recognition test, and the Moberg’s pickup test.

Quantitative measures of sensory threshold can also be obtained through vibrometry, current perception threshold testing, and devices that test temperature threshold detection. The traditional nerve conduction study (NCS) is a diagnostic test typically used for the evaluation of peripheral nerve injury. The NCS primarily evaluates the function of nerve fibers with the highest conduction velocity; the large myelinated A-beta fibers, within a segment of peripheral nerve, and cannot quantify hyperesthesia or hypoesthesia.

Hence, a sensitive, reliable, and quantitative test of pain and non-pain sensory nerve conduction from peripheral nerves to the central nervous system may be extremely useful in monitoring therapeutic outcomes after traumatic lesions and diagnosing any associated impairments (anesthesia, hypoesthesia, hyperesthesia). The electro diagnostic test performed by automated
Neurometer CPT/C device quantitatively measures the integrity of peripheral sensory nerves by utilizing transcutaneous nerve stimulator in a painless convenient way. The sensory nerve conduction threshold (sNCT) findings assist in the patient management in four primary areas: 1) Identifying abnormal sensory nerve function, 2) Localizing areas of abnormal function, 3) Quantifying the severity of an abnormality and 4) Monitoring the course of a progressive neuropathy or the efficacy of a treatment. 99, 100-102

1.2.4.3 Neurometer® CPT/C device (Neurotron Inc., Baltimore, USA):

Through determination of the minimum perceptible current perception thresholds (CPTs) over dermatomes, the Neurometer evaluates sensory nerve conduction from periphery to the brain and has been shown to detect differences in neural function in asymptomatic subjects when neural stress was administered. 215 This portable battery operated nerve stimulator has the ability to emit three different frequencies in sinusoidal waveforms to selectively target different subpopulations of nerve fibers dependent upon nerve fiber diameter. A frequency of 2,000 Hz is used to stimulate the large myelinated A-beta fibers which detect cutaneous touch and pressure; a 250-Hz stimulus will stimulate myelinated A-delta nerve fibers which are mechanoreceptive, and detect fast pain, pressure and temperature, while a frequency of 5 Hz is used to stimulate the small unmyelinated C-polymodal nociceptive fibers which detect slow pain, postganglionic sympathetic and temperature. 99 This device has been used in many studies to detect, screen, and diagnose the abnormalities of peripheral nervous system. 100-102 Ranged CPT (R-CPT) is a sensory perception threshold test typically completed in 3 to 6 min for each test site. It is used to confirm or rule out sensory involvement from vascular involvement in large sample trials. 99-102 In R-CPT, each frequency is repeated several times (7-10 times) to ensure accuracy
and reproducibility. The Neurometer reports values as the normal range (R-CPT Level, 6–13), hyperesthesia (R-CPT Level, 1–5), and hypoesthesia (R-CPT Level, 14–25).  

Hand function reflects through the integration of all systems and is thought to be affected by decreased blood flow, cold hands, and loss of sensation.  

After injury symptoms of pain due to vascular insufficiency, soft tissue lesions, edema and muscular strain may mimic neurologic conditions, suggesting a possible impairment either in the neural or vascular functions. The incidence of complications such as, median nerve injury and reflex sympathetic dystrophy after the distal radius fracture also suggests that using a baseline sensory and vascular assessment in the injured (and normal) hand would be advisable to assist with early detection of complications. Therefore, assessment of neurovascular function gives some important information about the possible etiology. The non-invasive evaluations conducted at important timelines, using the TiVi and Neurometer may be helpful in identifying and differentiating any sensory or vascular impairments during the course of rehabilitation, thus assisting clinicians and therapists in planning or modifying the treatment goals. Currently, there is a scarcity of published clinical trials that have looked at both the sensory (A beta and C fibre perception thresholds) and vascular responses to cold, ultrasound therapy and exercise in the uninjured and injured hands after DRF.

1.3 Rehabilitation after DRF

Majority of the distal radial fractures are treated conservatively (non-operatively). This usually involves the reduction of the fracture if displaced (closed reduction), and forearm immobilisation in a plaster cast or brace for around six weeks. Operative treatment usually involves either closed or open
reduction followed by external or internal fixation and a similar period of immobilisation. The aims of physiotherapy in distal radial fracture rehabilitation are to restore maximum movement and functional ability. Rehabilitation after DRF usually involves three phases: 1) Early protective phase or immobilization phase, 2) Mobilization phase and 3) Strength phase (Table 1). During the management of DRF, therapists use several different treatment techniques. The treatment plan for each patient is determined by various factors including the pattern of bone fracture, bone quality, degree of soft tissue damage, medical condition and compliance with treatment. The early rehabilitation program must be customized to meet the needs of the patient while considering aspects of the person, their injury, and their environment. Upon receiving initial treatment, for example fracture reduction and application of a plaster cast, patients are usually given instructions to carry out straightforward exercises. These typically include elevation of the injured arm in the first few days post-injury and exercising of the non-immobilised joints in order to alleviate and/or counter swelling and stiffness. More extensive and intensive rehabilitation intervention is more frequent post-immobilisation (cast removal), where limited range and quality of movement, reduced grip strength, and pain are typical reasons for initiating rehabilitation interventions. The later phases of rehabilitation requires that the therapist focus on any residual physical impairments, moving the patient towards their normal activities, and restoring functional strength and endurance.

1.3.1 Current evidence on rehabilitation after DRF:

Overall, there is weak evidence to support the need for rehabilitation after DRF with closed reduction and open reduction internal fixation. A recent Cochrane review on rehabilitation after DRF in adults identified an insufficient evidence for different therapeutic interventions in both immobilization and mobilization phase (after cast removal). In addition to
this, a recent review by the American Academy of Orthopedic Surgeons (AAOS) summarised few recommendations (Numbers; 21, 22, 27) for therapeutic management of DRF population. In that article the authors identified weak and insufficient evidence to support the effectiveness of home exercise (as per recommendation: 21 and 22), ice and PEMF, and ultrasound therapy (as per recommendation: 27) after DRF. These authors highlight gaps in the research and recommend to conduct high quality trials in the future to evaluate effectiveness of physical therapy after DRF using exercises (e.g. early formal physical therapy, self-supervised home programs) and mechanical adjuvants like, PEMF, ice, and ultrasound.

1.3.2 Rehabilitation during immobilisation phase:

For interventions started during immobilisation (plaster cast/external fixator), there is limited evidence of improved hand function for hand therapy in the days after plaster cast removal, with some beneficial effects continuing one month later. There was also limited evidence of improved hand function and of a lack of differences in outcome between the supervised and unsupervised exercises during immobilisation period.

1.3.3 Rehabilitation during mobilisation phase:

For interventions started post-immobilisation (after cast removal), there is limited evidence of a lack of significant differences in outcome in patients receiving formal rehabilitation therapy.

1.3.3.1 Exercise after immobilisation period in DRF:

Four trials evaluated the provision of routine therapy compared with no therapy following plaster cast removal. None of the trials found a significant effect with the routine provision of either occupational therapy (with exercises twice per week performed three times per day at home),
or physiotherapy (treatment at the discretion of PT) or “activity-focussed” physiotherapy (home exercises for up to six weeks plus a single advice session), when compared to no therapy at all.

Table 1.1: Phases of rehabilitation after DRF

<table>
<thead>
<tr>
<th>Rehab. Phase</th>
<th>Duration</th>
<th>Treatment goals</th>
<th>Treatment Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immobilization or protection</td>
<td>1–6 weeks (based on fracture stability)</td>
<td>Protect fracture, control pain, swelling, skin infections</td>
<td>Cast/orthosis, surgery/external or internal fixation; edema management, tendon gliding exercises.</td>
</tr>
<tr>
<td>Mobilization</td>
<td>Starts after cast removal or immobilization</td>
<td>AROM of uninvolved joints AROM of involved joint; forearm</td>
<td>AROM of proximal and distal joints like, shoulder, elbow and digits AROM/PROM of forearm, wrist, digits; or dynamic mobilization</td>
</tr>
<tr>
<td>Later rehab. or Strength phase</td>
<td>Starts after fracture Heals</td>
<td>Increase ROM; strength; improve ADL</td>
<td>Begin with isometric exercises, then isotonic/dynamic, and resisted exercises</td>
</tr>
</tbody>
</table>

Table legends: rehab.= rehabilitation, AROM=active range of motion; PROM=passive range of motion; ADL activities of daily living

There was a single trial which found better short term hand function with improved upper limb activity and reduced pain at three weeks, and six weeks in participants given exercise and advice, than in those with no intervention after cast removal. There were no other significant between group differences for the primary outcome measure of wrist extension or for the secondary outcomes of other ranges of motion and grip strength at weeks three or six. Similarly, Watt and colleagues found better grip strength and wrist extension following six weeks of therapy in the physiotherapy referral group (six therapy sessions plus home exercise programme and advice; passive joint mobilisation) than in those who were instructed for home exercise alone by a single surgeon after immobilization.
1.3.3.2 Therapeutic ultrasound after immobilization period in DRF:

There was only one trial which found the short term benefit of ultrasound therapy in DRF. Basso and co-workers compared the active versus sham application of low frequency, long-wave ultrasound to the back of the affected wrist for 5 min following plaster cast removal in 38 participants. Physiotherapy was provided only if “hand function was poor.” The authors found no significant difference between participant’s allocated active ultrasound and those allocated sham ultrasound, in the loss of active flexion-extension wrist motion relative to the unaffected wrist. The author concluded that ultrasound did not affect wrist motion but might have led to a lower referral rate for physiotherapy at eight weeks. Despite the lack of evidence, there are survey reports on the routine usage of ultrasound after DRF (in the year 1998 over 50% of therapist in the USA showed preference for both pulsed and continuous US). In contrast, a recent survey by the Australian physiotherapists in the year 2011, showed nil usage of US in the treatment of DRF. One possible reason might be the lack of trials on the effectiveness of US in general and in DRF rehabilitation.

1.3.3.3 Cryotherapy after immobilization period in DRF:

There is weak evidence to suggest a preference between different methods of pain and edema management after injury. However, treatment has been shown to be effective in reducing pain and swelling than control, after DRF.

There was only one study which evaluated the relative effectiveness of 5 daily applications of ice, pulsed electromagnetic field (PEMF) and a combination of ice and PEMF together with exercise in reducing forearm pain and swelling and improving the range of wrist motions after the period of immobilization following DRF. Eighty-three subjects were randomly
allocated to receive 30 min of either ice plus pulsed electromagnetic field (group A); ice plus sham pulsed electromagnetic field (group B); pulsed electromagnetic field alone (group C), or sham pulsed electromagnetic field treatment for 5 consecutive days (group D). All subjects received a standard home exercise programme. A visual analogue scale was used for recording pain, volumetric displacement for measuring the swelling of the forearm, and a hand-held goniometer for measuring the range of wrist motions before treatment on days 1, 3, and 5. The authors reported that by day 5, group B (ice pack) was significantly more effective than group D in reducing volumetric measurement. In addition, group B produced significantly greater improvement in pronation ROM than the control group. They recommended that addition of pulsed electromagnetic field to ice therapy may produce better overall treatment outcomes than ice alone, or pulsed electromagnetic field alone in pain reduction and range of joint motion after cast removal.

Even though there is absence of strong evidence to support different interventions after DRF, their preference in clinical practice was reported by Michlovitz et al... These authors surveyed 242 therapists (PTs, OTs, and CHTs) by questionnaire at an annual hand therapy meeting, to identify preferred practice patterns and physical and functional outcome measures used during DRF management. A descriptive analysis of data performed to identify preferred practice during the immobilization and the post-immobilization periods showed that more than 75% of the surveyed therapists used upper extremity range of motion (ROM) exercises and compressive wrap with retrograde massage during the immobilization phase. More than 90% of therapists included range-of-motion exercises and heat or cold modalities in the post-immobilization treatment to achieve the primary goals of edema control, increased ROM, and decreased stiffness. Most of these techniques were used during both phases of rehabilitation, although very few patients were seen during the immobilization phase.
1.3.4 Special considerations following DRF:

Whilst many people with these fractures will make a satisfactory recovery, it should be noted that the consequences of a bad outcome might include disabling pain, loss of independence and that, for many patients, these fractures indicate an increased risk of further fracture in the future, or complications, or serious functional impairment. Hence, early detection and prevention of secondary complications is crucial for DRF population.

A structured complication checklist to evaluate complication rates after DRF was used by McKay et al., to review a cohort of 250 patients. The authors found that most common complications following a distal radius fracture were compression of the median nerve (22%), reflex sympathetic dystrophy (20%), tendinitis/tenosynovitis (14%), and radial nerve compression (11%). These complications are often thought to be either missed or overlooked by the treating therapists. Furthermore, injury to the peripheral vasculature, defective vasoregulation, and nerve injury have been suggested as possible routes to cold intolerance. Smits et al., demonstrated that 38% of the patients with hand fractures developed cold intolerance according to the responses on the Cold Intolerance Symptom Severity (CISS) questionnaire. Pullock et al., reported cold intolerance in half of their study participants with confirmed diagnosis of RSD after exposing them to an Isolated Cold Stress Test (ICST) and Ruijs et al., found similar reports of cold intolerance in 56% of patients with an isolated ulnar or median nerve injury, and 70% with a combined ulnar and median nerve injury after an exposure to cold stress test (ICST) along with abnormal ratings on CISS questionnaire.

Cold intolerance, cold sensitivity or ‘‘trauma induced cold associated symptoms’’ is defined as abnormal pain after exposure to mild or severe
Cold, with or without discolouration, numbness, weakness, or stiffness of the hand and fingers. Cold intolerance is commonly reported by patients after hand fractures, which may arise within the initial months or may have a delayed manifestation, depending on the seasonal nature of the injury. The pathophysiology of cold intolerance is still unclear. However, it is postulated that post-traumatic cold intolerance has both a vascular and neural etiology among other contributing causes.

One major complication after DRF is reflex sympathetic dystrophy (RSD), also referred to as complex regional pain syndrome (CRPS) and shoulder-hand syndrome. In the early stages, it can be difficult to distinguish CRPS from the normal pain and swelling associated with the fracture or ORIF. As per the survey and randomised clinical trial, cold modality is used to reduce pain and swelling after DRF, but if an underlying neurovascular dysfunction exists, then it is detrimental for patients to continue treatments with cold therapy. In addition to this, cold intolerance as reported earlier in the patients with RSD, median and ulnar nerve injuries and hand fractures after cold exposure can be severely disabling for some patients. Serious cases of RSD may require many months of therapy to alleviate symptoms (pain, tenderness, impairment of joint mobility, swelling, dystrophy, vasomotor instability). Given that cold sensitivity is related to functional impairment and quality of life, but not only to sensibility, quantitative measurements like the cold stress test may be important in detecting cold intolerance or cold sensitivity in the hand after injury. Testing techniques that reflect fluctuations of both thermoregulatory and nutritional blood flow may be required for the accurate quantitation of how and where in the microcirculation derangements of function occur.

Immersion in Cold-water Evaluation protocol (ICE) is a simple and reliable objective measure to assess cold responses in the hand. Previous reports on the ICE used only skin temperature for the evaluation of thermoregulatory
responses\textsuperscript{21, 22} and did not include any vascular measures. Although blood flow has a thermoregulatory component (80% to 90%, mainly through arteriovenous anastomoses) and a nutritional component (10% to 20%, capillary system), skin temperature in the hands and digits is highly correlated with skin blood flow.\textsuperscript{94-97} The vasa nervosum and nervi vasorum control vasomotor response in arteries. If the nerve is injured and/or impaired, these sympathetic autonomic efferents may not be able to communicate with the nearby artery to signal the appropriate vasomotor response to an environmental temperature change and tissue damage may occur.\textsuperscript{106} Aberrations in the balance between thermoregulatory and nutritional blood flow have been documented after trauma (e.g., RSD).\textsuperscript{126} It is also possible that after cold exposure, nutritional blood flow diminishes to critical levels, leading to cellular ischemia, pain, and cold intolerance.\textsuperscript{23, 24} Hence, observation of vascular changes is important to understand the central and peripheral mechanisms of blood flow regulation after hand injury.

Neurovascular function is thus an important indicator of upper extremity condition (nutrition, thermoregulation, structural integrity, neuromuscular coordination). Effective rehabilitation interventions help in preventing complications associated with the fracture and/or treatment and in optimising functional recovery in order to achieve activities required for daily living.\textsuperscript{9, 34, 44, 110, 111} Hence, using baseline sensory, vascular, and cold responses to assess the injured (and normal) hand would be advisable to assist with early detection and prevention of secondary complications after DRF. Furthermore, monitoring of neurovascular function at important timelines (6 weeks/cast removal) after DRF during the rehabilitation process will be useful to plan or modify the future care.

1.4 Physical agents /therapeutic modalities (Ultrasound, Cold)
Physical agents are included in the plan of care for hand and upper extremity patients to decrease pain, increase range of motion, increase muscle strength, and facilitate tissue healing. 12, 19, 144, 145 Associated impairments may determine the selection of modality. This is particularly true for pain associated with edema and inflammation. Cryotherapy techniques or low-intensity, pulsed-wave ultrasound are thought to be the most beneficial by some authors. 49, 138-143 However, there is a lack of strong evidence to support this.

1. 4.1 Therapeutic ultrasound:

Ultrasound is typically used as a deep heating agent. 51 Ultrasound uses acoustic energy with wavelengths above the audible range (>17,000 Hz). 146 It is probably the most widely used physical agent in hand therapy practice. Electrical energy is converted into mechanical energy (sound propagation) via the piezoelectric effect. A ceramic or quartz piezoelectric crystal located within the transducer expands and contracts from the applied electrical current. The crystal creates an electric voltage potential that replicates the sound wave pattern determined by the selected frequency. The sound waves are initially propagated longitudinally into the target tissue and then transversely at bone or metal interfaces. These sound waves leave the transducer as a collimated focused beam similar to a flashlight. The larger the sound head, the more collimated the beam. Molecules and cells within the target tissue expand and contract to produce vibration. The vibration increases kinetic energy of the molecules, which increases tissue temperature, provided the ultrasound was delivered in the continuous mode with sufficient intensity. 146 Frequency determines the depth of penetration within the target tissue. The collimated beam is more divergent with the 1-MHz transducer, which will transmit sound waves through the superficial tissue layers so that the ultrasound energy will be absorbed in deeper tissues at 4 to 5 cm. Energy is absorbed in the superficial tissue layers up to 2 cm with the 3MHz frequency.
Ultrasound is absorbed within tissues with high protein content (e.g., collagen); thus, collagen-rich connective tissues such as tendon, ligament, and joint capsule absorb sound waves well. Standing waves are known as “hot spots” and have the potential to cause tissue damage. These can be avoided if the transducer is kept moving, if the 3-MHz frequency is selected, and if the intensity is not too high. The effective radiating area (ERA) is the portion of the transducer that actually produces and emits sound waves. The beam non-uniformity ratio (BNR) compares the maximum point intensity on the transducer (spatial peak intensity) with the average spatial intensity across the sound head (spatial average intensity). The lower the BNR is, the more evenly distributed the energy from the transducer. A coupling medium such as a commercially available water-soluble gel is spread in a layer between the applicator and skin surface to avoid attenuation of US waves in the air.

Therapists have the option to select continuous or pulsed-wave ultrasound treatments. With pulsed-wave ultrasound, the intensity is periodically interrupted so that no ultrasound energy is being produced during the off time in the duty cycle. Continuous-wave ultrasound is thought to produce thermal and nonthermal effects, whereas pulsed-wave ultrasound is thought to emphasize the nonthermal effects of ultrasound because heat does not really accumulate. This is a result of the dissipation of heat by conduction during the off time of the pulse period. Low-duty cycles of 10% or 20% have been studied in chronic wound healing, but no other work has been demonstrated at high-duty cycles. The physiologic effects of a particular duty cycle are unclear. There are no clear-cut guidelines on how to select treatment intensity, but the World Health Organization does set an upper limit of 3.0 W/cm² ultrasound units. The correct intensity will achieve the desired goal and do no harm. Treatments are likely to be ineffective if the ultrasound
treatment is not focused on the correct structure and dosing parameters are incorrect. 17, 144, 146 -148

Ultrasound has a multitude of clinical indications, 17, 51 and it primarily focuses on smaller treatment areas and may target structures greater than 2 cm in depth. Ultrasound is thought to promote tissue healing first by increasing blood flow and oxygenation due to thermal effects and second as a result of the nonthermal effects. Studies of delayed-healing wounds have demonstrated that low-intensity pulsed-wave ultrasound, which emphasizes nonthermal effects, releases growth factors from macrophages, increases angiogenesis, and facilitates collagen production. 149 These benefits promote the fibroplasia phase of tissue healing. During remodeling, tensile strength may increase when thermal ultrasound is combined with controlled stress exercises. Increased tissue extensibility will facilitate collagen reorganization and gains in tensile strength. 144,145 The use of therapeutic modalities in hand therapy to help strengthen, relax, and heal the injured part has been present for many years. 51,149,152,153 Therapeutic benefits of US remain largely speculative and are based mostly on laboratory based research and empirical evidence. 51,149,153 There remains a scarcity of high quality controlled trials examining the physiologic effects of US and how these effects might be influenced by the method of application (i.e., pulsed or continuous).

1.4.1.1 Blood flow, skin temperature and nerve conduction velocity responses after US:

Recently, Noble et al., 151 used laser Doppler flowmetry to assess cutaneous blood flow and concomitant measures of ambient and skin temperatures after applying 3 MHz pulsed (1:2) and 3 MHz continuous ultrasound at an intensity of 1 W/cm² for 6 min over the forearm. The authors noted that, after sonation, there was a significant increase in skin blood perfusion with
both pulsed US and continuous application of US. However, there was no significant difference in skin temperatures between the US groups.

Ware et al.,\textsuperscript{157} used laser Doppler flowmetry to measure dermal blood flow after applying 10 min of 3 MHz, 1.5 W/cm\textsuperscript{2} continuous US to the human calf. The authors noted that after sonation, there was a significant increase in skin temperature, but dermal blood flow decreased by an average of 12\%. Fabrizio et al.,\textsuperscript{155} also investigated blood flow velocity in the human popliteal artery using sham, control and US groups. Significant increases in blood flow velocity were found in the sham group and with applications of both 1 and 3 MHz ultrasonic frequencies. They proposed that this increase was attributable to a massage effect of the transducer head.

Finally, Robinson and Buono\textsuperscript{156} studied the effects of 1.5 W/cm\textsuperscript{2} continuous US on skin and muscle blood flow. Cutaneous blood flow was measured using laser Doppler flowmetry. Subtracting this figure from total forearm readings measured through occlusion plethysmography gave the values for muscle blood flow. The authors concluded that the administration of US had no significant effects on muscle blood flow. However, they further reported that, it was evident that skin blood flow increased in both the sham and intervention groups, suggesting that movement of the transducer head caused a massage-mediated thermal effect.

All the above mentioned trials did not measure sensory changes with ultrasound application, which may have explained the pain control and modulation along with the blood flow and temperature changes when using different modes of US therapy. We found one related investigation that measured sensory nerve conduction velocities in median nerve using different US intensities. Andrew et al.,\textsuperscript{158} studied the influence of ultrasound on the conduction velocity and amplitude of evoked sensory potentials in the median nerve. They assigned 13 subjects to either
experimental or control groups for ultrasound or placebo treatments. They compared sensory-nerve conduction velocity in the median nerve after 10 min of ultrasound treatment at three intensity levels (0.5, 1.0, and 1.5 W/cm²) with sensory-nerve conduction velocity in the median nerve after 10 min of placebo ultrasound treatment (0.0 W/cm²). No significant differences were noted between groups (placebo and US) at any of the three-ultrasound intensity levels.

The traditional nerve conduction study (NCS) is a diagnostic test used for the evaluation of peripheral nerve injury. The NCS primarily evaluates the function of nerve fibers with the highest conduction velocity; the large myelinated A beta nerve fibers but cannot measure the function of A-delta or C fibres like the Neurometer CPT /C device which can detect normal, increased or decreased sensation of all three subtype of nerve fibres. A 5-Hz stimulus will activate unmyelinated C-fibers; a 250-Hz stimulus will depolarize the sparingly myelinated A-delta nerve fibers, whereas a higher frequency stimulation of 2,000 Hz will activate the large, myelinated A-beta nerve fibers. It has been demonstrated that CPT detects improvement over time in both carpal tunnel syndrome and other neural dysfunctions. Hence both sensory and vascular measures should be included to examine whether the method of application in ultrasound has any additional beneficial effect on skin blood flow and sensation.

1.4.2 Cryotherapy:

Cryotherapy (or cold therapy) refers to the therapeutic use of cold. Cold is primarily used after acute injury or surgery to control pain and edema. The normal patient response to cold in terms of sensory changes is the feeling of cold followed by burning, pain/discomfort, tingling, and numbness. Although the timing is not standardized among patients, the order of these sensory changes is consistent. The application of cold results in decreased
blood flow and vasoconstriction in response to decreases in tissue temperature.\textsuperscript{167, 68} Vasoconstriction is an immediate response to attempt to regulate temperature. There is a decrease in blood viscosity, which further reduces blood flow. This response is usually observed in the skin, but it may occur in deeper tissues as well.\textsuperscript{167} Prolonged cold exposure such as in an ice bath below 10°C (50°F) may result in a reflex vasodilation called the ‘hunting response’, whereby a digit exposed to constant cool temperatures will display temperature cycling with alternating vasoconstriction and vasodilatation. When an individual’s fingers are immersed in an ice bath, the temperature initially decreases, reflecting vasoconstriction. However, after 15 min the temperature begins to cyclically increase and decrease, as the vessels alternate dilating and constricting.\textsuperscript{171} It is proposed that this vasodilatory response is mediated by an axon reflex in response to the pain of prolonged cold or very low temperatures or that it is caused by inhibition of contraction of the smooth muscles of the blood vessel walls by extreme cold.\textsuperscript{172} It is normal for the skin underlying the cold source to become red during cryotherapy because of hyperemia or vasodilation of skin blood vessels. Maintained vasodilatation without cycling has also been observed with cooling human forearms at 1°C for 15 min.\textsuperscript{173} For these reasons, it is important to be aware of the temperature being delivered during cold therapy and the period of time.\textsuperscript{12,175}

It has been found that cryotherapy reduces pain and edema, and shortens recovery time, if applied within the first 2 days after an injury. Decreasing tissue temperature slows the rate of the chemical reactions that occur during the acute inflammatory response and reduces the heat, redness, edema, pain, and loss of function associated with this phase of tissue healing.\textsuperscript{161-163} Reduced edema means that there will be less tissue distention and therefore less pain.\textsuperscript{164} A decrease in the circulating chemical mediators that promote inflammation and activate or sensitize nociceptors will also modulate pain.\textsuperscript{164}
Although muscle tension will decrease in response to cold, which may reduce muscle spasm, guarding, or spasticity, the muscles will be less flexible to movement.\textsuperscript{139-141} With cold exposure, decreased nerve conduction velocity, and muscle spindle and golgi tendon organ activity may also contribute to decreases in pain.\textsuperscript{169} The mechanism by which cooling elevates the pain threshold is unclear; hypotheses include cutaneous counter irritation (involving Melzack and Wall’s gate theory, 1965),\textsuperscript{189} diminished nerve conduction functioning,\textsuperscript{190} or reflex muscle relaxation.\textsuperscript{191} Decreased nerve conduction with cooling has been demonstrated by numerous investigators.\textsuperscript{192-198} Both motor\textsuperscript{192-196} and sensory fibers are affected.\textsuperscript{195-196} The reduction in velocity approximates 2 m/s for every 1°C of cooling.\textsuperscript{195-196} If cooling continues, frank conduction block with termination of axoplasmic transport and subsequent axonal degeneration (Wallerian) may ensue.\textsuperscript{17, 193}

### 1.4.2.1 Methods of cold application:

Clinical application of cold therapy comes in various forms including cold or ice packs, ice water immersion, ice cups, controlled cold compression units, frozen gel wraps, frozen towels, vapocoolant sprays, cold whirlpools, and contrast baths. Cold packs are usually filled with a gel composed of silica or a mixture of saline and gelatin, and are for the most part covered with vinyl. The gel is formulated to be semisolid between 0°C and 5°C for the pack to conform to the contours of the upper extremity. Ice packs are made of crushed ice placed in plastic bags, through which they provide more vigorous cooling at the same temperature. Immersion is an alternative most often used by athletes, whereby the water temperature ranges between 10°C and 15°C. Ice cups refer to small paper or Styrofoam cups of water that are frozen and used to apply a direct and focal ice massage to the affected area. Controlled cold compression units alternately pump cold water and air into a sleeve that is wrapped around the affected area and are more customarily used directly after surgery.\textsuperscript{12, 17} The temperature of the water is routinely set between 10°C and
Frozen gel wraps are an excellent alternative for wrapping single digits of the hand. Frozen wet towels are no longer commonly used because they are cumbersome and untidy. Vapocoolant sprays are generally used for rapid cutaneous cooling to allow for the treatment of trigger points, myofascial pain, and restricted motion. Cold whirlpool (temperatures range between 0°C and 26°C) is not commonly used; however, its effect and tolerance is similar to ice water immersion.12, 17

From the available literature it appears that the cooling efficacy of cryotherapy depends on many factors, including the duration of cold application, the anatomical location of the cryotherapy treatments, the use of compression, the level of prior or subsequent physical activity, and the specific mode of cryotherapy used.199

1.4.2.2 Blood flow, skin temperature and nerve conduction velocity response after local cold tests and therapeutic cold applications:

Altering tissue temperature (using thermal agents) can have a range of therapeutic effects through changes in metabolism, nerve transmission, hemodynamics, and mechanical properties.183,184 Cooling procedures could influence physiological responses, so the results obtained are difficult to compare. In most cases, the local cold tests consisted in immersion in cold water. However, the water temperature and the duration of the immersion have both been extremely variable according to the investigators. Some tests have consisted in immersion in water at 0°C, 4°C, 5°C, and their durations have varied from 1 to 30 min. The cooling procedures have also varied according to the part of the limb immersed. Leblanc et al.,209 carried out foot immersions, whereas some investigators have preferred an immersion of either one finger or hand, or forearm or finger, hand and forearm.186
Lewis \cite{171} has observed that alternating periods of vasoconstriction and vasodilatation occur during local cooling of the hands. These fluctuations, as measured by skin temperature, have been called the ‘hunting response’, or cold induced vasodilatation (CIVD). Similar reactions have been observed in other parts of the extremities in humans and animals. \cite{210} It has been shown that CIVD is related to an intermittent interruption of cold induced vasoconstriction by vasodilatation of arterioles and arteriovenous anastomoses of the skin. \cite{211} This phenomenon has often been mentioned as an effective prevention of the occurrence of local cold injuries \cite{208} and is therefore of great interest.

A study by Levy et al., \cite{212} investigated hand blood flow in response to wide range of general and local cutaneous thermal stimuli (0-36 °C and 4-42 °C respectively). The local stimulus consisted of thermostatically controlled water bath for right hand and the general stimulus consisted of the ambient room temperature. Blood flow was measured at right wrist by strain gauge plethysmography. A paradoxical vasodilatation was observed at 4 °C (Lewis hunting phenomenon). The author concluded that, hand (cutaneous) blood flow responds simultaneously to both local (wrist) and general stimuli (room temperature). The local stimulus seems to dominate at cold to comfortable ambient temperatures (10, 16 and 22 °C); and hand blood flow responds more significantly to variations in local than to general stimuli ≤ 22 °C.

Sendowski et al., \cite{186} studied the physiological responses induced by immersion in cold water at different areas of the upper limb. Subjects immersed their index finger or hand or forearm and hand for 30 min in 5°C water followed by a 15 min recovery period. Skin temperature of the index finger, skin blood flow (Qsk) measured by laser Doppler flowmetry, as well as heart rate (HR) and mean arterial blood pressure (BPa) were all monitored during the test. Cutaneous vascular conductance (CVC) was calculated as Qsk/BPa. Cold induced vasodilatation (CIVD) indices were calculated from index
finger skin temperature and CVC time courses. The results showed that no differences in temperature, CVC or cardiovascular changes were observed between hand and forearm. During finger test, CIVD appeared earlier compared to hand and forearm. The HR was unchanged in fingers, whereas it increased significantly at the beginning of hand and forearm and then decreased at the end of the immersion. Moreover, BPa increased at the beginning of finger but was lower than in hand and forearm. The rewarming during recovery was faster and higher in finger compared to hand and forearm. The results showed that general and local physiological responses observed during an upper limb cold water test differed according to the area immersed. Index finger cooling led to earlier and faster CIVD without significant cardiovascular changes, whereas hand or forearm immersion led to a delayed and slower CIVD with a bradycardia at the end of the test.

Another study by Music et al. investigated the effect of quantitatively measured cold perception (CP) thresholds on microcirculatory response to local cooling as measured by direct and indirect response of laser-Doppler (LD) flux during local cooling at different temperatures. The CP thresholds were measured in 18 healthy males using the Marstock method (thermode placed on the thenar). The direct (at the cooling site) and indirect (on contralateral hand) LD flux responses were recorded during immersion of the hand in a water bath at 20 °C, 15 °C, and 10 °C for a period of 5 min each. The cold perception threshold correlated (linear regression analysis, Pearson correlation) with the indirect LD flux response at cooling temperatures 20 °C and 15 °C. In contrast, there was no correlation between the CP threshold and the indirect LD flux response during cooling in water at 10 °C. The results demonstrated that during local cooling, depending on the cooling temperature used, cold perception threshold influences indirect LD flux response.

The studies mentioned earlier investigated physiological responses to cold stimuli or cold test as a part of physiological investigation. The use of ice
for treatments in clinical settings is different than the experimental studies,12,17,183 and this makes it difficult for the therapists to compare and draw conclusions for their clients. Even though ice packs have been shown to improve pain and function in DRF,46 the evidence is weak and needs further research. Moreover, the report on both neural and vascular functions after cold application in health and patient population is incomplete.

There were two studies which looked at only blood flow responses to ice therapy using Doppler flowmetry and Doppler ultrasound after the application of ice in healthy volunteers.182,214 Recently Gregson et al.,182 assessed the influence of different degrees of cooling on the limb blood flow of thigh muscles and skin, after 5 min of cold water immersion (8 °C and 22 °C) using Doppler flowmetry and Doppler ultrasound. These authors reported that 10 min of cold water immersion (5 min at 8 °C and 5 min at 22 °C in sequence) reduced the whole limb blood flow markedly along with a paradoxical increase in cutaneous blood flow immediately after immersion in colder water (8 °C) but not in the cool water (22 °C). Another study by Topp et al.,214 looked at the effects of menthol gel and ice pack (0.5 kg of 0 °C for 20 min) on radial artery blood flow using Doppler flowmetry in the forearms of healthy subjects. These authors found that menthol gel reduced blood flow in the radial artery 5 min after application (short acting) but not at 10, 15, or 20 min after application. While ice reduced, blood flow in the radial artery only after 20 min of application (prolonged cooling) and both these methods inhibited the forearm muscle strength after application of ice.214 However in these two trials,182,214 blood flow was measured from a single artery distal to the application of the experimental treatments214 or at a point marked on the leg,182 whereas the blood flow in the tissues directly adjacent to the treatments were not assessed nor the complete treatment area was included.
Thus, the effects of the interventions on the tissues most directly affected by the treatment were not measured.

There were two studies that looked only at the measures of sensation (sensory nerve conduction velocity-SNCV) after ice therapy in healthy individuals.\textsuperscript{49,213} Algafy et al.,\textsuperscript{213} determined the impact of cryotherapy application on sensory nerve conduction velocity (NCV), pain threshold (PTH) and pain tolerance (PTO) in the ankles of male sports players and compared them with the control. NCV of the tibial nerve was measured via electromyogram, PTH, and PTO via pressure algometer. All outcome measures were assessed at two sites served by the tibial nerve: one receiving cryotherapy and one not receiving cryotherapy. Analysis showed that in the control ankle, NCV, PTH and PTO did not alter when reassessed. However, in the ankle receiving cryotherapy, NCV was significantly and progressively reduced as ankle skin temperature was reduced to 10°C. Cryotherapy led to an increased PTH and PTO at both assessment sites. These authors concluded that cryotherapy could increase pain threshold and pain tolerance at the ankle along with a significant decrease in sNCV.

Similarly, Esperanza et al.,\textsuperscript{49} also reported a significant reduction in the sensory NCV of sural and posterior tibial nerves, immediately after the application of ice pack, ice massage and cold water immersion to leg. Each group received 1 of the 3 cold modalities, applied to the right calf region for 15 min at a temperature of 10°C. Skin temperature and nerve conduction parameters were measured before and immediately after cooling. All three modalities reduced skin temperature (mean, 18.2°C). There also was a reduction in amplitude and an increase in latency and duration of the compound action potential. Ice massage, ice pack, and cold water immersion reduced sensory nerve conduction velocity (NCV) but cold water immersion was thought to be the most effective modality in changing nerve conduction parameters probably because it involved a greater area.
All the above mentioned studies either used nerve conduction velocities or Doppler flowmetry to measure either the skin blood flow or sensation after cold exposure. However, they are found to have certain limitations; the NCV test is capable of evaluating large fibre conduction velocity (A-beta) within a segment of peripheral nerve but it cannot quantify hyperesthesia (increased sensation) or hypoesthesia (decreased sensation). Moreover, temperature sensation or cold sensation is carried by unmyelinated polymodal C fibres and in part by myelinated A-delta fibres, and not by the A-beta fibres which carry touch and pressure sensations. And those studies which assessed blood flow focussed on a single artery distal to the application of the experiment or treatments, instead of the blood flow in the tissues directly affected by cold application. Thus, the effects of the interventions on the tissues most directly affected by the treatment were not measured. Better understanding of the biological effects of cold water immersion should include monitoring of both vascular and neural functions. There is limited research evaluating the effectiveness of cold modalities using neurovascular function parameters in healthy as well as DRF population.

1.5 Exercise in the rehabilitation of upper extremity fractures; general and specific principles:

Therapeutic exercise is the systematic performance or execution of planned physical movements, postures, or activities intended to enable the patient/client to 1) remediate or prevent impairments, 2) enhance function, 3) reduce risk, 4) optimize overall health, and 5) enhance fitness and well-being. Effective therapeutic exercise program prescription requires 1) assessing the patient’s current status and 2) determining appropriate, relevant, and achievable goals. These two points mark the beginning and ending anchors for the structured rehabilitation program. Contained within these two points are a number of progression variables (i.e., exercise dosage parameters), supporting factors (i.e., good tissue quality, low pain levels, few comorbidities), barriers
(i.e., high demand occupation, poor tissue quality, multiple comorbidities), and benchmarks (i.e., short term goals). Once these issues are evaluated, therapeutic dosage parameters such as mode of delivery, type of muscle contraction, type of mobility activity, volume, frequency, intensity, duration, speed, sequencing, environment, and feedback are all considered and applied in the therapeutic exercise prescription.  

Exercise is the most common physiotherapy intervention, often used in conjunction with other therapeutic modalities to reduce impairment and increase activity in the rehabilitation of people with upper limb fractures.  

The results of a systematic review indicated that the strongest evidence for techniques to restore passive ROM in the upper extremity include active exercise, joint mobilization, and the use of an orthosis.  

Prescription of exercise after upper limb fractures is also consistent with the key principle of fracture management, movement. Despite this, there are currently no high quality trials that have evaluated the effects of exercise alone on rehabilitation outcomes. A majority of the previous trials did not clearly define the exercises included in the interventions like the intensity and frequency. It is unclear as to what is the “best dosage” for prescribed exercise was. From the trials that did outline the intensity of the program, adherence to the protocols was poorly reported.  

General principles of upper extremity exercise include avoiding painful active ROM (AROM) and passive ROM and the importance of working within the patient's comfort level. General AROM exercises for the hand include wrist flexion and extension, gentle digit flexion and extension, and thumb opposition. Shoulder and elbow AROM in the supine position is also beneficial for preventing stiffness. ROM exercise should be kept pain-free to prevent overstretched of joint structures, and the number of repetitions controlled to avoid overstretching vulnerable tissues.  

More specific guidelines for
exercises depend on the involved and vulnerable structures identified during the initial examination.\textsuperscript{111,165}

1.5.1 Exercise for the involved joints after DRF:

Exercise is the most frequently used active intervention during DRF rehabilitation.\textsuperscript{7-9,221} In patients with DRF, range of motion,\textsuperscript{223,224} volume,\textsuperscript{225} touch and threshold\textsuperscript{226,227} are the key physical impairments that should be monitored in the early phase. Later, grip strength,\textsuperscript{228} measures of functional ability, endurance, or dexterity may be more relevant.\textsuperscript{229} After DRF, wrist extension may be reduced because of adaptive shortening of the joint capsule, scar, or reduced flexor tendon gliding on the volar wrist. Supination loss may be attributed to volar soft-tissue injury or shortening, potentially involving the pronator quadratus, joint capsular adhesions, or distal radioulnar joint malalignment. These two can be addressed through exercise and orthotic wear. Active wrist flexion should be performed with the fingers relaxed or extended. Radial and ulnar deviation should be done with the wrist in neutral position in the sagittal plane and the forearm pronated. It is also helpful to have the patient use the opposite hand to stabilize the forearm to prevent the elbow from moving. Forearm rotation should be done with the elbow at approximately a 90-degree angle and tucked into the side to prevent shoulder substitution.\textsuperscript{111,165} Some patients can recover full range of motion solely by performing home exercises.\textsuperscript{8,43,44} Adherence to prescribed home exercise has been found to moderately-to strongly associated with short term outcomes of impairment and activity after DRF.\textsuperscript{221} Most recent survey on therapy patterns in DRF population showed that active interventions, including exercise and advice, were most frequently administered interventions for patients after a distal radial fracture irrespective of physiotherapist or patient factors.\textsuperscript{7}
Although the common use of exercise in DRF rehabilitation is consistent with the principles of fracture management and principles of self-management, these improvements are mostly attributed to theoretical benefits of movement. Recent systematic reviews also found that there is weak to moderate evidence to support exercise after DRF, that are managed conservatively. However, the exercise trials included in the previous reviews were found to use co-interventions along with hand exercises. This makes it difficult to draw definitive conclusions on the role of exercise alone after DRF and thus needs further investigation.

### 1.5.2 Exercise for the uninvolved joints after DRF:

Active ROM exercises of the uninvolved joints act to maintain joint mobility, prevent tendon adherence, and help reduce edema by the “pumping” action of the muscles transporting the fluid proximally. Full excursion of the flexor and extensor tendons can be prohibited by the flexed position of the wrist in the cast or external fixation device. The accompanying pain and edema may further restrict tendon gliding. Patients need to be instructed in specific exercises that need to be performed several times each day. In addition to active flexion and extension exercises for the fingers, patients should be instructed in individual tendon-gliding exercises for the superficialis and profundus tendons. Emphasis should be placed on moving to the end of the available range, rather than just wiggling fingers and “flapping the hand about in the air.” ROM exercises through multiple planes of motion can be done with the assistance of a wand.

### 1.5.3 Sensory and vascular responses after hand exercises in DRF:

Physiological responses to exercise are believed to be influenced by frequency (how often exercise is performed), intensity (resistance), and duration (number of repetitions or time the exercise is performed), muscle
contraction type, range of motion (ROM), speed of movement, and mode of exercise.\textsuperscript{217-19} Control of blood flow to skeletal muscles during exercise occurs through somatic (sensory) and sympathetic neural pathways. The activation of skeletal muscle fibers by somatic nerves results in vasodilation and functional hyperemia.\textsuperscript{238} Sympathetic activation results in vasoconstriction and maintenance of arterial blood pressure. The effects of these respective neural control systems interact throughout the vascular resistance network of skeletal muscle to facilitate coupling between the vascular supply of oxygen and the metabolic demands of the contracting muscle fibers.\textsuperscript{238} Dynamic physical exercise induces an increase in the production of heat in active muscles and increases core body temperature.\textsuperscript{240} Core body temperature is the main thermal input which stimulates the thermoregulatory centre (the hypothalamus), which in turn induces vasodilation in the skin.\textsuperscript{241} Control of skin blood flow is thus influenced by myogenic activity and local concentrations of muscle metabolites (CO\textsubscript{2}, hydrogen ion etc.) which elicit an exercise pressor reflex to increase muscle blood flow.\textsuperscript{90,92,236,248} Based on the amount of activity and oxygen demand in the exercising muscle tissue, increase in muscle blood flow is contributed via redistribution from the splanchnic circulation and cutaneous circulation to meet the metabolic demands.\textsuperscript{217,218} As skin vasomotion is influenced by thermal and non-thermal factors associated with the exercise, the thermal input–output relationship in the control of cutaneous circulation during the exercise differs from that at rest.\textsuperscript{241,248} Hence, monitoring sensory and vascular responses in skin during exercise provides an indication of changes in the neurovascular functions. The skin vascular responses to exercise have also been shown to differ between glabrous regions such as the palm and sole, and non-glabrous regions such as the dorsal hand and forearm.\textsuperscript{234-237} But there is a lack of reports on blood flow and sensory responses to different intensities of hand exercises in both healthy and patient populations.
1.6 Summary of limitations in knowledge base

1.6.1 Assessment tools:

Complications like CRPS, median nerve compression, tendonitis etc., may occur either in the early (in six weeks) or later phase (after cast removal) of DRF, and may further lead to cold intolerance. Such impairments have been thought to be missed or overlooked by the treating therapist. Hence monitoring of cold intolerance and neurovascular functions at important timelines (six weeks/cast removal) during the rehabilitation process will be useful to plan or modify the future care.

A majority of the studies which included the vascular measures, used laser Doppler probe (LDF probe) to capture responses from small areas of skin, distal to the treatment area. These measurements were typically obtained from a single blood vessel, instead of the total area of treatment directly affected by the intervention or exposure. There is lack of studies on blood flow measures that capture responses from the whole treatment area to give a better understanding of treatment effects.

There are a number of studies which assessed sensory nerve function parameters using nerve conduction velocity (NCV) tests. But the sensory nerve conduction studies primarily evaluate the function of nerve fibers with the highest conduction velocity i.e., the large myelinated A-beta nerve fibers and thus are not that useful in assessing the function of A-delta or C nerve fibers which carry different sensory signals to brain. There were hardly any trials which looked at the impact of therapeutic interventions on different sensory nerve fibre responses (A-beta, C fibres etc.).

There is also scarcity of trials that have included both neural and vascular measures to monitor therapeutic outcomes. Thermal agents are
thought to have a range of therapeutic effects through changes in metabolism, nerve transmission, hemodynamics, and mechanical properties. Inclusion of both measures would give important information about the tissue viability, oxygen supply, thermoregulation, and neuromuscular coordination. Hence, choosing both measures deemed important to have a better understanding of neurovascular function.

1.6.2 DRF management:

Previous surveys and reviews on DRF management have demonstrated the benefits of cold as an adjuvant in the treatment of DRF after cast removal, but if an underlying neurovascular dysfunction or complication exists then it would be detrimental for patients to undergo treatment with cold or therapeutic modality.

There is also a scarcity of trials in the literature that examined techniques and effective dosage for physical agents or therapeutic modalities in hand conditions.

Ultrasound therapy is an option for adjuvant treatment in DRF after cast removal. But the clinical guidelines regarding timing, duration and intensity of application have not been established to select parameters for tissue healing, associated pain or for treating complications such as tendonitis/tenosynovitis in DRF.

Exercise program (supervised/home) is commonly used in the rehabilitation of DRF after cast removal and there is also evidence on its short term benefits in hand function. However, the details regarding mode, intensity and duration of exercise is not clear in healthy as well as patient populations.
While all these interventions are commonly used in the rehabilitation of patients after distal radius fracture in spite of the weak evidence, to date there is only limited research evaluating their effectiveness after immobilization period.

Thus, therapists do not have the evidence required to make informed choices nor to justify their services to fund organizations in light of the need to practice within an evidence-based framework. Hence, to maximize the effectiveness of these modalities/interventions we planned to test the short term effects of two approaches in ultrasound therapy and hand exercise in the healthy volunteers.

The normative data on sensory and vascular functions obtained after control condition (rest), ultrasound and hand exercise in healthy individuals might allow for useful clinical comparisons in future research studies, in particular the DRF population.

Therefore, the evidence on the effects of cold exposure in DRF hands, and the impact of different dosages of ultrasound and different intensities of hand exercises on the sensory and vascular function parameters are incomplete in both healthy as well as DRF population. Hence there is a need to fill this gap in the knowledge base, by initiating these trials in the healthy subjects and then apply these findings to the patient population.

### 1.7 Thesis objectives and hypothesis:

This thesis is a manuscript-style thesis. The overarching objective is listed below, followed by the 3 specific objectives which are then addressed in 3 manuscripts each forming a chapter of the thesis (chapters. 2, 3, and 4). A consequence of presenting the thesis in ‘Integrated Article’ format is that some repetition is apparent.
**Overall thesis objective:** To determine the short term sensory and vascular responses to thermal, ultrasound and exercise interventions in healthy volunteers and patients with DRF. The specific objectives are:

**Objective 1:** To determine the impact of immersion in cold water evaluation (ICE) protocol on sensation and superficial blood flow: comparing injured and uninjured hands in patients with DRF after cast removal.

**Hypotheses:** Our hypothesis is that cold water immersion will alter superficial blood flow, skin temperature and sensation differently between affected and unaffected hands following DRF.

**Objective 2:** To determine the impact of continuous (1MHz) and pulsed (3MHz) ultrasound therapy on sensation and superficial blood flow in the forearms of healthy volunteers. And to see if responses are affected by age and gender.

**Hypotheses:** Our hypothesis is that skin blood flow, temperature and sensation will be altered differently with continuous US and pulsed US in both males and females belonging to two age categories.

**Objective 3:** To determine the impact of low intensity and high intensity hand grip exercise on sensation and superficial blood flow in the hands of healthy volunteers. And to see if responses are affected by age and gender.

**Hypotheses:** Our hypothesis is that two different exercise intensities will have different effects on skin blood flow and sensation in both males and females belonging to two age categories.

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CHAPTER 2

‘Short term sensory and vascular responses to cold water immersion in patients with distal radius fracture (DRF).’

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2.1 ABSTRACT

**Study Design:** Randomized trial, repeated measures design (pretest post-test).

**Introduction:** From the literature currently available it is unclear which components of physiotherapy intervention are effective for patients with DRF after the immobilisation period. Cold is used for therapeutic effects to reduce pain and swelling. Cold exposure is also used to assess nerve and vascular function.

**Purpose:** To determine the short term impact of cold water immersion on sensory and vascular functions in patients with DRF and compare responses in their injured and uninjured hand.

**Methods:** Twenty DRF participants aged 18 to 65 yrs. (Mean age: 52 ±12 yrs.) were recruited after the cast removal for this study. Superficial blood flow in the palm and distal forearms was determined using the Tissue viability imaging system. Sensory perception thresholds (sPT) for ulnar and median nerves (at 2000 Hz and 5Hz) were determined from ring finger (C7, C8) to assess A-beta and C fibre function. Following baseline testing each hand was exposed to the Immersion in Cold-water Evaluation (ICE) protocol and the order of application in the hands was randomly assigned. ICE consisted of 5 min of hand immersion (up to mid forearm in an insulated container) in cold water, maintained at 12 °C. Scores were obtained before, immediately after immersion and 10 min later. Differences in these were analyzed using general linear models.
**Results:** In the DRF hand, ICE increased blood flow from pretest (Mean, SD: 82.27 ±9.22 A.U., p<0.05) to immediately after immersion (0 min) (124.49 ± 34.61 A.U., p<0.05), then remained constant for over a minute (118.09 ± 32.82 A.U., p<0.05) and returned to pre-exposure levels by 10 min (83.25 ± 8.45 A.U., p<0.05). Skin temperature was reduced in the index finger from the baseline level (31.69 ± 3.15 °C, p<0.05) to immediately after immersion (0 min) (21.72 ±5.10 °C, p<0.05) and 10min later (27.62 ±5.98 °C, p<0.05). A similar trend was noted in little fingers from baseline (32.12 ± 3.10 °C, p<0.05) to both immediately (0 min) (23.06 ±5.83; p<0.05) and 10min (28.02 ±5.94, p<0.05) after immersion. The sPT’s at 5 Hz remained unaltered by ICE in both injured and uninjured hands (p>0.05). sPT at 2000 Hz changed only on the DRF side and showed an increased response from baseline (8.95 ±2 mA, p<0.05) to both immediately (1 min) (10.7 ±1.65 mA, p<0.05) as well as 10 min later (10.70 ±1.72 mA, p<0.05). Except for the changes in sPT at 2000Hz on the DRF side, no other significant difference in sensory and vascular responses were observed between the injured and uninjured hands on all outcome measures(p>0.05).

**Conclusion:** Normal thermo-physiological responses consistent with ‘hunting reaction’, digital rewarming, and unaltered C fibre activity were observed in both the injured and uninjured hands after ICE protocol. ICE was effective in increasing sPTs at 2000 Hz in the fractured hand after cast removal. These findings suggest that cold water immersion, as applied in this study, can induce some therapeutic effects associated with ‘hunting response’ like reducing pain and swelling and might also induce a hypoalgesic effect through its reductions in skin temperature and increases in sPT’s of large diameter, myelinated A-beta fibres during the rehabilitation of uncomplicated DRF.

**Key words:** sensation, skin blood flow, cold intolerance, cold immersion, distal radius fracture
2.2 INTRODUCTION

Fracture of the distal radius (DRF) can occur after a fall on an outstretched hand and is one of the most common fractures seen by orthopaedic surgeons with an incidence of 195.2/100,000 persons per year. DRF is more common in females and in older populations. It has been estimated that a 50 year old white woman in the USA or Northern Europe has a 15% lifetime risk of a DRF; whereas a white man of the same age has a lifetime risk of a little over 2%. Interventions following distal radius fractures are directed at restoring the anatomic alignment of the fractured bones, promoting the repair of injured structures and fostering the normal function of these structures during the healing process. The treatment plan for each patient is determined by various factors including the pattern of bone fracture, bone quality, degree of soft tissue damage, medical condition and compliance with treatment. DRF can result in an increased morbidity, with long-term functional impairment, pain, and deformity.

The focus of rehabilitation during the early rehabilitative phase includes decreasing pain, minimizing oedema, improvement in range of motion (ROM) of hand, wrist and forearm and improvement in functional activities. Progressive resistive exercises, joint mobilizations, passive ROM exercises, and heat are all used to help increase ROM and decrease pain during this phase. A recent systematic review of 15 trials on the effectiveness of various rehabilitation techniques following DRF, managed either conservatively or surgically (involving 746 adults), has concluded that there is insufficient evidence to support the relative effectiveness of different interventions during the immobilization as well as mobilization phase after DRF. However a survey of 242 therapists by Michlovitz et al., found that an exercise program and the use of heat or cold modalities (90%) were the most frequent interventions provided by therapists for this patient group.
Altering tissue temperature (using thermal agents) can have a range of therapeutic effects through changes in metabolism, nerve transmission, hemodynamics, and mechanical properties. Biochemical, histological and mechanical changes occur during immobilization after DRF and may contribute to pain and swelling. Cryotherapy or ice therapy is thought to reduce pain and swelling and subsequent capillary damage in acute and sub-acute stages via a ‘hunting response,’ a counter-irritation effect, and through the gate control theory of pain. Controlling pain and swelling in the early stage of DRF may restore maximal function and mitigate complications that can occur later in recovery. However, there is little evidence to suggest a preference between different methods of pain and edema management, although treatment has been shown to be more effective than control.

Cheing et al. evaluated the effectiveness of thermal agents and exercise on forearm pain, swelling, and wrist ROM in patients with DRF. These authors compared 5 daily applications of ice, pulsed electromagnetic field (PEMF) and a combination of ice and PEMF together with exercise after the cast removal. The study demonstrated the effectiveness of ice at 3 and 5 days (p<0.05). When comparing the 4 groups receiving adjuvant treatments (i.e. ice therapy, PEMF therapy, or ice and PEMF therapy) versus sham, the only statistically significant difference was for ice therapy which reduced swelling and associated pain more than the PEMF therapy or sham for up to 5 days. However, previous reports have shown that melted ice water has better efficacy than any of a variety of newer cooling methods (including frozen gel packs, endothermic chemical packs, and refrigerant-filled packs). The findings from Esperanza et al., and Gregson et al. also provide an important insight into the possible mechanisms responsible for the use of cold water immersion in alleviating inflammation in clinical and sporting environments, as well as a basis for improving treatment outcomes.
There are also reports of complications with DRF from a large cohort study (275 patients), like reflex sympathetic dystrophy (RSD) (20%), median nerve compression (22%), tendonitis or tenosynovitis (14%), and radial nerve compression (11%), which are often found to be either missed or overlooked by the treating therapist. Injury to the peripheral vasculature, defective vasoregulation, and nerve injury have been suggested as possible routes to cold intolerance. Smits et al., reported that 38% of patients developed cold intolerance after hand fractures. Pullock et al., reported cold intolerance in half of their study participants with confirmed diagnosis of RSD after exposing them to an Isolated Cold Stress Test (ICST) and Ruijs et al., found similar reports in 56% of patients with an isolated ulnar or median nerve injury and 70% with a combined ulnar and median nerve injury after an ICST and Cold Intolerance Symptom Severity (CISS) questionnaire.

Cold intolerance, cold sensitivity or “trauma induced cold associated symptoms” is defined as abnormal pain after exposure to mild or severe cold, with or without discolouration, numbness, weakness, or stiffness of the hand and fingers. Patients commonly report cold intolerance after hand fractures, that may arise within the initial months or may have a delayed manifestation, depending on the seasonal nature of the injury. The pathophysiology of cold intolerance is still unclear. However, it is postulated that post-traumatic cold intolerance has both vascular and neural etiology among other contributing causes.

The forearm (non-glabrous) and palmar skin (glabrous) is innervated by sensory nerves and sympathetic vasoconstrictor and/or vasodilator nerves, which respond to thermal, chemical, and mechanical stimuli to provide feedback to the central nervous system and influence cutaneous arteriolar tone (vasoconstriction or vasodilation) via the release of neuropeptides and other vasoactive agents. Skin temperature is another valuable indicator
of tissue viability which is directly related to digital vessel patency. In a healthy person, after extensive cooling of the extremity, the thermoregulatory system increases the blood flow to the extremity to counteract the decrease in hand temperature and prevent pain or frost bite. Thermoregulation of skin in part relies on input from temperature sensors and nerves located in the peripheral extremities. Thermal and pain sensations are both mediated through small-diameter, slowly conducting nerve fibers: unmyelinated C and lightly myelinated A-delta fibers. Normally, these two types of afferent fibers in the distal axons of primary sensory neurons respond to nociceptive stimuli, including temperatures below 15°C, if the intensity of the stimulus is high enough. In cold-intolerant subjects, it may be that this cold stimulus threshold is lowered, requiring less intensity to elicit a pain response. These fibers are also thought to contribute to autonomic control. Small fibers are therefore implicated in sensory and autonomic dysfunctions such as pain manifestation and enhancement. Therefore, peripheral neuropathies would consequently have a detrimental effect on vasomotor function. Sometimes, after injury the symptoms of pain due to vascular insufficiency may mimic neurologic conditions. Hence, it is important to consider vascular, sensory, sympathetic and temperature measures while assessing the healthy and injured tissues.

When neurovascular dysfunction exists in hands, cutaneous thermoregulation, nutritional blood flow, and autonomic functions may get impaired. One of the major complications after DRF is RSD and it was reported previously that in the early stages, it can be difficult to distinguish RSD from the normal pain and swelling associated with the fracture or ORIF. Serious cases of RSD may require many months of therapy to alleviate symptoms (pain, tenderness, impairment of joint mobility, swelling, dystrophy, vasomotor instability). Cryotherapy is used to reduce pain and swelling after DRF, but if an underlying neurovascular
dysfunction exists, then it is detrimental for patients to continue treatments with cold modalities. In addition to this, cold intolerance as reported earlier in patients with RSD, median and ulnar nerve injuries and patients with hand fractures can be severely disabling for the patients. Given that cold sensitivity is related to functional impairment and quality of life, but not to sensibility, quantitative measurements like the cold stress test may be important in detecting cold intolerance in the hand after injury. Testing techniques that reflect fluctuations of both thermoregulatory and nutritional blood flow may be required for the accurate quantitation of how and where in the microcirculation derangements of function occur.

Immersion in cold water evaluation (ICE) is a simple and reliable objective measure to assess cold responses in the hand. Previous reports on the ICE used only skin temperature for the evaluation of thermoregulatory responses, and did not include any vascular measures. Although blood flow has a thermoregulatory component (80% to 90%, mainly through arteriovenous anastomoses) and a nutritional component (10% to 20%, capillary system), skin temperature in the hands and digits is highly correlated with skin blood flow. Aberrations in the balance between thermoregulatory and nutritional blood flow have been documented after trauma (e.g., reflex sympathetic dystrophy). It is also possible that after cold immersion, nutritional blood flow diminishes to critical levels, leading to cellular ischemia, pain, and cold intolerance. Hence, observation of vascular changes is important to understand the central and peripheral mechanisms of blood flow regulation after hand injury.

Neurovascular function is an important indicator of upper extremity condition (nutrition, thermoregulation, structural integrity, neuromuscular coordination). Effective rehabilitation interventions may help in preventing complications associated with the fracture and/ or treatment and in optimising functional recovery in order to achieve activities required for daily living.
Hence, using baseline sensory, vascular, and cold responses to assess the injured (and normal) hand would be advisable to assist with early detection of complications after the DRF. Furthermore, monitoring of neurovascular function at important timelines (6 weeks/cast removal) after DRF during the rehabilitation process will be useful to plan or modify the future care.

In addition to this, there is also a scarcity of published trials that have looked at both the sensory and vascular responses to cold application in the DRF population. Hence, the specific aim of this study is to determine whether distal radius fracture would result in alteration of blood flow, sensory function in an area innervated by median and ulnar nerves, and/or cold sensitivity after brief exposure to an ICE protocol. These evaluations might also inform our understanding for potential mechanisms of therapeutic effect that operate through beneficial effect on skin blood flow and sensory function.

2.3 METHODS

Participants:

The sample size required for this research was based on the number needed to detect a moderate effect size according to Cohen. A moderate effect (ES r=0.50) using two-tailed alpha (α = 0.05) at 80% power, requires a sample of 28 participants in each group for a between subject design and a sample of 14 participants for a within subject design. As this is a within subject design and variance within individuals is less than between subjects a sample size of 20 was considered and approved by the ethics board. Statistical significance was considered if p<0.05.

Patients with DRF were recruited by the treating surgeon or therapist during the 6th week following cast removal. Testing was done in the Hand and Upper
Limb Research Lab, at St Joseph’s Health Care, London, Ontario, Canada. Participants aged 18 to 65 yrs. with stable DRF, treated by either closed reduction or open reduction internal fixation (ORIF), and had no other injury or disease to the neck, shoulder, elbow, wrist, or hand within the past year were included in the study. The control hand was included if it had no recent injury or disease to neck, shoulder, elbow, wrist, or hand within the past year. All subjects were informed to refrain from drinking beverages and to avoid exercise 4 hours prior to testing. Subjects were excluded if they had skin infection, open wound, pregnancy, presence of a pacemaker/monitoring device, malignancy, heart disease, confirmed diagnosis of CRPS, inflammatory arthritis, peripheral vascular diseases, previous fractures, revision surgeries, complex fractures with neurovascular injuries, autoimmune disorders, cancer, local hot or cold insensitivity, cold adverse reactions, hypertension and cardiac failure, diabetes, internal haemorrhages, neural diseases, deficits in sensation in the area to be treated (sensory test to identify sharp and dull sensation; hot or cold), decreased circulation (Digital patency test for fingers) and inability to understand instructions. This study was approved by the Western University Research Ethics Board. All participants read the letter of information, had his/her questions answered, and signed a consent form prior to participation in this study.

**Outcome measures:**

**Immersion in cold water Evaluation (ICE)** (Traynor and MacDermid 2008):

ICE is a reliable, objective measure of cold response to assess cold intolerance in hands after injury. This protocol was centered predominantly on the former etiology, examining peripheral blood flow and the associated temperature recovery. A cold-provocation test is initiated by immersing hands in cold water maintained at a temperature of 12° C (± 1° C) and the digital temperatures in the index and little fingers are measured using
an infrared skin thermometer during the recovery period. All tests are performed with the patient seated comfortably in a thermo-neutral environment (20°C ± 2°C).

**TiVi (Tissue Viability Imager) 600 polarization spectroscopy camera (version 7.4 Wheels Bridge AB, Linköping, Sweden):**

The TiVi is a small and portable device for high-resolution instantaneous imaging of Red Blood Cell (RBC) concentration in upper human dermal tissue. TiVi software was used to quantify RBC concentration on the anterior aspect of palm and distal forearm on both arms using a digital camera (Canon Rebel EOS model 450D, Japan) with a polarization lens. The camera was supported by a multijointed metal arm provided by Wheels Bridge and the arm was secured to a desk. The camera was adjusted to point downwards towards the surface of the desk. A royal blue colored cushion was used to rest the forearm and to fill the camera view. An outline was drawn to standardize hand positioning. Each participant was required to keep their shoulder in neutral, elbow in 90° flexion; forearm (s) supinated and placed approximately at the level of the heart. Each image was captured with the polarized lens set at the cross polarization setting and the camera was positioned at a distance of 300mm from the participant’s hand. Image quality was set to medium normal. One photo was taken every 5 seconds (12 photos /min) and uploaded into the attached laptop computer. The camera has a light penetration depth between 400 to 500 micrometers, and this light contains information about the main chromophores in the epidermis (melanin) and dermis (hemoglobin).

Once the images were captured, the TiVi images were processed using the TiVi software. For each participant, one image at baseline and at each follow up point (0 min, 1 min and 10 min after immersion) was used for processing and analysis, for a total of 4 images per hand. Regions of Interest (ROI’s)
were selected over the immersed area at palms and the distal forearms (up to 2 inch from ulnar styloid process). The magnitude of RBC concentration over the selected ROI’s was obtained using ‘group image analysis.’ Values for the TiVi are measured by Arbitrary Units (A.U.) as defined by the manufacturer. Data was first exported from the TiVi software into Microsoft Excel 2010 spreadsheets and then imported into SPSS version 20.0 for statistical analysis. The technique has shown many uses in drug development, burn investigations, pressure studies, and general research maneuvers due to the ease of use, portability, and low cost. The TiVi has been validated for construct validity to measure superficial RBC concentrations with in vitro fluid models and computer simulations. The TiVi software is able to accurately calculate the oxygen saturation level of 91.5% in vivo, which is within the physiological range of oxygen saturation within blood. It has been shown to be sensitive to change during blood occlusion testing, and drug testing on skin, and has also demonstrated good inter-laboratory reliability.

**Neurometer® CPT/C device (Neurotron Inc., Baltimore, USA):**

The Neurometer evaluates sensory nerve conduction from the periphery to the brain and has been shown to detect differences in neural function in asymptomatic subjects when neural stress was administered. This portable battery operated nerve stimulator has the ability to emit three different frequencies in sinusoidal waveforms to selectively target different subpopulations of nerve fibres dependent upon nerve fibre diameter. A frequency of 2,000 Hz is used to stimulate the large myelinated A-beta fibres (A_β fibres) which detect cutaneous touch and pressure; a 250-Hz stimulus will stimulate myelinated A-delta nerve fibres (A_δ fibres) which are mechanoreceptive, and detect fast pain, pressure and temperature, while a frequency of 5 Hz is used to stimulate the small unmyelinated C-polymodal nociceptive fibres which detect slow pain and temperature and are post
ganglionic sympathetic fibres. This device has been used in numerous studies to detect, screen and diagnose the abnormalities of peripheral nervous system and normal ranges for all nerve fibre types (A-beta, A-delta and C fibres) have been established to assess normal sensation, increase in sensation (hyperesthesia), decrease in sensation (hypoesthesia) and no sensation at all (anesthesia). The Neurometer has been shown to be a reliable and valid measure in the evaluation of mechanical neck disorders (MND). It has been shown to be both specific (73%) and sensitive (74%) in the clinical examination of carpal tunnel syndrome and hence considered as a good quantitative sensory function test.

Ranged CPT (R-CPT) is a sensory perception threshold test which can be completed in 3 to 6 min for each test site. It is typically used to confirm or rule out sensory involvement in large samples such as screening. In R-CPT, each frequency is repeated several times to ensure accuracy and reproducibility. The average time needed to complete the tests has been reported as less than 10 min. The Neurometer reports values as the normal range (R-CPT Level, 6–13), hyperesthesia (R-CPT Level, 1–5), and hypoesthesia (R-CPT Level, 14–25). R-CPT was tested at two frequencies, 2000Hz and 5Hz, to target two different nerve fibre types. To begin 2000 Hz stimulation, the skin was cleaned with a skin paste and then the 1 cm gold electrodes coated with small amount of gel were attached to the ring finger with an adhesive tape. Then, the participants were asked to press and hold the red “Test cycle” button on the remote control box and release it as soon as they begin to feel the tingling or buzzing sensation. The machine records the response when the button is released and the same process is repeated 7-10 times until a score is displayed. In total three scores are obtained at 2000Hz. The same procedure is was repeated at 5Hz. These test cycles end automatically after few repetitions (7-10 times) and the CPT displays score for 5Hz.
**Experimental procedure:**

**Study design and procedures:**

We used a randomized, repeated measures design in this study. Random allocation to hand was achieved through subject’s selection of assignment contained in an opaque envelope. Subjects were required to acclimate to the testing room temperature upon arrival for 15 min. During this time, subjects were instructed about the ICE protocol (Immersion in Cold water Evaluation). After explaining the protocol and obtaining consent, each participant was asked to pick up one sealed envelope from a bundle, which had information on the side of hand (either normal or DRF) to begin intervention. Once the side was picked, participant underwent cold water immersion in the hand first selected. After this, the opposite hand received the ICE. The study procedure was administered in a closed room at a temperature of 20º±2 ºC. Outcome assessments and testing were all provided by single physiotherapist. Testing was completed in two hands one after the other on same day. Please refer to Figure. 2.1 outlining the study design.

**ICE protocol:**

Each subject was directed to rest her hand comfortably, palmar surface up, on a table as mentioned earlier. The subject was instructed to maintain a stable upper body position and refrain from moving her hands, both while on the table and during cold water immersion. Subjects were first measured on TiVi over the palmar aspect and distal forearms (up-to 10 cm from ulnar styloid process), then skin temperature was recorded from index and little fingers using King’s infrared digital thermometer, and this was followed by Ranged CPT test measured from the tip of ring finger (over C7/C8 dermatome level) to record sensory perception thresholds at 2000Hz and 5Hz before starting cold water immersion. The participant subsequently
immersed her hand up to 10 cm proximal to the ulnar styloid process in cold water at 12 °C (±1°C) for 5 min, in an insulated container. Temperature in the insulator was monitored throughout the experiment using a floating Aquarius digital spa and pool thermometer and a mercury-inglass thermometer to verify the temperature readings. The water temperature was maintained within 1°C of the target value with the administration of additional ice or warm water, as required. The investigator stirred the contents of the container three times every minute to evenly disperse the water warmed by the subject’s hand. This protocol was timed with a stop watch. Instructions were given to stop the test if the participants felt any kind of discomfort during immersion. Following 5 min of immersion in cold water, the subject removed her hand and placed it again palmar surface up on a towel on the table. The hand was quickly pat-dried and then placed under the TiVi camera to measure superficial blood flow, finger temperatures and sensory perception thresholds using R-CPT test. The TiVi measurements were taken immediately (0 min to 1 min) and after 10 min of immersion, whereas R-CPT was measured at 1 min and 10 min post immersion. Skin temperatures were measured immediately (0 min) and 10 min after immersion. The delay between the removal of hands from the water and start of the recordings on the three measures was less than 3 min. TiVi took 12 photos for 1 min (0 min to 1 min), temperature was recorded during the 5 second gap in TiVi, and R-CPT was initiated at the end of TiVi. The protocol was repeated on the subject’s opposite hand for comparison in similar order.

TiVi software was used to calculate the mean blood flow (A.U.) over the area of immersion in both arms (palms and forearm up to 5 cm from ulnar styloid process) and then the data was transferred to an Excel sheet (Microsoft 2010). The sensory perception thresholds obtained from R-CPT test at 2000Hz and 5Hz (m. A.) were recorded directly from the digital display of the Neurometer.
CPT/C device onto a separate data collection sheet along with the temperature (°C) readings.

**Data analysis:**

Data was entered in SPSS and random checks of 10% of the data against the hard copies of data sheets was used to ensure data quality (100% were correct so no further data audits were performed). Descriptive statistics were run to further investigate data quality and assess data normality. The majority of data was normally distributed as assessed by Kolmogorov-Smirnov Test (p>0.05), hence parametric tests were used for data analysis. General linear model (GLM, using SPSS version 20, IBM Inc.) was used to determine if participants normal and injured hand had different measures of superficial blood flow (RBC concentration), sensory perception thresholds, and temperature at baseline, immediately after cold water immersion and then again after 10 min. A 2 × 4 (hand × time) design was used to assess changes in skin blood flow, and a 2 × 3 (hand × time) design was used to assess changes in temperature and sensory perception thresholds at 2000 Hz and 5 Hz (A-beta and C fibre) for normal and injured hands. Interactions were examined for significance between time and hand. Post hoc analyses were performed using Bonferroni correction, wherever necessary. Pair wise comparisons were used to perform within-group comparisons wherever needed. Significance level was set at p<0.05 level unless otherwise noted. All values were expressed as means, standard deviation and 95% confidence intervals.

**2.4 RESULTS**

Twenty patients with DRF were recruited after the cast removal between November 2012 to May 2013. No data points were missing. Patients were primarily females who were treated non-surgically (casted) (See Table 2.1).
Table 2.2, 2.3 and 2.4 displays group means, standard deviation and 95% confidence interval obtained from the GLM to assess the changes in skin blood flow, skin temperature and sensory perception thresholds at 2000Hz and 5Hz. Seventeen participants felt comfortable during the ICE protocol in the injured hand. On the uninjured side, they described a slight numbing sensation until two minutes, but eventually after the third minute, it was free from any discomfort. Only three participants removed both the injured and uninjured hands before five minutes; one due to pain and others due to discomfort during immersion. No long-term discomfort was reported.

**Superficial blood flow response:**

*Differences following cold exposure within the uninjured hand:* Skin blood flow significantly increased from baseline (Mean, SD: 82.18 ±7.52) to immediately after immersion (0 min) (Mean, SD: 106.03 ± 25.92; p<0.05), remained high for over a minute (1 min) (Mean, SD: 104.44 ±24.86) and then decreased significantly after 10 min post immersion (Mean, SD: 84.17 ± 8.91; p<0.05). Post hoc comparisons between baseline value and immediately (0 min) after immersion as well as between baseline and 1 min after immersion showed a significant difference. Post hoc comparisons between baseline and 10 min after immersion as well as between 0 min and 1 min after immersion were not significantly different (p>0.05) (Table 2.2, Figures. 2.2, 2.3, 2.4).

*Differences following cold exposure within the injured hand:* Skin blood flow significantly increased from baseline (Mean, SD: 82.27 ±9.22, p<0.05) to immediately after immersion (0 min) (Mean, SD: 124.49 ± 34.61, p<0.05), remained high for over a minute (1 min) (Mean, SD: 118.09 ± 32.82, p<0.05) and then decreased significantly after 10 min of immersion (Mean, SD: 83.25 ± 8.45; p<0.05). Post hoc comparisons between baseline value and immediately (0 min) after immersion as well as between
baseline and 1 min after immersion showed a significant difference (p<0.05). Post hoc comparisons between baseline and 10 min after immersion as well as between 0 min and 1 min after immersion were not significantly different (p>0.05) (Table 2.2, Figures. 2.2, 2.3, 2.4).

**Differences between the injured and uninjured hands:** The observed changes in skin blood flow were not significantly different between the normal and DRF hand (p >0.05). However, there was a significant difference in skin blood flow response across the time points with a significant interaction between the hand and time (p<0.05) (Table 2.2, Figures. 2.2, 2.3, 2.4).

**Skin temperature response:**

**Differences following cold exposure within uninjured index and little fingers:** There was a significant decrease in skin temperatures at the tip of index and little fingers from baseline (Mean, SD: 31.91 ±3.12 and 32.55 ±2.94; p<0.05, respectively) to immediately after cold water immersion (Mean, SD: 22.23± 5.9 and 22.21± 5.17; p<0.05, respectively) and after 10 min (Mean, SD: 27.21± 6.70 and 27.48± 6.14; p<0.05, respectively). Post hoc comparisons between baseline and immediately after immersion (0 min), and between (0 min) immediate test and 10 min after immersion, as well as between baseline and 10 min after immersion showed significant difference in both index and little fingers (p<0.05) (Table 2.3, Figures. 2.5,2.6).

**Differences following cold exposure within the injured index and little fingers:** There was significant decrease in skin temperatures at the tip of index and little fingers from baseline (Mean, SD: 31.69 ± 3.15 and 32.12 ± 3.10; p<0.05, respectively) to immediately after cold water immersion (0 min) (Mean, SD: 21.72 ±5.10 and 23.06 ±5.83; p<0.05, respectively) and after 10min (Mean, SD: 27.62 ±5.98 and 28.02 ±5.94; p<0.05, respectively).
Post hoc comparisons between pretest and immediately after immersion (0 min), and between immediate measures (0 min) and at 10 min after immersion as well as between baseline and 10 min after immersion showed a significant difference in both the index and little fingers (p<0.05) (Table 2.3, Figures. 2.5, 2.6).

*Differences between the injured and uninjured fingers:* The observed changes in skin temperature at the index and little fingers were neither significantly different between the normal and DRF hands (p >0.05), nor an interaction for hand and time was seen (p>0.05) (Table 2.3, Figures. 2.5, 2.6).

**Sensory perception threshold at 5 Hz (for C fibres):**

*Differences following cold exposure within the injured and uninjured hand:* There was no significant difference in perception threshold at 5Hz between baseline and immediately after (1 min) and between baseline and 10 min after immersion in both injured and uninjured hands (p>0.05). (Table 2.4, Figure 2.7)

*Differences between injured and uninjured hand:* There was no significant difference in perception threshold at 5 Hz between the injured and uninjured hands (p >0.05) across the time points (p>0.05) nor an interaction was found (p>0.05) (Table 2.4, Figure 2.7).

**Sensory perception threshold at 2000 Hz (for A-beta fibres):**

*Differences following cold exposure within the uninjured hand:* There was no significant difference in perception threshold at 2000Hz between baseline and immediately after (1 min) or between baseline and 10 min after immersion (p>0.05). (Table 2.4, Figure 2.8)

*Differences following cold exposure within the injured hand:* There was a significant increase in perception threshold at 2000Hz, from baseline
(Mean, SD: 8.95 ±2; p<0.05) to immediately after (1 min) cold water immersion (Mean, SD: 10.7 ±1.65; p<0.05) as well as after 10 min (Mean, SD: 10.70 ±1.72; p<0.05) in the DRF hand. Post hoc comparisons between baseline value and immediately (1 min) after immersion as well as between baseline and 10 min after immersion showed a significant difference (p<0.05). Post hoc comparisons between values immediately after (1 min) and 10 min after immersion were not significantly different (p>0.05) (Table 2.4, Figure 2.8).

Differences between the injured and uninjured hand: Neither a significant difference in perception threshold at 2000Hz was observed between the uninjured and DRF hands (p >0.05), nor was an interaction between the hand and time (p>0.05). However, a significant difference in perception values was observed between the injured and uninjured hands across all time points (p <0.05) (Table 2.4, Figure 2.8).

2.5 DISCUSSION

The responses observed in this study are consistent with ‘hunting reaction’ or the ‘cold induced vasodilatation’ phenomenon that has been postulated to explain cold exposure responses. This study found no differences in skin perfusion and rewarming patterns between the previously fractured hand and the unaffected hand of patients presenting at 6th week following a closed reduction. Since patients with vascular injuries were not included in the study, this finding suggests that in the absence of such injury vascular function is relatively “normal.” Similarly no difference was observed in C fiber activity after ICE (which carry temperature, pain sensation and sympathetic signals) between the injured and uninjured hands, indicating that these pain fibers were operating at similar detection levels after brief exposure to cold. In contrast A-beta fibers (which carry touch and pressure sensation) responded by an increase in threshold only on the affected side.
However, the A-beta perception thresholds were within the normal range (R-CPT Level, 6-13); indicating that the fractured hand was less sensitive following the ICE exposure.

The demonstrated changes in skin blood flow immediately after cold water immersion in this study are consistent with changes in limb blood flow reported by Levy et al.,20 These authors noted an increase in cutaneous blood flow measured by plethysmography after hand immersion in cold water at 4 °C. Even though the cold water temperatures and the methodology used in the study were different than the ICE protocol, the observed vasodilatation in the present study is consistent with that reported by Levy et al., and the previously described "hunting reaction" phenomenon.7 The term hunting reaction or hunting response7 is described as the alternating periods of vasodilation and vasoconstriction during cold exposure until a steady state is reached. Maintained vasodilatation without cycling has also been observed with cooling human forearms at 1°C for 15 min. 42 This reaction has implications for assessment and treatment since the clinical rationale for doing each must be consistent with the underlying physiological mechanisms. When the ICE is used to assess abnormal physiological responses to cold, there can be a variety of indicators of this, including abnormal pain in response to cold exposure (detected by numeric pain rating and test completion), failure to achieve appropriate vasodilation and vasoconstriction during the test, or inability to re-stabilize vascular supply and temperature following exposure. Similarly, the same impairments could negate therapeutic value of cold exposure for selected indications.

The extremities mitigate the detrimental effects of local cold extremes. In healthy subjects, about 5 to 10 min after the initiation of cold exposure of the hand in a 15 °C or cooler environment, the blood vessels suddenly vasodilate to increase peripheral blood flow and maintain fingertip temperatures.7,14,17.
Others have reported that this response is stronger when cooling occurs in water in comparison to air. This cold induced vasodilation (CIVD) is followed by a new phase of vasoconstriction to reduce blood flow to the peripheries in favor of a central pooling of blood in the torso and deep body core. This process repeats itself and is called ‘the hunting reaction’ or CIVD reaction. Daanen et al., observed that this hunting reaction was present in 210 out of 226 investigated healthy male subjects (93%) who immersed their fingers in ice water. This was also observed in the injured and uninjured fingers/hands of patients with Reflex Sympathetic Dystrophy, and patients with median and ulnar nerve lesions after an Isolated Cold Stress Test (ICST). This phenomenon is principally attributed to the opening of arterio-venous anastomoses but the exact mechanism is still subject to debate.

The changes observed in skin temperature immediately after ICE in both index and little fingers is consistent with changes reported by Traynor et al., and Smits et al., in the healthy controls and patients with hand fractures. These authors showed that normal active rewarming of the fingers starts approximately 50 to 80 sec after removing the hand from cold water (12 °C) and lasts up to 5 or 10 min. Thus, after an extensive cooling of the extremities, the thermoregulatory system increases the blood flow to the extremity to counteract the decrease in hand temperature and prevent pain and/or frostbite.

This study provided new information about the response patterns in different nerve fibers to cold exposure. No alteration in small C fibre functionality was demonstrated. A small increase in threshold for the larger A-beta fibres was demonstrated in the injured hand. Since this is the first report of this finding, we cannot verify it from other studies on cold water immersion. However, there are previous reports on sensory nerve conduction velocities observed after cryotherapy in healthy subjects using ice packs and cold water
immersion. These studies have demonstrated that peripheral nerve conduction is slowed by cold application. Because nerve conduction studies can measure conduction velocities of large diameter nerve fibres, the increase in A-beta perception thresholds (threshold increase corresponds to hyposensitivity or numbness) observed after cold water immersion in this study are consistent with the decrease in sensory nerve conduction velocities observed by Esperanza et al.,. Previous studies have demonstrated that topical cold treatment decreases the skin temperature in underlying tissues to a depth of 2 to 4 cm, decreasing the conduction velocity of pain nerve signals. This results in a local anesthetic effect called cold-induced neuropraxia. We did not demonstrate evidence of this in our 5 Hz thresholds which target the small unmyelinated pain fibers. The fact that injured and uninjured hands showed no variation in C fibre perception thresholds with the brief cold exposure, suggests that the ICE exposure resulted in minimal thermal, nociceptive or sympathetic physiological responses.

Nerve fibre sensitivity is also presumed to vary according to the diameter and myelination of the nerve. The large diameter, myelinated nerve fibres are thought to be most responsive to cold exposure whereas the small, unmyelinated fibres are thought to be least affected by the cold. The increase in sensory perception thresholds of large diameter, myelinated A-beta fibres in the present study, might help with pain modulation. The pain signals from the injured tissue can be reduced via counter-irritant effect or pain gate mechanism or hypoesthesia after uncomplicated DRF.

The observed trends in skin blood flow and skin temperature from the time of immersion to 10 min post immersion in this study are consistent with some of the previous physiological responses to local cold application. Hence, we summarize the possible physiological mechanisms that might have led to the observed findings as per the previous reports (Figure 2.9):
Shortly upon exposure to cold water, a sympathetically mediated vasoconstriction resulted in reduced blood flow to the peripheries in favor of a central pooling of blood in the torso and deep body core.\textsuperscript{18,19} According to the laws of thermodynamics, heat transfer is always unidirectional from high heat to low heat, so there was a transfer of thermal energy from the higher-energy tissues to the lower-energy cold water.\textsuperscript{37} Due to the vasoconstriction of the peripheral microvasculature and the high surface area-to-volume ratio, the skin temperature of the fingers tends to rapidly decrease to a level approaching that of the ambient environment.\textsuperscript{22}
After 5 min the hand was removed from cold water and a seemingly paradoxical and temporary increase in blood flow over the digits and palmar regions \(^{20,100}\) was observed (Figures 2, 3), while the index and little fingers were at a lower temperature. \(^{39}\) Then the temperature in the fingers started to rise, and the skin blood flow started to revert to its pre-immersion values. This observed pattern as mentioned earlier is called ‘hunting response’ \(^{7}\) or the cold induced vasodilation (CIVD phenomenon). \(^{17,18}\)

The current study objectively examined thermoregulatory, sensory and vascular function after DRF by evaluating cutaneous blood flow, skin temperature, A-beta and C fibre responses before and after the delivery of a cold provocation test (ICE) to the hands. Normal thermo-physiological responses such as CIVD reaction, \(^{7,17}\) and digital rewarming patterns, \(^{7,17,23}\) after ICE were noted in both the injured and uninjured hands after the cast removal in patients with uncomplicated DRF. We can therefore presume that a normal thermo-physiological response to cold stimuli in the injured and uninjured hands has some clinical implications. The similar responses observed between the normal and DRF hands on all outcome measures indicate that there is a possibility of some therapeutic benefit after brief exposure to cold water immersion. Cryotherapy in the form of ice packs or immersion has been shown to effectively reduce pain and swelling during the inflammatory response after injury. \(^{29,30}\) Previous findings have shown that, an optimal reduction of tissue temperature between 10\(^\circ\) to 15\(^\circ\)C may be necessary to maximize the therapeutic effects of cryotherapy. \(^{29,74}\)

Cryotherapy induces effects both locally (at the site of application) and at the level of the spinal cord via neurologic and vascular mechanisms.

Cryotherapy is believed to help control pain by inducing local anesthesia around the treatment area. \(^{24,31}\) Investigators have also shown that it decreases edema, \(^{32}\) cellular metabolism, \(^{34}\) and local blood flow. \(^{15,30}\)
Cheing et al.,\textsuperscript{10} demonstrated the beneficial effects of ice pack at 3 and 5 days for pain, swelling and range of motion in DRF patients after cast removal. Whereas, Stockle et al.,\textsuperscript{25} showed that continuous cold-water treatment is preferable to cool packs for reducing posttraumatic edema in injured tissues. Cold water immersion is thought to cause the least skin temperature reduction, possibly due to the fact that a greater area receives the treatment, leading to a faster activation of the thermoregulatory responses that protect the body from abrupt temperature changes\textsuperscript{26} and consequently, the skin temperature is quickly stabilized and does not adequately reflect the effects of cooling on subcutaneous tissues.\textsuperscript{8, 27} The temperature reductions of approximately 10 °C in both hands along with the changes in superficial blood flow, sensory perception thresholds in A-beta fibres and the possible mechanisms behind these changes led us to a conclusion that cold water immersion for 5 min has a potential to reduce pain via analgesic effects; and can act as a counter-irritant via pain gate mechanism through the activation of large diameter A-beta fibres. Cold water immersion might also help to reduce swelling (if any) in the DRF patients after cast removal, if applied regularly for few days as demonstrated by Cheing et al..\textsuperscript{10} The increase in A-beta perception thresholds only on the affected side after immersion could be attributed to the ongoing healing process and presence of associated pain signals in the injured tissues which were possibly absent in the normal tissue. When cold is used to reduce edema, then the position of the extremity must be considered. Some have used contrast baths, alternating immersion in cold and hot water. A systematic review and effectiveness of contrast baths was inconclusive.\textsuperscript{102} It might be useful to examine different approaches to cold application using the approach conducted in this study to determine potential differences in physiological effects across methods of administering thermal agents.
A normal thermophysiological response does not prevent the presence of subjective symptoms of post traumatic cold intolerance. Even with normal CIVD reaction on digital thermography, in both injured and uninjured digits, patients with median and ulnar nerve injuries have still reported cold intolerance according to the CISS questionnaire. In contrast, previous findings on digital thermography have shown normal digital rewarming or CIVD reaction after local cold exposure in the injured hands with subjective symptoms of cold intolerance. There are also studies that demonstrated a lack of correlation between the subjective symptoms of cold intolerance (CISS) and the objective evaluation of skin temperature in patients with hand fractures, and healthy controls. Since previous reports have questioned the relationship between skin thermography and symptoms of cold intolerance in people with or without hand pathology, the importance of assessing vascular function through physiological measures, clinical tests (like ICE) and self-report measures of cold intolerance requires further examination.

**Limitations and research recommendations**

There are a number of limitations in the current study that may have affected the study findings and generalizability. Only one therapist provided the treatment and assessments, which meant that the evaluator was not blinded. However, no three measures were under control of the therapist. The sensory threshold was determined by patient and TiVi and temperature were not controlled by either the patient or the therapist so minimal bias was expected with respect to outcome evaluation. For the sensory evaluation, we used the rapid CPT assessment which has fewer repetitions than the full CPT protocol based on a repeated force choice protocol. While this may have made our sensory measurements less precise, it was deemed appropriate given we were looking for transient changes and use of time consuming protocols leads to missed short term responses.
Simultaneous measurements of skin blood flow, skin temperature and sensation was not possible and this is considered a minimal limitation since very transient effects are unlikely to have therapeutic value. The TiVi testing (for 1 min) and sensory testing (for 8 min) took approximately 10 min to complete, hence we could not capture changes at 5 min after immersion and jumped directly to 10 min from 0 min. Thus, the responses at regular intervals up to 10 min were not reported. We did not use any patient rated scale to note numeric pain ratings during or after the experiment, hence we had no indicator of its beneficial effect on patients who felt good during cold water immersion on the injured side. Although our repeated measures design was statistically efficient, sampling a greater number of people may have contributed to greater diversity and results. Future studies may wish to specifically target patients with cold intolerance to determine to what extent they behave differently than the uncomplicated cases used in this study.

The sensory perception thresholds were recorded from the tip of ring fingers (dermatome supplied by C7 and C8), instead of the treatment area in order to follow the recommended guidelines of the manufacturer, and to avoid any unwanted motor point stimulation (muscle contraction) and thus may not reflect sensory changes in the whole area of immersion. Ruch et al., demonstrated that blood flow to a specific digit, digital pain, and/or cold sensitivity is altered within the nerve's sensory innervation territory after an isolated peripheral nerve lesion. Furthermore, since the ring finger is innervated by both the median and ulnar nerves, differential effects in these nerves were not directly explored in this study. Therefore, future research on ICE should focus on single peripheral nerve and observe the effects on cutaneous perfusion and thermoregulatory function in single nerve territory instead of two nerves simultaneously.
Cold induced vasodilation (CIVD) is thought to vary according to age, gender, ethnicity, acclimatization to cold weather and body heat etc. \(^{18,19}\) Hence future research can include people based on these factors and assess their responses to have an individualized assessment and treatment approach. Even though no correlation was found between the subjective symptoms of cold intolerance and digital rewarming patterns after the ICE protocol, \(^{61,62}\) inclusion of both biological and self reported cold intolerance measures would have given a complete understanding of both subjective and objective responses in these patients. Hence, this should be investigated in future trials.

The normal thermo-physiological responses observed after ICE are thought to induce some therapeutic effects in patients with uncomplicated DRF. Knowledge about the short term and long term physiologic effects informs our understanding of the safety and therapeutic benefit of cold water immersion protocol. Future study is needed to explore the effects in patients with hand injuries and observe responses on outcomes of pain, swelling, range of motion and number of days to return to work.

### 2.6 CONCLUSION

This study concluded that brief cold (ICE) exposure resulted in a higher blood flow and lowered skin temperature to the digital extremities for around 10 min in the injured and uninjured hands of people recovering from DRF. Concurrently, no changes were found in sensory perception threshold of the pain carrying fibers (5 Hz) or large diameter touch fibers (2000 Hz) of uninjured hands. A small increase in sensory threshold of the large diameter fibers was measurable on the injured hand. The findings were consistent with physiological underpinnings of cold exposure if used as therapeutic agent or test exposure. Though the evidence for best interventions after DRF is weak and limited and more randomized trials are needed to facilitate best treatment
decision, we think that the responses observed in this study enhance the value of cold modality during the rehabilitation of uncomplicated DRF.

2.7 REFERENCES


### Tables and Figures:

#### Table 2.1: Demographic characteristics of participants

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in yrs. (mean± SD)</td>
<td>52± 12.2</td>
</tr>
<tr>
<td><strong>Gender:</strong></td>
<td></td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>18 (90%)</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td><strong>Side of injury:</strong></td>
<td></td>
</tr>
<tr>
<td>Right, n (%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Left, n (%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td><strong>Type of Injury:</strong></td>
<td></td>
</tr>
<tr>
<td>Fall n (%)</td>
<td>18 (90%)</td>
</tr>
<tr>
<td>Others (%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td><strong>Reduction</strong></td>
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<tr>
<td>CR n (%)</td>
<td>100%</td>
</tr>
<tr>
<td>ORIF (%)</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table legends: SD= Standard deviation; n = number of participants; CR=closed reduction; ORIF= surgery
Table 2.2: Summary of results showing superficial blood flow responses in both hands

<table>
<thead>
<tr>
<th>Hand</th>
<th>Normal</th>
<th>DRF</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Pretest</td>
<td>Post 0 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD: 7.5</td>
<td>SD: 26</td>
</tr>
<tr>
<td>CI:</td>
<td>(79-86)</td>
<td>(94-118)</td>
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</tbody>
</table>

DRF – distal radius fracture; Post0 – immediately after cold water immersion; Post1 min - after 1 min; Post 10min-after 10 min
M=mean; CI= 95% confidence interval; SD= standard deviation
Table 2.3: Summary of results showing skin temperature responses in both hands

<table>
<thead>
<tr>
<th>Hand</th>
<th>Normal</th>
<th>DRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pretest</td>
<td>Post 0 min</td>
</tr>
<tr>
<td>Temp. Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M:</td>
<td>31.9</td>
<td>22.2</td>
</tr>
<tr>
<td>SD:</td>
<td>3</td>
<td>5.9</td>
</tr>
<tr>
<td>CI:</td>
<td>(30.4-33.3)</td>
<td>(19.4-25)</td>
</tr>
<tr>
<td>Temp. Little</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M:</td>
<td>32.5</td>
<td>22.2</td>
</tr>
<tr>
<td>SD:</td>
<td>2.9</td>
<td>5.1</td>
</tr>
<tr>
<td>CI:</td>
<td>(31-33.9)</td>
<td>(19.7-24)</td>
</tr>
</tbody>
</table>

DRF – distal radius fracture; Post0 – immediately after cold water immersion; Post 10min – after 10 min; Temp: Temperature; M = mean; CI = 95% confidence interval; SD = standard deviation
Table 2.4 Summary of results showing sensory perception responses in both hands

<table>
<thead>
<tr>
<th>Hand</th>
<th>Normal</th>
<th>DRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pretest</td>
<td>Post 1 min</td>
</tr>
<tr>
<td></td>
<td>SD: 2.1</td>
<td>SD: 1.8</td>
</tr>
<tr>
<td></td>
<td>CI: (7.4-9.4)</td>
<td>CI: (8.2-9.9)</td>
</tr>
<tr>
<td></td>
<td>SD: 3.5</td>
<td>SD: 3.1</td>
</tr>
<tr>
<td></td>
<td>CI: (11-14)</td>
<td>CI: (9.6-13)</td>
</tr>
</tbody>
</table>

DRF –distal radius fracture; Post 1 min - after cold water immersion; Post 10 min - after 10 min; M=mean; CI= 95% confidence interval; SD= standard deviation; RCPT = ranged current perception threshold test
Figure 2.1: Flow chart for study design (Randomized, repeated measures, pretest post-test design)
Figure 2.2: Responses in DRF hand shown on TiVi: 1) pretest; 2) post 0 min; 3) post 1 min; 4) post 10 min of cold water immersion.

*Basal blood flow appears blue and as the blood flow increases color changes to green, yellow and red as shown in the scale
Figure 2.3: Responses in normal hand shown on TiVi: 1) pretest; 2) post 0 min; 3) post 1 min; 4) post 10 min of cold water immersion.

*Basal blood flow appears blue and as the blood flow increases color changes to green, yellow and red as shown in the scale.
Figure 2.4: Superficial blood flow responses (mean values) across time

Figure 2.5: Skin temperature responses (mean values) in index finger across time
Figure 2.6: Skin temperature responses (mean values) in little finger across time

Figure 2.7: Sensory perception threshold responses at 5Hz (mean values, C fibre)
Figure 2.8: Sensory perception threshold responses at 2000Hz (mean values, A-beta fibres) across time
CHAPTER 3

“Short term sensory and vascular responses to therapeutic ultrasound in the hands of healthy volunteers.”

Shaguftha Sultana Shaik, Joy C. MacDermid, Ruby Grewal
3.1 ABSTRACT

Study design: Randomized Cross-over, repeated measures, pretest post-test design.

Introduction: Ultrasound (US) is used for a variety of clinical pathologies. The evidence on the effects of ultrasound on vascular and sensory functions in humans is incomplete.

Purpose: To determine the short term impact of two doses of therapeutic Ultrasound (1 MHz continuous and 3 MHz pulsed) on sensory and vascular functions in the hands of healthy volunteers.

Methods: Twenty healthy volunteers were recruited (10 men and 10 women; aged 18 to 50 yrs. (Mean age: 29.6±8.8 yrs.) for the study. Superficial blood flow in the distal forearms was determined using the Tissue viability imaging system. Sensory perception thresholds for ulnar and median nerves (at 2000 Hz and 5Hz) were determined from tip of ring finger (C7, C8) to assess A-beta and C fibre function. The cross over trial included the following: a control condition, 1 MHz continuous and 3 MHz pulsed US. Subject’s forearms were randomised to continuous US group (control followed by US) and pulsed US group (US followed by control). Scores were obtained before and immediately after the application of US and control. Differences in these were analyzed using general linear models (GLM).
Results: Both 3 MHz pulsed US and 1 MHz continuous US showed small to moderate (ES r = 0.12 to 0.68), statistically significant reductions in skin blood flow (3 MHz, Mean change = 2.8 A.U. and 1 MHz, Mean change = 3.9 A.U., p<0.05 respectively); skin temperature (2.5 °C and 1.1 °C, p<0.05 respectively); and sensory perception thresholds at 5 Hz (1.3 m. A. and 1 m. A., p<0.05 respectively) across time. There was a significant decrease in these measures overtime without the treatment as well, but the changes were very small (ES r = -0.04 to 0.3) compared to US therapy. Sensory perception thresholds at 2000Hz remained unaltered by all three conditions (p>0.05). Age and gender also had no effect on all the outcome measures (p>0.05).

Conclusion: The responses observed in this study suggest that small to moderate changes in skin blood flow, skin temperature and sensory nerve perceptions should be expected with brief exposure to US therapy. While our study does not provide an indication about a therapeutic dosage, it does suggest that 3 to 5 min applications may not be producing substantial superficial therapeutic effects. This would suggest that future studies looking at physiological effects of ultrasound on blood flow, temperature and sensory function should move towards investigating larger dosages and study the effects in patient populations.

Key words: sensory perception, skin blood flow, ultrasound, forearm
3.2 INTRODUCTION

Therapeutic ultrasound (US) is a physical agent modality that has been used in hand clinics for the management of various musculoskeletal injuries for over 50 yrs. 1, 2, 3, 38, 43, 44 Physiological and therapeutic properties of US are attributed to various non-thermal and thermal responses. 4, 9, 38, 39, 44 The tissue response to non-thermal ultrasound includes acceleration of tissue healing through cavitation and its associated effects, 3, 9, 10, 17, 44 while the responses to thermal ultrasound include, increases in tissue temperature at superficial and deep levels such as tendons, ligaments, joint capsules, and fascia without overheating underlying fat. 3, 4, 5, 6, 10, 17 Both continuous and pulsed ultrasound are thought to show non-thermal effects and accelerate tissue repair, 1, 2, 3, 7, 8, 17, 44; while continuous ultrasound is thought to add additional therapeutic effects due to heating. 6, 22, 17, 44

Although US has been used for decades, the lack of definitive studies defining its benefit in different musculoskeletal conditions 9, 10, 38, 39, 40, 41 has questioned the traditional view of its therapeutic benefits. 10 Multiple systematic reviews and meta-analyses of US has failed to provide definitive conclusions about the effectiveness (or lack of effectiveness) of US because of insufficient evidence. 9, 10, 11, 38, 39, 40, 41, 44 Several reviews also report disagreement and confusion about the most efficacious treatment parameters for US. 9, 10, 15, 38, 39, 40, 41, 44 Despite this lack of strong evidence, previous reports on US usage in the form of questionnaires and surveys have shown that US is being used frequently in the clinical practice for musculoskeletal conditions. 12, 21, 39, 42, 58, 59 It was found that over 70 to 95% experienced and advanced-practice clinicians continue to use US regularly for specific impairments encountered in orthopedic and sports settings, indicating that US is perceived as an important component in the management of selected impairments. 12, 21, 39, 42, 58, 59 Although dosage is
based on the theoretical rationale, there are insufficient dosage trials to define the optimal dosage of ultrasound across different conditions. 11, 12, 38, 39, 44

Ultrasound is thought to affect tissue thermodynamics and as such might result in changes in the peripheral circulatory system. A therapeutic modality capable of altering peripheral circulation could affect the health of human tissue, and facilitate tissue healing. 9,15 The forearm skin (non-glabrous) is innervated by sensory nerves and sympathetic vasoconstrictor and vasodilator nerves, which respond to thermal, chemical, and mechanical stimuli to provide feedback to the central nervous system and influence cutaneous arteriolar tone (vasoconstriction or vasodilation) via the release of neuropeptides and other vasoactive agents. 23, 30, 31 After injury, symptoms of pain can occur because of vascular insufficiency which affects metabolic function in the injured soft tissue or edema and muscular strain etc. 46 Alterations in pain can also be related to neural transmission in sensory and pain fibers. 46 Better understanding of the biological effects of ultrasound should include monitoring all these pathways (vascular and neural).

There is currently a scarcity of published clinical trials that have looked at the neural and vascular responses to ultrasound therapy. Noble et al., used laser Doppler flowmetry (LDF) to assess cutaneous blood flow and concomitant measures of ambient and skin temperatures after applying 3 MHz pulsed (1:2) and 3 MHz continuous US at an intensity of 1 W/cm² for 6 min over the mid-forearm. 13 The authors noted that, after sonation there was an increase in skin blood perfusion with pulsed US and continuous application of US without any significant difference in skin temperature between the US groups. However, these authors measured skin blood flow distal to the US application from single vessel (single point LDF) instead of the tissues directly affected by the treatment. Further, they did not include sensory monitoring to establish changes in nerve function with ultrasound application. 13
The effects of US are thought to vary with the type of tissue, site and the dosage used. There is a scarcity of information regarding the effects of ultrasound on hemodynamics resulting from altered treatment times, intensities, and frequencies in human subjects. These evaluations might inform our understanding for potential mechanisms of therapeutic effect that operate through beneficial effect on skin blood flow and sensory function. Hence, the purpose of this study was to determine the effects of two different doses of US (1MHz continuous and 3MHz pulsed) on superficial blood flow, skin temperature, and sensory perception thresholds in the distal forearms of healthy volunteers. A secondary purpose was to determine if the responses were affected by age and gender.

3.3 METHODS

Participants:

The sample size required for this research was based on the number needed to detect a moderate effect size according to Cohen. A moderate effect (ES r=0.50) using two-tailed alpha (α= 0.05) at 80% power, requires a sample of 28 participants in each group for a between subject design and a sample of 14 participants for a within subject design. As this is a within subject design and variance within individuals is less than between subjects, a sample size of 20 was considered and approved by the Ethics Board. Statistical significance was considered if p<0.05.

Subjects were recruited by poster advertisement and word of mouth in the university campus. Testing was done in Hand and Upper Limb Research Lab, at St Joseph’s Health Care, London, Ontario, Canada. Healthy subjects aged 18 to 50 yrs. with no recent injury or disease at neck, shoulder, elbow, wrist, or hand, within the past year were included in the study. Subjects were divided into two age categories: 18–34 and 35–50 yrs. There were 10 males
and 10 females in total. Please refer to Table 3.1 for subject demographics. All subjects were informed to refrain from exercise and drinking beverages 4 hours prior to testing. Subjects were excluded if they had ecchymosis, skin infection, open wound, swelling, neurovascular injuries, deficits in sensation in the area to be treated (sensory test to identify sharp and dull sensation; hot or cold), decreased circulation (digital patency test for fingers), pregnancy, presence of a pacemaker/monitoring device, malignancy, hypertension and cardiac failure. This study was approved by the Western University Research Ethics Board. All participants read the letter of information, had his/her questions answered, and signed a consent form prior to participation in this study.

**Equipment:**

**Ultrasound machine:**

A ‘Phyaction U’ ultrasound machine (GymnaUniplay N V, Pasweg 6A, and BILZEN) with the capabilities for 1 MHz and 3 MHz frequency operation was used to deliver the ultrasound treatments. The transducer, model U92, had an effective radiating area of 4.0 cm² and a beam nonconformity ratio (BNR) of <4.0, and was calibrated before research was initiated. An aqueous Eco Gel (Eco-med Pharmaceuticals, Ontario, Canada) was used as the coupling medium for all treatments.

We could not find any clear standard guidelines for US dosage in the literature hence, we adopted the framework proposed by Tim Watson. Based on the previous evidence on the effectiveness of ultrasound, he put forth a framework for the treatment parameter selection. The basic principle is that the more acute and irritable the tissue in question, the lower the required dose to achieve a stimulating effect. The frequency selection (1 or 3 MHz) will influence the effective treatment depth (3MHz is more superficial
i.e. a depth of approximately 2 cm, 1MHz is effective to a depth of 4 or 5 cm). The pulse ratio needs to be higher for the more acute lesions (1:4) and lower for the more chronic (1: 1 or continuous). Intensities vary from 0.1 to 0.3 W/cm² for the acute lesions to 0.4 to 0.7 or 0.8 W/cm² for the chronic lesions.

Table 3.2: US dosage chart

<table>
<thead>
<tr>
<th>Freq.</th>
<th>Intensity</th>
<th>Duty cycle</th>
<th>Duration</th>
<th>US DOP</th>
<th>TiVi DOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1MHz</td>
<td>0.80 W/cm²</td>
<td>100% (Continuous)</td>
<td>3 min</td>
<td>4-5cm</td>
<td>0.4mm-0.5mm</td>
</tr>
<tr>
<td>3MHz</td>
<td>0.25 W/cm²</td>
<td>20% (1:4)</td>
<td>5 min</td>
<td>2-2.5cm</td>
<td>0.4mm-0.5mm</td>
</tr>
</tbody>
</table>

Table legends: Freq. =frequency; DOP=depth of penetration; TiVi= tissue viability imager

Treatment times are based on the principle of one minute of ultrasound per treatment head area. **Hence, we derived two experimental dosages from the above framework which may be applicable to an acute condition (3MHz) and a chronic condition (1MHz) at the distal forearm (Table. 2).**

Pilot testing on healthy subjects (n=6 i.e., 12 hands) also revealed that the current dosage used for continuous US was tolerable for 3 min and further increase in treatment time caused mild heating and discomfort on the forearm skin. It has been suggested that when bone is superficial, as in the hand and wrist, ultrasound at 1 MHz causes tendons adjacent to bone to heat more quickly than skin. It appears that tendon-heating to skin-heating in an ultrasound field could be in the ratio of 2:1. **Hence, subjective skin warmth is considered a good indicator to know that dense tissue adjacent to bone has become heated.** It must also be noted that recent research on the use of continuous ultrasound by Merrick et al., demonstrated that the extent
and rate of heating can vary between different brands of ultrasound devices. Frye et al., also reports about blister formation within 24 hrs. in three healthy women, on the anterior aspect of tibial shin when sonated with continuous US (1 MHz) at an intensity of 1.5 W/cm², on the calf for 10 min. Hence, a 3 min time period was chosen for continuous US in this study to avoid any discomfort.

**TiVi (Tissue Viability Imager) 600 polarization spectroscopy camera (version 7.4 Wheels Bridge AB, Linköping, Sweden):**

The TiVi is a small and portable device for high-resolution instantaneous imaging of red blood cell (RBC) concentration in upper human dermal tissue. TiVi software was used to quantify RBC concentration on the anterior aspect of the distal forearm on both arms using a digital camera (Canon Rebel EOS model 450D, Japan) with a polarization lens. The camera was supported by a multi-jointed metal arm provided by Wheels Bridge and the arm was secured to a desk. The camera was adjusted to point downwards and parallel to the surface of the desk. A royal blue colored cushion was used to rest the forearm and to fill the camera view. An outline was drawn to standardize hand positioning. The participants were positioned with their shoulder in neutral, elbow in 90° flexion, wrist in neutral position and the forearm fully supinated and placed approx. at the level of heart. Each image was captured with the polarized lens set at the ‘cross polarization’ setting and the camera was positioned at a distance between 300mm from the participant’s hand. Image quality was set to ‘medium normal’. One photo was taken every 5 sec and uploaded into the attached laptop computer. The camera has a light penetration depth between 400 to 500 micrometers, and this light contains information about the main chromophores in the epidermis (melanin) and dermis (hemoglobin), while the surface reflections contain information about the surface topography, such as texture and wrinkles. Once the images were captured, the TiVi images were processed using the TiVi software.
For each participant, one image at baseline and immediately after US therapy and control (no US) were used for processing and analysis. There were a total of 8 images per participant (4 in each arm). Regions of Interest (ROI) were selected over the treatment area (2x Effective Radiating Area or ERA) at the distal forearms. The magnitude of RBC concentration over the selected ROI’s was obtained using ‘image analysis.’ Values for the TiVi are measured by Arbitrary Units (A.U.) as defined by the manufacturer. Data was first exported from the TiVi software into Microsoft Excel 2010 spreadsheets and then imported into SPSS version 20.0 for statistical analysis. The technique has shown many uses in drug development, burn investigations, pressure studies, and general research maneuvers due to the ease of use, portability, and low cost. The TiVi has been validated for construct validity to measure superficial RBC concentrations with in vitro fluid models and computer simulations. TiVi software is able to accurately calculate the oxygen saturation level of 91.5% in vivo, which is within the physiological range of oxygen saturation within blood. It has been shown to be sensitive to change during blood occlusion testing, and drug testing on skin, and has also demonstrated good inter-laboratory reliability.

**Neurometer® CPT/C device (Neurotron Inc., Baltimore, USA):**

The Neurometer evaluates sensory nerve conduction from the periphery to the brain and has been shown to detect differences in neural function in asymptomatric subjects when neural stress was administered. This portable battery operated nerve stimulator has the ability to emit three different frequencies in sinusoidal waveforms to selectively target different subpopulations of nerve fibers dependent upon nerve fiber diameter. A frequency of 2000 Hz is used to stimulate the large myelinated A-beta fibers (Aβ fibers) which detect cutaneous touch and pressure; a 250-Hz stimulus will stimulate myelinated A-delta nerve fibers (Aδ fibers) which are mechanoreceptive, and detect fast pain, pressure and temperature, while a
frequency of 5 Hz is used to stimulate the small unmyelinated C-polymodal nociceptive fibers which detect slow pain and temperature and are post ganglionic sympathetic fibres. This device has been used in numerous studies to detect, screen and diagnose the abnormalities of peripheral nervous system and normal ranges for all nerve fibre types (A-beta, A-delta and C fibres) have been established to assess normal sensation, increase in sensation (hyperesthesia), decrease in sensation (hypoesthesia) and no sensation at all (anesthesia). The Neurometer has been shown to be both specific (73%) and sensitive (74%) in the clinical examination of carpal tunnel syndrome and is considered a reliable and valid measure of quantitative sensory function.

Ranged CPT (R-CPT) is a sensory perception threshold test which can be completed in 3 to 6 min for each test site. It is typically used to confirm or rule out sensory involvement in large samples such as in screening and monitoring therapeutic outcomes. In R-CPT, each frequency is repeated several times to ensure accuracy and reproducibility. The average time needed to complete the tests is reported to be less than 10 min. The Neurometer reports values as the normal range (R-CPT Level, 6–13), hyperesthesia (R-CPT Level, 1–5), and hypoesthesia (R-CPT Level, 14–25). Sensory nerve perception thresholds at two frequencies, 2000Hz and 5Hz, to test two different nerve fibres were used in this study. To begin 2000 Hz stimulation, the skin was cleaned with a skin paste and then the 1 cm gold electrodes coated with small amount of gel were attached to the ring finger (area innervated by C7, C8) with an adhesive tape. Then, the participants were asked to press and hold the red “Test cycle” button on the remote control box and release it as soon as they begin to feel the tingling or buzzing sensation. The machine records the response when the button is released and the same process is repeated 7-10 times until a score is displayed. In total three scores are obtained at 2000Hz. The same procedure
is repeated at 5Hz. These test cycles end automatically after few repetitions (7-10 times) and the machine displays score for 5Hz.

**Experimental Procedure**

**Randomization:**

We used a randomized cross over, repeated measures design in this study. Random allocation to treatment order and hand was achieved through subject’s selection of assignment contained in an opaque envelope. After explaining the protocol and obtaining consent, each participant was asked to pick up two different colored sealed envelopes from two bundles, which had information on the side of hand and sequence of therapy to be initiated. Once the hand side was picked, the participant was then randomized to either pulsed US group or continuous US group based on the labeling on cards inside these envelopes. There were 3 conditions for testing; a control condition (or rest), pulsed ultrasound and continuous ultrasound. If the card showed pulsed US group, then the order of therapy was pulsed US followed by rest in the hand first selected. After this the opposite hand received therapy in reverse order (continuous US group), beginning with rest and then followed by the continuous US. A 25 min gap was established between each treatment condition (control/ rest, pulsed and continuous US) to provide a washout period and to minimize any potential carry over effects of US. Therapy instructions and outcome assessments were all provided by a single physiotherapist. The two group sequences were completed on the two hands one after the other on same day. The flow chart outlining the study design is in Figure 3.1.

**Ultrasound protocol:**

After acclimatization to room temperature for 10 min, participants were first measured using the TiVi over the treatment area in distal forearms. This
was followed by skin temperature measurement using King’s infrared digital thermometer. Then a Range –CPT test was recorded from the tips of ring finger (over C7/C8 dermatome level) to assess sensory perception thresholds at 2000Hz (for A-beta fibres) and 5Hz (for C fibres). These three measurements (TiVi, temperature, R-CPT) were done before (pretest or baseline) and immediately (post-test) after each control condition/ rest and ultrasound application in similar order. After completing baseline assessments, based on the group order selection, participants either underwent therapy with continuous US or pulsed US or were informed to rest for 3 to 5 min without any treatment, during the control conditions. The next therapy was initiated after 25 min during which the skin temperature returned to its pre-treatment level. To ensure that the ultrasound was directed at the target tissue, a template equivalent to twice the area of ultrasound applicator (2 X ERA) was placed on the anterior aspect of distal forearm (distal border coinciding with ulnar styloid process). Pulsed US was delivered at 3 MHz pulsed mode, with 1:4 duty cycle, at an intensity of 0.25 W/cm² for 5 min. Whereas, continuous US was delivered at 1 MHz, continuous mode, with an intensity of 0.8 W/cm² for 3 min. Dosage details are shown in Table 3.2 (adapted from T. Watson). The ultrasound applicator was moved back and forth (circular motion) in the template at a rate of 3 to 4 cm/sec continuously and was timed with a metronome. Instructions were given to the participants to inform if the therapy was uncomfortable, in order to stop the machine and note the time of discomfort free therapy. After US therapy the treatment area was cleaned with a towel and then TiVi, skin temperature and R-CPT responses were measured immediately after (post-test). The same process was repeated after control/ rest.

TiVi software was used to calculate the mean blood flow (A.U.) in the treatment area and then the data was transferred to an Excel sheet (Microsoft
The sensory perception thresholds obtained at 2000Hz and 5Hz (m. A.) were recorded directly from the digital display of the Neurometer CPT/C device along with temperature (°C) readings onto a separate data collection sheet. Subjects were instructed to keep the area clean and covered and to self-monitor for any signs of local skin irritation after they leave.

**Data analysis:**

Data was entered in SPSS and random checks of 10% of the data against the hard copies of data sheets was used to ensure data quality (100% were correct so no further data audits were performed). Descriptive statistics were run to further investigate data quality and assess data normality. The majority of data was normally distributed as assessed by Kolmogorov-Smirnov Test (p>0.05), hence parametric tests were used for quantitative data analysis. The outcome measures (RBC concentration, temperature and sensory perception thresholds) were assessed for differences using General Linear Models (GLM, using SPSS version 20, IBM Inc.). Models assessed whether there were differences between baseline and immediately after control or ultrasound therapy (1MHz and 3MHz). Interactions were examined for significance between time and treatment group. Post hoc analyses were performed using Bonferroni correction wherever necessary. Pair wise comparisons were used to perform within-group comparisons for treatment and control. The GLM model was run without covariates and then repeated with age and gender as a covariate to test for differential responses. Significance level was set at p<0.05 level unless otherwise noted. All values were expressed as means, standard deviation, and confidence intervals.

**3.4 RESULTS**

Twenty healthy volunteers were recruited between November 2012 to February 2013. No data points were missing. Demographic information of
participants is presented in Table 3.1. The group means, standard deviation (SD), 95% confidence interval (CI), effect size (ES), and change scores (CS) for skin blood flow, skin temperature and sensory perception thresholds at 2000Hz and 5Hz are shown in Table 3.3 and are summarized by outcome measure below.

**Sensory perception threshold at 2000Hz from ring finger:**

No significant difference in sensory perception threshold at 2000 Hz was observed in the ultrasound or control, across the time points. There was no significant interaction between time and treatment. (Table 3.4 and Figure 3.2)

**Sensory perception threshold at 5 Hz from ring finger:**

A significant decrease in perception threshold at 5 Hz was observed from pretest to post-test with US (either 1 MHz or 3MHz) as well as control condition (p<0.05). A significant interaction was also found between time and treatments (p<0.05). Post hoc comparisons revealed that control condition resulted in a statistically significant decrease in threshold (13.4 m. A. to 10.6 m. A.) when compared to pulsed US at 3 MHz (13.4 m. A. to 12.2 m. A.) (p<0.05) in the pulsed US group. The post hoc comparisons between continuous US at 1 MHz (12.4 m. A. to 11.4 m. A.) and control condition (12.0m. A. to 10.8 m. A.), showed no significant difference (p>0.05). However, the change in perception threshold was greater after control (2.8 m. A. in pulsed US group and 1.6 m. A. in continuous US group; p<0.05) than after the pulsed US (1.1 m. A.) or continuous US therapy (1.0 m. A.) (p<0.05). (Table 3.4 and Figure 3.3)

**Skin blood flow over treatment area:**
There was a significant decrease in skin blood flow over the treatment area from baseline to post-test after the ultrasound (1MHz or 3MHz) and control condition (p<0.05). A significant interaction was also found between time and treatments (p<0.05). Post hoc comparisons revealed that pulsed US at 3 MHz resulted in a statistically significant decrease in superficial blood flow (60.3 A.U. to 57.6 A.U.) as compared to control condition (60.3 A.U. to 60.1 A.U.) (p<0.05) in the pulsed US group. Similarly the post hoc comparisons between continuous US at 1 MHz showed a significant decrease in blood flow (60.6 A.U. to 56.9 A.U.) as compared to control (60.6 A.U. to 59.9 A.U.) (p<0.05) in the continuous US group. The change in blood flow was very small after control (1.1 A.U. in pulsed US group and 1 A.U. in continuous US group; p<0.05) than after the pulsed US (2.5 A.U.) or continuous US therapy (3.5 A.U.) (p<0.05). (Table 3.3 and Figures. 3.4, 3.6)

**Skin temperature over the area of treatment:**

A significant decrease in temperature was also observed over the treatment area from pretest to post-test with ultrasound (1 MHz or 3MHz) as well as control condition (p<0.05). A significant interaction was also found between time and treatments (p<0.05). Post hoc comparisons revealed that pulsed US at 3 MHz resulted in a statistically significant decrease in skin temperature (33.0 °C to 30.9 °C) when compared to control condition over the treatment area (33.1 °C to 33.0 °C) (p<0.05). Similarly the post hoc comparisons between continuous US at 1 MHz showed statistically significant decrease in skin temperature (33.1 °C to 32.1 °C) when compared to the control condition (33.4 °C to 33.1 °C) (p<0.05). The change in temperature was very small with control (0.05 °C in pulsed US group and 0.3 °C in continuous US group) than after the pulsed US (2 °C) or continuous US (1.5 °C) (p<0.05). However, participants reported that they felt the skin and the transducer head became slightly warmer during or after continuous
US (1MHz) but did not report this during or after pulsed US therapy (3MHz). (Table 3.3 and Figure 3.5)

**Effect of age and gender:**

Analysis with age and gender as covariates revealed no significant effect of age (across the two categories; 18–34, 35–50 age groups) as well as the gender on the R- CPT scores or superficial palmar blood flow or skin temperature (p>0.05) after US therapy.

### 3.5 DISCUSSION

Ultrasound therapy (pulsed US and continuous US) demonstrated a small to moderate effect on skin blood flow (RBC concentration), skin temperature and sensory perception thresholds at 5 Hz (C fibres) over the treatment area in the distal forearms of healthy volunteers. This study resulted in a significant reduction in skin blood flow, skin temperature and C fibre perception thresholds immediately after the pulsed US, continuous US and rest. Whereas, the sensory perception thresholds at 2000Hz (A beta fibres) remained unaltered by all three conditions (pulsed US, continuous US and rest).

Previous studies have demonstrated that US has the potential to decrease blood flow in rat models, \(^33, 34, 35\) and human calf skin. \(^20\) In the present study, the results demonstrated that application of US (whether pulsed or continuous) significantly decreases skin blood flow immediately after therapy, thus supporting the work by Ware et al. There was a decrease in skin blood flow over time without the treatment (control/rest) as well, but the changes observed were smaller (≤1.0 A.U.) when compared to continuous US (3.5 A.U.) or pulsed US therapy (2.5 A.U.). Our findings are consistent with Ware et al., who reported an average decrease of 12% in dermal blood flow, and elevated skin temperatures averaging 1.4°C with
continuous, 3MHz US, using different measurement and treatment procedures. They used laser Doppler flowmetry measured from calf muscles, and a higher US dosage was implemented including an intensity of 1.5 W/cm² and a duration of 10 min. Thus the total energy delivered was quite different than what was used in this current investigation. In contrast, our study found decreased skin temperature along with decreased skin blood flow immediately after the US application (both pulsed and continuous US) (Figure 3.5). The current findings on temperature in our study are similar to the previous reports which have revealed that skin temperature decreases with US intervention. Bickford et al., and Paul et al., attributed their findings to the use of a water-cooled applicator for the data collection, while Kramer et al., attributed the temperature changes to US transmission gel. It is known that, when in contact with cold materials the skin tends to freeze at higher temperatures than when exposed only to cold air, due to a reduction in the amount of supercooling. This may further be explained by the thermal responses to local cooling of skin (mild), which stimulates the cold-sensitive afferents to activate sympathetic nerves to release norepinephrine, leading to a local cutaneous vasoconstriction. Thus, the underlying mechanism of the demonstrated changes in superficial blood flow and skin temperature in this study might have been due to the US transmission gel and the metal plate of the US transducer head.

The current study demonstrated that there was no change in A-beta perception threshold in the ring finger after the application of pulsed US, continuous US or after control/ rest (Figure 3.2). We could not find any study that has looked at the sensory perception thresholds before and after US therapy in the distal forearms of healthy volunteers. However, there are some previous reports on median and radial nerve sensory nerve conduction velocities (sNCV) observed after US in healthy subjects using
variable intensities for different durations. 64, 65, 66, 67 Because conventional nerve conduction studies can measure the conduction velocities of large diameter nerve fibres, 60 the responses most similar in our study would be the 2000 Hz R-CPT scores. Andrew et al., 64 found no significant differences in the median nerve sNCV when comparing the experimental groups (at 3 intensities; 0.5, 1.0, and 1.5 W/cm²), and control group (no US) with the placebo group (0.0 W/cm²) after 10 min of US therapy. 64 Therefore, it could be assumed that the application of ultrasonic waves, either pulsed or continuous, has no effect on the touch and pressure sensations in the area supplied by median and ulnar nerves.

The present study also demonstrated that there was a decrease in C fibre perception threshold in the ring finger after the application of pulsed US, continuous US or after control/ rest (Figure 3.3). We could not find any study which looked at the sensory perception thresholds after US therapy. But we can relate these findings to the previous reports which have demonstrated that, peripheral nerve conduction responses after US vary according to the subtype of nerve fibres. Several investigators have shown that “B” peripheral nerve fibres are most sensitive to US, followed by “C” fibres, while “A” nerve fibres were the least sensitive to US therapy. 48,56,57 Decrease in sensory perception threshold corresponds to hypersensitivity or increased sensitivity, hence we can presume that changes observed in this study might have been due the increased responsiveness of C fibres to US therapy. These changes in C fibre perception threshold may be thought to help with pain modulation. 45 C fibers transmit polymodal nociceptive, slow pain, temperature sensations and carry post ganglionic sympathetic signals; hence, the decrease in sensory perception thresholds associated with pulsed US and continuous US might have been influenced by changes in skin temperature through a thermal-cooling effect of the US transmission gel or by the ultrasound itself. The temperature of the forearm
skin was comparatively higher than the treatment area (2xERA) where gel was applied, hence we can presume that this temperature difference caused a mild cooling effect on skin and lead to the stimulation of sympathetic vasoconstriction and thus reduced blood flow and temperature as mentioned earlier. These immediate vasoconstrictor responses after mild local cooling of skin requires both intact sensory and sympathetic functions and are thought to manifest through a complex combination of sensory, autonomic, and direct effects. This can further be explained by several underlying mechanisms, involving effects on receptor translocation, transmitter secretion and vascular smooth muscle contractile function. 23

Differing construct parameters, methods of blood flow measurement, skin temperature measurement, and treatment protocols do not allow direct comparisons to be made between the research studies that have been published to date (Table. 3.4). Another issue to be considered in our dosage was that we were sonating normal tissue, and the physiological effects might be more dramatic if we were dealing with injured tissue. We elected to study the physiological effects in normal tissue because of a lack of research in this area and it is important to start with a simpler construct. Further ethics boards are often unwilling to allow research on human subjects with injuries or disease until the testing has been applied to normal individuals. However, the US dosage used in this study was close to the preferred practice patterns of therapists around the world. Recent survey reports from experienced and advanced-practice clinicians shows that US usage is continuing regularly for specific impairments encountered in the orthopedic and sports settings, indicating its important role in the management of selected impairments. Over the past 10 yrs., researchers from Australia, 12 Canada, 42 Netherlands, 58 USA, 39 and Brazil, 59 have examined the usage of US therapy in their countries. Ultrasound was found to be widely available and frequently used modality in primary health care centres, 58 in sports, 12
orthopedics and traumatology. Despite differences in questions, clinicians responses indicated that US usage was more common and consistent among the therapists (70-96%), across countries, across studies. A majority of clinicians have reported its usage either on a regular basis, or at least once per day. Ultrasound is shown to be used in a wide range of clinical scenarios and at a range of dosages across the countries (Table 3.5). The US duration and mode selection in this study were consistent with the clinical practice patterns of the therapists in Australia and Brazil. They opted pulsed mode for acute condition and continuous mode for the chronic, and applied US for a duration ranging between 2 to 10 min for an acute and 2 to 20 min for a chronic condition. The dosage range for US frequency and intensity (based on the depth of tissue injury) were consistent with the preferred practice patterns of the therapists in North-East and mid-Atlantic regions of USA (0.10 W/cm² to 3.30 W/cm² for superficial tissues and 0.40 W/cm² to 4.00 W/cm² for deeper tissues).

It is also possible that the low intensities (0.25 W/Cm² and 0.8 W/Cm²) and short durations (5 min and 3 min) used in the current study might have accounted at least in part for the observed changes in skin blood flow, skin temperatures and C fibre perception thresholds; thus indicating that, US is not ineffective as a treatment modality but can have some minor effects on the superficial tissues. However, some of the previous reports on the effects of US on superficial blood flow and skin temperature response at low intensities (1 W/cm²) and short durations (5 to 6 min) showed conflicting results (Table 3.4). Superficial skin blood flow either increased, decreased or showed no variation after US therapy. Noble et al., demonstrated an increased skin blood flow in the mid-forearm, after 6 min of sonation with 1 W/cm² intensity, using 3 MHz-continuous, and 3 MHz-pulsed US. Similar changes were observed by Robinson et
al., after 5 min of sonation with continuous US, at an intensity of 1.5 W/cm². The studies observing skin temperature responses to US, using low intensities and short durations also reported variable findings. The skin and subcutaneous tissue temperatures in these trials either decreased, increased or showed no variation after US therapy.

Kramer et al., demonstrated a linear relationship between subcutaneous tissue temperature and US intensity. In their study subcutaneous temperature increased linearly with increasing intensity after 5 min of sonation, using a frequency of 0.87 MHz. These authors observed a significant decrease in skin temperature during the first minute of sonation at 0.0 and 0.5 W/cm² demonstrating a rapid cooling effect, and also during the recovery periods at 1.5, 2.0, and 2.5 W/cm² after the gel was wiped off from the skin. It was not until US intensity had been increased to 2.0 W/cm² that the thermal heating effect of US negated the immediate superficial thermal-cooling effect of the gel to produce significantly increased subcutaneous tissue temperature during sonation. It was suggested that, as US provided a deep heating effect, the US transmission gel on the skin surface provided a superficial cooling effect.

In the present study, we too observed a similar temperature response to US therapy. Skin temperatures decreased with 0.25 W/cm² pulsed US as well as with 0.8 W/cm² continuous US, but the largest drop in skin temperature was seen with pulsed US at 0.25 W/cm² (2 °C p<0.05) and not with the continuous US at 0.8 W/cm² (1.5 °C, p<0.05) or with control/rest (≤ -0.3 °C, p<0.05). Therefore, it is suggested that there will be minimal cooling in skin after the US application, if the cooling of the gel was counteracted by continuous US or with use of higher intensities.

While the changes with US therapy are deductible from the previous findings, the underlying mechanism of the demonstrated changes in skin blood flow,
skin temperature and sensory perception thresholds obtained with 5Hz stimulation in the control are still unclear. The small changes observed in skin temperature and skin blood flow after the control or rest period (3 to 5 min), might have been due to the emotional factors, which were not under participants’ control. Whereas the changes in sensory perception threshold at 5 Hz after control/rest in both groups (pulsed or continuous US group), may have been due to the ‘wind-up phenomenon,’ which is described as a frequency-dependent increase in the excitability of spinal cord neurons in response to the C fiber activity (repetitive stimulation). The lowering of sensory perception thresholds at 5 Hz in this study following repetitive stimulation of C fibres is consistent with the previous CPT findings of Wallace et al., and Farajidavar et al., in the control group. The changes observed after control condition can also be explained by order effect or learning effect from the repeated testing on the Neurometer. TiVi and infrared skin thermometer are objective outcome measures and they could not have influenced the participants’ blood flow or temperature responses while at rest. But the Neurometer is both subjective, (subjects have to respond to 5 Hz stimuli and stop the test when they begin to feel the tingling or buzzing sensation near the electrodes) and objective assessment tool, and this might have had an influence on the observed threshold responses. At the beginning, participants were unaware of the transcutaneous electrical stimulation from the Neurometer and might have responded with higher thresholds (higher baseline values), but as the tests continued and repeated several times, they become familiar with the test and type of stimulations thus performing subsequent tests more fast and more conveniently, indicating a possible learning effect. It is also known from previous reviews that therapeutic ultrasound is often used as a deep heating rehabilitation modality for hand conditions. 38, 44
The present investigation only examined the effect of ultrasound from superficial tissues in the distal forearms. TiVi can reflect red blood cell concentrations from the skin at a depth of 400 µm to 500µm (well into the reticular dermis), while the digital thermometer and R-CPT tests record temperature and sensation superficially. Adequate washout was attained before each pre-test for all measures. However, it is not known, whether the dosage used for pulsed US and continuous US in this study actually increased or decreased the tissue blood flow and tissue temperatures at a depth of 2 cm (3 MHz) and 5 cm (1MHz) or had no effect at all. Bickford et al., reported some conflicting responses, like decreased subcutaneous and skin temperatures (superficial) along with increased muscle blood flow (at a depth of 1 to 3 cm) after sonating healthy tissues with 0.8 MHz, using higher intensities (ranging from 2.0-3.0 W/cm²). These authors demonstrated that, consistent sustained increase in blood flow and tissue temperature in the deep muscles occur only with higher intensities of US treatment (over 3.0 W/cm²), while the moderate intensities causes reduction in skin blood flow and skin temperature due to the effect of contact cooling with US applicator. Lehmann et al. reported that vigorous heating requires higher total power outputs (up to 40 W) and higher US intensities (up to 4 W/cm²). Most joints covered with a significant amount of tissue (shoulder, hip) may be moderately heated with a total power output of 10 to 20 W (at 1 to 2 W/cm² US intensity). For very mild treatments, or for small joints with minimal soft tissue cover, a total output of 1 to 10 W (at 0.1–1.0 W/cm² US intensity) may be used for adequate heating.

Though tissue heating is regarded as beneficial, Merrick et al., cautioned that it is difficult to predict temperature increases when ultrasound is applied clinically owing to a number of unknown variables, including the distance to reflecting soft tissue–bone interfaces, variability among ultrasound machines,
the thickness of each tissue layer, and the amount of circulation. 4, 5, 55 Hence, further research is needed to determine how different dosage of therapeutic ultrasound influences the damaged tissues. While our study does not provide an indication about a therapeutic dosage, it does suggest that 3 min to 5 min applications may not be producing substantial superficial therapeutic effects. This would suggest that future studies looking at physiological effects of ultrasound on blood flow, temperature and sensory function should move towards investigating larger dosages and patient populations.

**Limitations and research recommendations:**

There are a number of limitations in the current study that may have affected the study findings and generalizability. Only one therapist provided the treatment and assessments, which meant that the evaluator was not blinded. However, three of these measures were not under control of the therapist. The sensory threshold was determined by the participant while the TiVi and thermometer were not controlled by either the participant or therapist, so minimal bias was expected with respect to outcome evaluation. However, the TiVi system while accurate is only able to measure superficial blood flow and the US effects in deeper tissue were not measured. For the sensory evaluation, we used the rapid CPT assessment which has less repetition than the full CPT protocol, which involves a repeated force choice protocol. While this may have made our sensory measurements less precise, it was deemed appropriate given we were looking for transient changes and the forced choice protocol can be more time consuming and we may have lost the opportunity to see the short term changes. The sensory perception thresholds were recorded from the tip of ring fingers (dermatome supplied by C7 and C8), instead of the treatment area in order to follow the recommended guidelines of the manufacturer, and to avoid any unwanted motor point stimulation.
(muscle contraction) and thus may not reflect sensory changes in the treatment area. Furthermore, since the ring is innervated by both the median and ulnar nerves differential effects in these nerves were not directly explored. Real time measurements of skin blood flow and skin temperature over the treatment area during the application of US was not possible because of the continuous movement of transducer head which was in-turn blocking the view of images. This is considered a minimal limitation since very transient effects are unlikely to have therapeutic value.

As there is no standard for US dosage, the two US doses (1MHz continuous and 3 MHz pulsed) selected in this study were based on the empirical evidence and therapeutic principles of US therapy.\textsuperscript{15} Hence, there is a need to develop US therapy dosage guidelines for different disorders. The responses observed in this study suggest that small to moderate changes in skin blood flow, skin temperature and sensory nerve perceptions should be expected with brief exposure to US therapy. Hence, there is a possibility that the observed changes may have some beneficial effect on the injured tissues. Knowledge about the short term and long term physiologic effects of US also informs our understanding of the safety and therapeutic benefit of US therapy. Thus, future research should explore the effects of US in patients with hand injuries and with comorbid health problems, using different dosages commonly used in the clinical practice. Furthermore, responses from US can be compared with the responses from other physical agents commonly used in hand rehabilitation to help choose the best treatment for patients.

### 3.6 CONCLUSION

In conclusion, this study demonstrated that both pulsed (3 MHz, 1:4, 0.25W/cm\textsuperscript{2}, 5 min), and continuous US (1 MHz, continuous, 0.8 W/cm\textsuperscript{2}, 3 min), significantly decreased skin blood flow and skin temperatures and C
fibre perception thresholds immediately after therapy. There was no significant change in A-beta perception thresholds, detecting touch and pressure sensations with US therapy, indicating the negligible effect of US on these fibres. The changes observed in C fibre perception thresholds after US, indicate that these fibres are more sensitive to US therapy and may have a potential role in modulating pain. It is presumed that all these physiologic responses observed could have been due to a sympathetic vasoconstrictor effect as a result of thermal changes (thermo-cooling effect of gel and transducer head), or biochemical tissue responses to ultrasound or due to a direct effect of US on C fibers belonging to median and ulnar nerves. However, further research using different US dosages commonly used in clinical practice settings, would be required to definitively establish the putative therapeutic effects and underlying physiologic mechanism(s) of action of US and how they are influenced by different parameter settings.

3.7 REFERENCES


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60. Weseley SA, Sadler B, Katims JJ. Current perception: preferred test for evaluation of peripheral nerve integrity. ASAIO Trans.


Tables and Figures:

Table 3.1: Demographic characteristics of participants

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<tr>
<th>Age, yrs. (M± SD)</th>
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<td><strong>Gender:</strong></td>
<td></td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td><strong>Dominance:</strong></td>
<td></td>
</tr>
<tr>
<td>Right, n (%)</td>
<td>19 (95%)</td>
</tr>
<tr>
<td>Left, n (%)</td>
<td>3 (5%)</td>
</tr>
</tbody>
</table>

Table legends: M= mean; SD= Standard deviation; n = number of participants
Table 3.3: Summary of results for skin blood flow and skin temperature over the treatment area

<table>
<thead>
<tr>
<th>Gp</th>
<th>Pulsed US group</th>
<th>Control-p</th>
<th>Control-c</th>
<th>Continuous US group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>CS</td>
<td>ES</td>
</tr>
<tr>
<td>Bf</td>
<td>M: 60</td>
<td>M: 57.6</td>
<td>2.8*</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>SD: 10.6</td>
<td>SD: 11.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: (55-65)</td>
<td>CI: (52-62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>St</td>
<td>M: 33.1</td>
<td>M: 30.9</td>
<td>2.1*</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>SD: 1.1</td>
<td>SD: 1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: (33-34)</td>
<td>CI: (30-34)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table legends: Gp= groups; I = Pulsed US group; II = Continuous US group; † Pulsed mode - 3 MHz, 2.5 W/cm², 3min.; ‡ Continuous mode - 1 MHz, 0.8 W/cm², 3 min.; Control_p = no US therapy in pulsed US group; Control_c = no US therapy in Cont. US group; Tx= treatment; M= mean; CI= 95% confidence interval; SD= standard deviation; CS= change scores; ES= Effect Size x(pre-post/pooled SD); * significance level at p=0.05; Bf= Skin blood flow; St= skin temperature
Table 3.4: Summary of results for sensory perception thresholds at 2000Hz and 5 Hz from ring finger

<table>
<thead>
<tr>
<th>Gp</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pulsed US (3MHz)†</td>
</tr>
<tr>
<td>Tx</td>
<td>Before</td>
</tr>
<tr>
<td></td>
<td>M: 8.5</td>
</tr>
<tr>
<td></td>
<td>SD: 3.8</td>
</tr>
<tr>
<td></td>
<td>CI: (6.8-10)</td>
</tr>
<tr>
<td></td>
<td>M: 13.4</td>
</tr>
<tr>
<td></td>
<td>SD: 3</td>
</tr>
<tr>
<td></td>
<td>CI: (12-15)</td>
</tr>
</tbody>
</table>

Table legends: Gp = groups; I = Pulsed US group; II = Continuous US group; † Pulsed mode - 3 MHz, 2.5 W/cm², 5min.; ‡ Continuous mode - 1MHz, 0.8 W/cm², 3 min.; Control_p = no US therapy in pulsed US group; Control_c = no US therapy in Cont. US group; Tx = treatment; M = mean; CI = 95% confidence interval; SD = standard deviation; CS = change scores; ES = Effect Size r(pre-post/pooled SD); * significance level at p<0.05; Aβ = R-CPT at 2000Hz; C = R-CPT at 5Hz; R-CPT = Ranged Current Perception Threshold test.
Table 3.5: Summary chart of previous reports on blood flow, temperature, and sensory nerve conduction velocity after US therapy

<table>
<thead>
<tr>
<th>Study (N, S)</th>
<th>US parameters</th>
<th>Groups</th>
<th>Blood flow measures</th>
<th>Temp. measures</th>
<th>Sensory measures</th>
<th>Assessing time lines</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noble et al., 2007. N= 10 (5male; 5 female) S= Healthy</td>
<td>a) Pulsed mode Pulse ratio: 1:2 F: 3 MHz I: 1 w/cm² T: 6 min b)Continuous mode F: 3 MHz I: 1 w/cm² T: 6 min Site: Lateral aspect of forearm.</td>
<td>4 experiment conditions random order: i) control, ii) placebo, iii) pulsed iv) continuous</td>
<td>Skin blood flow velocity with Laser Doppler flowmetry</td>
<td>Ambient &amp; skin temperature skin with thermistor probe</td>
<td>N/A</td>
<td>Pre-post treatment; One condition applied each week, at same time of the day.</td>
<td>↑ Skin blood flow after 3 MHz pulsed US ↑ Skin blood flow after 3 MHz continuous US ≠ Ambient or skin temperature</td>
</tr>
<tr>
<td>Fabrizio et al., 1996. N=20 S= Healthy</td>
<td>a) Continuous mode 4 Frequencies &amp; 4 intensity levels: Tx-l F: 1.0 MHz I: 1.5 w/cm²</td>
<td>6 experiment conditions random order: i)US ii)sham iii)control</td>
<td>Blood flow velocity in the popliteal artery with Doppler Ultrasound</td>
<td>N/A</td>
<td>N/A</td>
<td>Pre-post treatment; All six treatment sessions applied with 2 days gap</td>
<td>↓ Arterial blood flow after control ↑ Arterial blood flow after Tx 2 &amp; Tx 3 ↑ Arterial blood flow after Sham ≠ Arterial blood flow</td>
</tr>
<tr>
<td>Tx-2</td>
<td>F: 1.0 MHz</td>
<td>I: 1.0 w/cm²</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Tx-3</td>
<td>F: 3.0 MHz</td>
<td>I: 1.2 w/cm²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx-4</td>
<td>F: 3.0 MHz</td>
<td>I: 1.0 w/cm²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx-5</td>
<td>= sham</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx-6</td>
<td>= control</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>T: 15 min</td>
<td></td>
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<tr>
<td>Site: Triceps surae muscle mass.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Ware et al., 2001.</th>
<th>a)Continuous mode</th>
<th>Dermal blood flow with Laser Doppler flowmetry</th>
<th>Skin temperature</th>
<th>N/A</th>
<th>Pre-Post treatment</th>
<th>↓ Dermal blood flow after Tx 1; Tx 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>S= Healthy</td>
<td>F: 3 MHz</td>
<td>I: 1.5 W/cm²</td>
<td>Site: Human calf</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>T: 10 min</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>a)Continuous mode</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>F: NS</td>
<td>I: 1.5 W/cm²</td>
<td>2 experiment conditions</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Skin blood flow with Laser Doppler flowmetry</td>
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<td></td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Pre-Post treatment</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>↑ Skin blood flow after US</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>↑ Skin blood flow after sham</td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Conditions</td>
<td></td>
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<tr>
<td>N= 20 (10 male, 10 female)</td>
<td>S= Healthy</td>
<td>T: 5 min</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Site: anterior forearm</td>
<td>i) US</td>
<td>Muscle blood flow with Occlusion plethysmography</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ii) Sham</td>
<td></td>
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</tr>
<tr>
<td>Bickford &amp; Duff, 1953.</td>
<td></td>
<td>3 experiment condition</td>
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</tr>
<tr>
<td>N= 26 (20 male, 6 female)</td>
<td></td>
<td>i) US at two intensity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site: mid forearm</td>
<td></td>
<td>ii) sham</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Skin &amp; muscle blood flow with Venous occlusion plethysmography</td>
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</tr>
<tr>
<td>Paul &amp; Imig, 1954.</td>
<td>S= Humans</td>
<td>T: 20 min</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>2 experiment conditions</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>i) US</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>ii) control</td>
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<tr>
<td></td>
<td></td>
<td>Blood flow with Venous occlusion plethysmography</td>
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</tr>
</tbody>
</table>

**NS** = Not specified

- **↑** Skin blood flow after US
- **↑** Muscle blood flow after US
- **↓** Skin temperature
- ≠ blood flow & subcutaneous temp after Sham

Pre-Post treatment
<table>
<thead>
<tr>
<th></th>
<th>Tx2</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F: NS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I: 3-3.5 W/cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T: 15 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clemente et al., 1992. S= Humans</td>
<td>a) Pulsed mode F: 1.0MHz I: 1.5 W/cm² T: 5min</td>
<td>2 experiment conditions i) US</td>
<td>Blood flow with Doppler ultrasound</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>b) Continuous mode F: 1.0MHz I:1.5 W/cm² T: 5 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wyper et al., 1978. S= Humans</td>
<td>a) Pulsed mode 4 Frequency levels &amp; 4 Intensity levels &amp; 4 durations: Tx1 F:1.0 MHz I: 1.0 W/cm² T: 10 min</td>
<td>6 experiment conditions i) US</td>
<td>Muscle blood flow using xenon washout technique</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Tx 2 F: 1.0 MHz I: 2.0 W/cm² T: 8min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx3</td>
<td>F: 3.0MHz</td>
<td>I: 0.5 W/cm²</td>
<td>T: 13 min</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
<td>--------------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>Tx 4</td>
<td>F: 3.0MHz</td>
<td>I: 1.0 W/cm²</td>
<td>T: 10 min</td>
<td></td>
</tr>
<tr>
<td>b) Continuous mode 2 Frequency levels &amp; 2 Intensity levels at 2 durations:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx1</td>
<td>F: 1.0MHz</td>
<td>I: 1 W/cm²</td>
<td>T: 6 min</td>
<td></td>
</tr>
<tr>
<td>Tx2</td>
<td>F: 3.0MHz</td>
<td>I: 2.0 W/cm²</td>
<td>T: 12 min</td>
<td></td>
</tr>
</tbody>
</table>

Klemp et al., 1982. S=Fibromyalgia Humans

<table>
<thead>
<tr>
<th>Mode: NS</th>
<th>F: NS</th>
<th>I: 1.0 W/cm²</th>
<th>T: 6 min</th>
</tr>
</thead>
</table>

one experiment condition
i) US

Muscle blood flow
using Xenon washout technique

N/A
data

Pre-post treatment
d
downarrow muscle blood flow
| Cosentini et al., 1983. | Mode: NS 4 Intensity levels: Tx1 F: 1 MHz I: 0.5 W/cm²  
Tx2 F: 1 MHz I:1.0 W/cm²  
Tx 3 F: 1 MHz I:1.5 W/cm² T: 10min  
Tx 4 placebo= 0.0W/cm² T: 10 min Site: Middle finger | 4 experiment conditions  
i) US ii)Placebo control | N/A | N/A | Sensory-nerve conduction velocity (sNCV)  
Evoked sensory potentials in median nerve | Pre-post treatment | ≠ s NCV after US or placebo control |

Table legends: N= total participants; S= type of subjects; NS= not specified ; Tx= treatment/condition ; US =ultrasound; F= US frequency; I: US intensity ; T: duration ; N/A = not applicable ; ↑ = increase ; ↓ = decrease; ≠ no observed change
Table 3.6: Summary of survey reports on US usage and preferred practice patterns across 3 countries

<table>
<thead>
<tr>
<th>US parameters</th>
<th>Australia $^{12}$</th>
<th>USA $^{39}$</th>
<th>Brazil $^{59}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode</strong></td>
<td>Acute: Pulsed mode (80%)</td>
<td>NS</td>
<td>Acute: Pulsed mode</td>
</tr>
<tr>
<td></td>
<td>Chronic: Continuous mode (90%)</td>
<td></td>
<td>Chronic: Continuous mode</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>NS</td>
<td>3MHz: superficial tissue</td>
<td>3MHz: superficial tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1MHz: deep tissues</td>
<td>1MHz: deep tissues</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Acute: 0.51 to 1.5 W/cm$^2$ (86%)</td>
<td>Superficial tissues: 0.10 W/cm$^2$ to 3.30 W/cm$^2$</td>
<td>Acute: 0.6 to 1.0 W/cm$^2$</td>
</tr>
<tr>
<td></td>
<td>Chronic: 1.01 to 2.0 W/cm$^2$ (90%)</td>
<td>Deep tissues: 0.40 W/cm$^2$ to 4.00 W/cm$^2$</td>
<td>Chronic: 1.1 to 1.5 W/cm$^2$</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Acute: 5 min (range, 2 to 10)</td>
<td>NS</td>
<td>Majority of conditions: 2 to 4 min</td>
</tr>
<tr>
<td></td>
<td>Chronic: 5 min (range, 3 to 20)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table legends: Acute: for acute conditions; Chronic: for chronic conditions; % = denotes usage by therapists; NS: not specified
Figure 3.1: Flow chart for the study design (Cross-over AB/BA):

Figure legends: R= randomization; Cont. = continuous; 25 min= washout period; TiVi= tissue viability imager; Temp = temperature; R CPT= Range current perception threshold at 2000 Hz & 5 Hz.
Figure 3.2: Sensory perception thresholds at 2000 Hz before and after US and control

Figure 3.3: Sensory perception thresholds at 5 Hz before and after US and control
Figure 3.4: Skin blood flow responses before and after US and control

Figure 3.5: Skin temperature responses before and after US, control
Figure 3.6: i) TiVi images over the treatment area (2X ERA) in Pulsed US group (3MHz US followed by No US/ rest)
If blood flow increases, images appear yellow, orange or red (160-400) on scale and if it decreases images appear blue (0-80)
Figure 3.6: ii) TiVi images over the treatment area (2X ERA) in Continuous US group (No US/rest followed by 1MHz US)

If blood flow increases, images appear yellow, orange or red (160-400) on scale and if it decreases images appear blue (0-80)
CHAPTER 4

“Short term sensory and vascular responses to hand exercise.”

Shaguftha Sultana Shaik, Joy C. MacDermid, Ruby Grewal
4.1 ABSTRACT

Study design: Randomised Cross-over, repeated measures, pretest post-test design.

Introduction: Hand exercise is used for a variety of clinical conditions. There is scarcity of literature on the normal effects of different intensities of hand exercise on sensory and vascular function.

Purpose: To determine the normal short term impact of two different intensities of hand exercises (high and low) on sensory and vascular functions.

Methods: Twenty healthy volunteers were recruited (7 men and 13 women; aged 18 to 50 yrs. (Mean age: 29.6 ± 8.83 yrs.) for the study. Superficial palmar blood flow in the hands was determined using Tissue viability imaging system. Sensory perception thresholds for ulnar and median nerves (at 2000 Hz and 5Hz) were determined from tip of ring finger (C7, C8) to assess A-beta and C fibre function. The cross over trial included 3 conditions: no exercise or rest, high intensity exercise and low intensity exercise. Subject’s hands were randomized to either a high intensity group (no exercise followed by exercise) or a low intensity group (exercise followed by no exercise). Scores were obtained before and immediately after the hand exercises and rest. Differences were analyzed using general linear models.

Results: Neither low intensity nor high intensity hand exercise had a significant effect on R-CPT scores or superficial palmar blood flow as there were no differences over time (p>0.05); nor was there treatment condition and time interaction (p>0.05). Similar results were found for rest (p>0.05). Age and gender also had no significant effect on either measures (p>0.05).
**Conclusion:** This study found a lack of short term physiological changes in superficial palmar cutaneous blood flow and sensory perception thresholds following brief low intensity or high intensity hand exercises. The exercise protocol used in this study may not have elicited cutaneous thermoregulatory responses (no change in internal tissue temperature), but there is a possibility that the non-thermoregulatory responses might have played some role in the observed findings.

*Key words:* sensory perception, skin blood flow, palm, exercise
4.2 INTRODUCTION

Regular exercise is used to improve muscle function and functional ability in healthy and patient populations. Physiological responses to exercise are affected by dosage and type of exercise and so can vary with: frequency (how often exercise is performed), intensity (resistance), and duration (number of repetitions or time the exercise is performed), muscle contraction type, range of motion (ROM), speed of movement, and mode of exercise.\textsuperscript{1,2,3,4} Control of blood flow to skeletal muscles during exercise occurs through somatic (sensory) and sympathetic neural pathways. The activation of skeletal muscle fibers by somatic nerves results in vasodilation and functional hyperemia.\textsuperscript{47} Sympathetic activation results in vasoconstriction and maintenance of arterial blood pressure.\textsuperscript{47} The effects of these respective neural control systems interact throughout the vascular resistance network of skeletal muscle to facilitate coupling between the vascular supply of oxygen and the metabolic demands of the contracting muscle fibers.\textsuperscript{47}

Skin is the only readily accessible organ for which blood flow can be measured noninvasively through noncontact imaging. Due to the essential link between microcirculation function and adequate tissue oxygen delivery, the tissue blood supply has been noted as a crucial indicator of injury and disease.\textsuperscript{5} Hence, skin is sometimes used as a model of generalized microvascular function.\textsuperscript{6, 7, 8} Dynamic physical exercise induces an increase in the production of heat in active muscles and increases core body temperature. Core body temperature is the main thermal input which stimulates the thermoregulatory center (the hypothalamus), which in turn induces vasodilation in the skin.\textsuperscript{9} Skin blood flow thus plays an important role in temperature control via thermoregulation, through its responses to heat and cold stress.\textsuperscript{9} Non-thermal factors associated with exercise such as the sympathetic stimulation, baroreflex and exercise pressor reflex also
affects cutaneous circulation, through its responses to changes in arterial and central venous pressure (CVP). The baroreceptors reflexively modulate skin blood flow, regulate central blood volume and maintain blood pressure (BP) during a BP challenge, exercise and heat stress environments. Local vasoactive substances (e.g., carbon dioxide, hydrogen ions etc.) released by the active muscle during exercise are responsible for the increase in blood flow to muscle through the exercise pressor reflex which is elicited by these substances. Control of blood flow is thus influenced by myogenic activity and local concentrations of muscle metabolites. As skin vasomotion is influenced by thermal and non-thermal factors associated with the exercise, the thermal input–output relationship in the control of cutaneous circulation during the exercise differs from that at rest. Hence, monitoring sensory and vascular responses in skin during exercise provides an indication of changes in the neurovascular functions.

Cutaneous microcirculation differs according to the location in human body and has few anatomical variations. Most of the body surface is covered with "hairy" or non-acral (also called non-glabrous) skin, whereas the fingers, lips, ears, forehead, palms, and plantar aspects of the feet are covered with acral or non-hairy (also called glabrous) skin. In the non-glabrous skin, the cutaneous microcirculation is organized as two horizontal plexuses: a lower horizontal plexus composed of large arterioles and venules positioned at the dermal subcutaneous interface, and an upper horizontal network of smaller arterioles and venules in the papillary dermis (1-1.5 mm below the skin surface) from which the capillary loops of the dermal papillae arise. The two plexuses are connected by ascending arterioles that are paired with descending venules and spaced at intervals of 1.5-7 mm. In addition to these two plexuses, glabrous skin also contains a high proportion of arterio-venous anastomoses (direct vascular connections between arterioles and
Arterioles in glabrous skin are innervated solely by noradrenergic sympathetic nerves, whereas arterioles in non-glabrous skin are innervated by both noradrenergic and cholinergic sympathetic nerves. The skin vascular responses to exercise have been shown to differ between glabrous regions such as the palm and sole, and non-glabrous regions such as the dorsal hand and forearm.

Previous literature on the effects of exercise on cutaneous vascular responses report muscle activity at one site and measurement of skin blood flow at a different site. For example, previous investigators measured skin blood flow either after a short bout of isometric hand grip exercise or after few weeks of hand grip training from the volar aspects of forearm, instead of the palmar region where the muscle activity takes place. Also, the effects of the intervention (exercise) on the tissues most directly affected by the treatment were not measured in these previous trials. Skin blood flow is typically obtained with laser-Doppler flowmetry (LDF) or laser-Doppler imaging using a single-point LDF (probe) either from the forearm or the finger pad. As described earlier, there is a higher vessel density and high proportion of arteriovenous anastomoses in the palms and finger pads when compared to the forearm region. Hence, LDF responses obtained through the single point LDF is prone to variability according to the anatomy of underlying vasculature.

An index of skin blood flow can also be obtained using a novel technique called Tissue Viability Imager (TiVi), which has the capability to measure the red blood concentration in upper dermal tissue (skin depth of 400 to 500 µm). The TiVi responses can be explained by physiological understanding and can be analyzed directly without any equation as in LDF (LDF flux/MAP). Unlike the LDF which uses a small single-point LDF probe (which is very small compared to the treatment area) to capture the
red blood cell flux in a finger pad, TiVi imager directly captures the red blood cell concentration over the whole treatment area. Dynamic hand grip exercise involves all muscles in the palm and the images can be captured over the whole palmar aspect using TiVi imager which are much larger than those obtained through single point LDF probe. TiVi imager is not affected by the velocity or movement of blood flow in circulation as in LDF, because it only captures the amount of red blood concentration in the area at that time point. \(^{32}\)

Palmar skin is also richly populated by sensory nerves, which respond to thermal, chemical, and mechanical stimuli to provide feedback to the central nervous system and influence cutaneous arteriolar tone via the release of neuropeptides and other vasoactive agents. \(^{20, 33}\) It is possible to perform direct measurement of the functional integrity of sensory nerve fibers using the current perception threshold (CPT) test. \(^{36}\) The CPT is the minimum amount of transcutaneously applied current that an individual consistently perceives as evoking a sensation. It is a quantitative sensory test used for functional analysis of A-beta (touch, pressure), A-delta, and C fibres (temperature, pain and postganglionic sympathetic). \(^{36}\) This method is increasingly used for assessment of sensory function in clinical practice such as epidural anesthesia, \(^{37}\) skin graft surgery, \(^{38}\) and chronic lumbar radiculopathy etc. \(^{34}\)

Currently, there is a scarcity of published reports on clinical trials which have looked at the short term effects of low intensity and high intensity exercises on the neural and cutaneous vascular responses in the hands of healthy individuals. Hence, the purpose of this study was to see the impact of two types of hand grip exercises on the superficial palmar blood flow and sensory perception thresholds in an area innervated by median and ulnar nerves (C7,C8). A secondary purpose was to determine if the responses were affected by age and gender.


4.3 METHODS

Participants:

The sample size required for this research was based on the number needed to detect a moderate effect size according to Cohen. \(^{64}\) A moderate effect (ES \( r=0.50 \)) using two-tailed alpha (\( \alpha = 0.05 \)) at 80% power, requires a sample of 28 participants in each group for a between subject design and a sample of 14 participants for a within subject design. As this is a within subject design and variance within individuals is less than between subjects a sample size of 20 was considered and approved by the ethics board. Statistical significance was considered if \( p<0.05 \).

Subjects were recruited by poster advertisement and word of mouth in the university campus. Testing was done in Hand and Upper Limb Research Lab at St Joseph’s Health Care, London, Ontario, Canada. Healthy subjects aged 18 to 50 yrs. with no recent injury or disease at neck, shoulder, elbow, wrist, or hand, within the past year were included in the study. Subjects were divided into two age categories: 18–34 and 35–50 yrs. There were 7 males and 13 females in total. Please refer to Table 1 for subject demographics. All subjects were informed to refrain from any kind of exercise or drinking beverages 4 hours prior to the testing. Subjects were excluded if they had skin infection, open wound, swelling, neurovascular injuries, deficits in sensation in the area to be treated (sensory test to identify sharp and dull sensation), decreased circulation (digital patency test for fingers), pregnancy, menstruation, presence of a pacemaker or monitoring device, malignancy, osteoporosis, dislocations, ligament tears or injuries, heart disease, hypertension and cardiac failure. This study was approved by the Western University Research Ethics Board. All participants read the letter of information, had his/her questions answered, and signed a consent form prior to participation in this study.
Outcome Measures:

**TiVi (Tissue Viability Imager) 600 polarization spectroscopy camera (version 7.4 Wheels Bridge AB, Linköping, Sweden):**

The TiVi is a small and portable device for high-resolution instantaneous imaging of Red Blood Cell (RBC) concentration in upper human dermal tissue. TiVi software was used to quantify RBC concentration on the palmar aspect in both arms using a digital camera (Canon Rebel EOS model 450D, Japan) with a polarization lens. The camera was supported by a multijointed metal arm provided by Wheels Bridge and the arm was secured to a desk. The camera was adjusted to point downwards towards the surface of the desk. A royal blue colored cushion was used to rest the forearm and to fill the camera view. An outline was drawn to standardize hand positioning. The participants were positioned with their shoulder in neutral, elbow in 90° flexion, wrist in neutral position and the forearm fully supinated. Each image was captured with the polarized lens set at the cross polarization setting and the camera was positioned at a distance of 300mm from the participant’s hand. Image quality was set to medium normal. One photo was taken every 5 sec and uploaded into the attached laptop computer. The camera has a light penetration depth between 400 to 500 micrometers, and this light contains information about the main chromophores in the epidermis (melanin) and dermis (hemoglobin), while the surface reflections contain information about the surface topography, such as texture and wrinkles. Once the images were captured, the TiVi images were processed using the TiVi software.

For each participant, one image at baseline and at each follow up point after exercise and control/rest were used for processing and analysis. A total of 8 images per participant (4 in each palm) were analyzed. Regions of Interest (ROI’s) were selected over the treatment area up to the wrist crease. The magnitude of RBC concentration over the selected ROI’s was obtained
using ‘image analysis.’ Values for the TiVi are measured by Arbitrary Units (A.U.) as defined by the manufacturer. Data was first exported from the TiVi software into Microsoft Excel 2010 spreadsheets and then imported into SPSS version 20.0 for statistical analysis. The technique has shown many uses in drug development, burn investigations, pressure studies, and general research maneuvers due to the ease of use, portability, and low cost. The TiVi has been validated for construct validity to measure superficial RBC concentrations with in vitro fluid models and computer simulations. The models performed in vitro demonstrated that the TiVi software was able to accurately calculate the oxygen saturation level of 91.5%, which is within the physiological range of oxygen saturation within blood. It has been shown to be sensitive to change during blood occlusion testing, and drug testing on skin, and has also demonstrated good inter-laboratory reliability.

**Neurometer © CPT/C device (Neurotron Inc., Baltimore, USA):**

The Neurometer evaluates sensory nerve conduction from the periphery to the brain and has been shown to detect differences in neural function in asymptomatic subjects when neural stress was administered. This portable battery operated nerve stimulator has the ability to emit three different frequencies in sinusoidal waveforms to selectively target different subpopulations of nerve fibers dependent upon nerve fiber diameter. A frequency of 2000 Hz is used to stimulate the large myelinated A-beta fibers (Aβ fibers) which detect cutaneous touch and pressure; a 250-Hz stimulus will stimulate myelinated A-delta nerve fibers (Aδ fibers) which are mechanoreceptive, and detect fast pain, pressure and temperature, while a frequency of 5 Hz is used to stimulate the small unmyelinated C-polymodal nociceptive fibers which detect slow pain and temperature and are post
ganglionic sympathetic fibres. This device has been used in numerous studies to detect, screen and diagnose the abnormalities of peripheral nervous system and normal ranges for all nerve fibre types (A-beta, A-delta and C fibres) have been established to assess normal sensation, increase in sensation (hyperesthesia), decrease in sensation (hypoesthesia) and no sensation at all (anesthesia). The Neurometer has been shown to be both specific (73%) and sensitive (74%) in the clinical examination of carpal tunnel syndrome and are considered reliable measures of quantitative sensory function.

Ranged CPT (R-CPT) is a sensory perception threshold testing which can be completed in 3 to 6 min for each test site. It is typically used to confirm or rule out sensory involvement from vascular involvement in large sample trials. In R-CPT, each frequency is repeated several times to ensure accuracy and reproducibility. The average time needed to complete the tests is reported to be less than 10 min. The Neurometer reports values as the normal range (R-CPT Level, 6–13), hyperesthesia (R-CPT Level, 1–5), and hypoesthesia (R-CPT Level, 14–25). Two nerve fibres were assessed in this study using R-CPT tests at 2000Hz and 5Hz. To begin 2000 Hz stimulation, the skin was cleaned with a skin paste and then the 1 cm gold electrodes coated with small amount of gel were attached to the ring finger with an adhesive tape. Then, the participants were asked to press and hold the red “Test cycle” button on the remote control box and release it as soon as they begin to feel the tingling or buzzing sensation. The machine records the response when the button is released and the same process is repeated 7-10 times until a score is displayed. In total three scores are obtained at 2000Hz. The same procedure is repeated at 5Hz. These test cycles end automatically after few repetitions (7-10 times) and the CPT displays score for 5Hz.
Experimental Procedure:

Randomization:

We used a randomized cross-over, repeated measures design in this study. Random allocation to treatment order and hand was achieved through subject’s selection of assignment contained in an opaque envelope. After screening for inclusion criteria, the study protocol and rate of perceived exertion (10 point RPE scale, by Borg’s) were explained and then the informed consent was obtained from each participant. Each participant was then asked to pick two different colored sealed envelopes from two bundles, which had information on the side of hand and sequence of exercise to be initiated. Once the hand side was picked, the participant was then randomized to either high intensity group or low intensity group based on the labeling on cards. There were three conditions: a control condition (rest or no exercise), high intensity hand grip exercise and low intensity hand grip exercise. If the card showed high intensity group, then the order of therapy was rest followed by high intensity exercise in the hand first selected. After this the person was asked to perform exercise on the opposite hand in a reverse order (low intensity group), beginning with low intensity exercise and followed by rest. A 10 min gap was established between each condition (rest, exercise) to provide a washout period and to minimize any potential carry over effects of exercise. Exercise instructions and outcome assessments were all provided by a single physiotherapist. The two group sequences were completed on the two hands one after the other on same day. The flow chart outlining the study design is in Figure 1.

Exercise intervention:

After acclimatization to room temperature for 10 min, participants were first measured on TiVi over the palmar region (up-to wrist crease) and
then the Range –CPT test was recorded from the tips of ring finger (over C7/C8 dermatome level) to assess sensory perception thresholds at 2000Hz (for A-beta fibres) and 5Hz (for C fibres). These two measurements were done before (pretest or baseline) and immediately (post-test) after each control condition and hand exercise in similar order. After completing baseline assessments, participants were either asked to rest for 5 min during the no exercise period, or perform a low intensity hand exercise or a high intensity hand exercise based on the group order selected. There was a 10 min washout period between each condition. Participants were asked to perform a warm up of hand muscles prior to the initiation of exercise. a) Low intensity (or low resistance and high frequency) exercise consisted of squeezing a low resistance thera ball (pink colored, soft, 15° hardness) for a total of 5 min. One set of hand exercise consisted 25 repetitions (1 sec contraction and 1 sec relaxation; each set was paced at <30 sec) and each set was separated by a 30 sec rest interval (25 reps- 30 sec rest-25 reps-30 sec rest). b) High intensity (high resistance and low frequency) exercise consisted of squeezing a high resistance thera ball (black colored, firm, 35° hardness) for a total of 5 min. One set of hand exercise consisted 12 repetitions (1 sec contraction and 2 sec relaxation; each set was paced at > 30 sec or 36 sec) and each set was separated by a 30 sec rest period (12 reps-30sec rest-12 reps-30sec rest) [Adapted from ACSM progression model, 2009]. The speed and time of contraction were paced with a stop watch and metronome. Rate of perceived exertion was used to monitor the level of exertion or fatigue after the exercise. TiVi and R–CPT responses were recorded immediately after exercise (post-test). The same process was repeated after control condition. TiVi software was used to calculate the mean blood flow (A.U.) in the palmar region up-to the wrist crease and then the data was transferred to an Excel sheet (Microsoft 2010). The sensory perception thresholds obtained at
2000Hz and 5Hz (m. A.) were recorded directly from the digital display of the Neurometer CPT/C device onto a separate data collection sheet.

**Data analysis:**

Data was entered in SPSS and random checks of 10% of the data against the hard copies of data sheets was used to ensure data quality (100% were correct so no further data audits were performed). Descriptive statistics were run to further investigate data quality and assess data normality. The majority of data was normally distributed as assessed by Kolmogorov-Smirnov Test (p>0.05), hence parametric tests were used for quantitative data analysis. The outcome measures (RBC concentration and sensory perception thresholds) were assessed for differences using General Linear Models (GLM, using SPSS version 20, IBM Inc.). Models assessed whether there were differences between baseline and immediately after control or exercise therapy (low intensity and high intensity). Interactions were examined for significance between time and treatment group. Post hoc analyses were performed using Bonferroni correction wherever necessary. Pair wise comparisons were used to perform within-group comparisons for treatment and control. The GLM model was run without covariates and then repeated with age and gender as a covariate to test for differential responses. Significance level was set at p<0.05 level unless otherwise noted. All values were expressed as means, standard deviation and 95% confidence intervals.

**4.4 RESULTS**

Twenty healthy volunteers who satisfied all eligibility criteria and agreed to participate were recruited between November 2012 to February 2013. No data points were missing. Demographic information of the participants is presented in Table 4.1. The group means, standard deviation (SD), 95% confidence interval (CI) and change scores and effect size for skin blood flow
and sensory perception thresholds at 2000Hz and 5Hz are shown in the Table 4.2 and are summarized by outcome measure below.

Neither of these exercise intensities (low and high) had a significant effect on R-CPT scores or superficial palmar blood flow as there were no differences over time (p>0.05); nor was an exercise condition and time interactions (p>0.05). Similar results were found for control condition (p>0.05) (Figures 4.2, 4.3, 4.4, 4.5). The effect sizes were small (ES r = <0.2) for both outcomes before and after the exercise and control. GLM with age and sex as covariates reveals no significant effect of age (across the two categories; 18–34, 35-50 age groups) as well as the gender on the R-CPT scores or superficial palmar blood flow (p>0.05).

4.5 DISCUSSION

This study found a lack of short term physiological changes in superficial palmar cutaneous blood flow and sensory perception thresholds following brief low intensity or high intensity hand grip exercises. The responses were also not affected by age or gender. We could not find any similar study in the literature which reported neural and vascular responses in the palm (glabrous skin) after high intensity and low intensity hand exercises. The closest findings related to our study which measured vascular and neural responses after resistant hand exercise was by Akira et al. These authors looked at the effects of vibration and noise on sympathetic nerve activity in fingers and palm (glabrous skin) of five healthy volunteers. One of the three experiments in their study was to observe the effect of isometric handgrip exercise (a constant gripping force of 2 kg) on skin blood flow, skin temperature and median nerve sympathetic activity in the hands before and after 5 min. No significant changes were observed in the sympathetic nerve activity or skin blood flow during and after isometric handgrip exercise when compared to the values at rest.
Our results were consistent with the reports by Akira et al.,\textsuperscript{26} with respect to skin blood flow and sensory nerve function (C fibres are post-sympathetic ganglionic). But direct comparison was not possible because the current study looked at superficial palmar blood flow and sensory perception thresholds from ring finger noninvasively (median and ulnar innervation zone) before and after two types of dynamic exercises, while Akira et al., assessed sympathetic neural activity at elbow level directly by inserting needle into the median nerve and measured skin blood flow from the tips of middle finger using laser Doppler flowmetry, before and after a constant isometric hand exercise.

Another study by Bartholomew et al.,\textsuperscript{27} investigated the effects of 20 min of self-selected resistance exercise (circuit weight training and stationary cycling) on pressure pain thresholds and pain tolerance in healthy volunteers. These authors found that pressure pain thresholds remained unchanged following exercise and control conditions, but pain tolerance increased across time.\textsuperscript{27} In the present study A beta perceptions did not change after control and after the two hand exercises. Because A beta function is to detect and transmit touch and pressure, the sensory perception thresholds at 2000Hz can be presumed to have responded similar to pressure pain thresholds in Bartholomew’s experiment.\textsuperscript{27} However there was pain component along with pressure component in the pressure pain threshold test. Hence, direct comparisons were not possible due to differences in site (legs), methods (exercise protocol was cycling) and assessments used in these studies.

Differing methods of skin blood flow measurements and treatment protocols do not allow direct comparisons to be made between the research studies that have been published to date. The observed changes in skin blood flow and sensory nerve perception thresholds before and after exercise and control may be explained by the body’s physiological responses. Skin blood flow
in the palm has been reported to be regulated by 3 mechanisms: 1) Thermoregulatory reflex control, 2) Non-thermoregulatory reflex control, and 3) Auto regulation. Thermoregulatory reflexes, which include skin blood flow responses to heat and cold stresses, exert their effects on the skin circulation through two branches of the sympathetic nervous system: a noradrenergic vasoconstrictor branch and an active vasodilator branch. Nonthermoregulatory reflexes, which include skin blood flow responses to changes in arterial and central venous pressure (CVP) and exercise stresses, also operate through the two aforementioned branches of the sympathetic nervous system; however, the glabrous/palmar skin operates only through the vasoconstrictor branch. In the auto-regulation process, throughout a specific range of arterial blood pressure, steady-state blood flow is maintained at a fairly constant level. Previous reports on cutaneous circulation have shown that, independent of neural control of blood flow, glabrous or palmar skin has the ability to buffer blood pressure oscillations and demonstrates a degree of dynamic auto-regulation. Conversely, nonglabrous or hairy skin has a diminished dynamic auto regulatory capacity.

We first tried to relate observations in the present study to some of the physiological findings reported earlier on the cutaneous responses to exercise on non-glabrous or hairy skin in terms of thermoregulatory control. These authors showed that the onset of acute dynamic exercise involves a transient reduction in skin blood flow mediated by increased cutaneous sympathetic (vasoconstrictor) outflow. As dynamic exercise progresses, core temperature (internal body temperature) begins to rise while skin blood flow remains unchanged until a temperature threshold ($T_c$) is reached ($T_c < 37\, ^\circ C$). Once this threshold is crossed in internal body temperature ($T_c \geq 38\, ^\circ C$), or exceeds a specific level in the deep tissue temperature of a local exercising muscle.
the skin blood flow begins to rise linearly with increasing temperature.\textsuperscript{51,53,57} This post-exercise elevation in core body temperature is intensity dependent, hence higher post-exercise temperatures were found to be associated with higher exercise intensities.\textsuperscript{31} Also the thermal afferents from an exercising tissue (muscle, vein or bone around the muscle etc.) might directly affect thermoregulatory responses.\textsuperscript{57,58,59} Hence, it is possible that the hand exercises used in this study did not cause a persistent post exercise thermal load that was substantial enough to stimulate an increase in core temperature.\textsuperscript{31,56} In the present study we monitored rate of perceived exertion (RPE) during and after the exercise to note level of fatigue or exertion (if any). All the participants described their rate of perceived exertion to be ‘weak’ or very weak’. From this we can presume that both low intensity and high intensity exercise protocols were not so intense to rise the local muscle tissue temperature,\textsuperscript{57,58,59} thus causing no variation in superficial palmar blood flow. There was no variation in superficial palmar blood flow and sensory perception thresholds after control as well. We presume that this response might have been due to the resting condition of the participants during ‘no exercise period’ in a thermo-neutral environment.

Secondly, it is also possible that the superficial palmar blood flow and sensory perception thresholds did not change after exercise due to the non-thermo regulatory control of skin blood flow (from muscle’s exercise pressor reflex or baroreflex etc.). It has been reported that control of blood flow in the cutaneous microcirculation depends primarily on cutaneous arteriolar tone, which is influenced by many factors including sympathetic stimulation, myogenic activity, and local concentrations of specific metabolites in muscle (e.g., carbon dioxide, hydrogen ions).\textsuperscript{20} In addition to this, skin is also richly populated by sensory nerves, which responds to thermal, chemical, and mechanical stimuli to provide feedback to the central
nervous system and influence cutaneous arteriolar tone. A-beta fibres play a key role in providing tactile sensory inputs from palmar skin to the brain. Hence, intact touch and pressure sensations are important to initiate voluntary contraction as well as maintain the muscle work according to the different force loads generated during hand grip exercise. So there is a possibility that the observations in the present study could have been due to the mechanical stimuli from rhythmic finger squeezing movements and the corresponding muscle vascular responses during the hand grip exercises.

Blood flow to active skeletal muscle is required to meet metabolic demands. Blood flow redistribution from other regional circulations contributes to the enhanced muscle blood flow. It has been previously reported that after exercise, oxygen consumption \((\text{VO}_2 \text{ max})\) and energy expenditure in the muscle remain above resting values for a period of time, denoting high energy expenditure during this period. The extra oxygen consumption is known as excess post-exercise oxygen consumption (EPOC). Evidence from past reports suggests an exponential relationship between exercise intensity and the magnitude of the EPOC for specific exercise durations. Furthermore, work at exercise intensities 50–60% \(\text{VO}_2 \text{ max}\) stimulate a linear increase in EPOC as exercise duration increases. During recovery from relatively high-intensity exercise, it may take approximately 60 min or more for \(\text{VO}_2\) and the anaerobic metabolic rate to return to values recorded before exercise. There is a possibility that the hand exercises used in this study might have increased the oxygen demand in the muscle tissue for a brief period after the exercises. Thus, causing blood flow redistribution from the skin to the active skeletal muscles, to suffice the post exercise oxygen consumption, which is thought to remain above resting levels for a period of time, before returning to their pre-exercise state.
Hence, we summarize all possible physiological mechanisms that might have led to the observed findings in this study as follows: The responses observed in palmar blood flow and sensory perception thresholds are more likely to be linked to the non-thermo regulatory control of skin blood flow (from muscle activity, exercise pressor reflex, post exercise oxygen consumption). We exclude the influence of a thermoregulatory control and the baroreflex control from our findings. A dynamic exercise in which a significant percentage of muscle mass is engaged (~50%) generates thermoregulatory demands that are met in part by increases in skin blood flow.\textsuperscript{9,60} The exercise protocols used in this study involved small muscles of the hand which contributes to <50% of the total body muscle mass.\textsuperscript{60} The localized rhythmic hand exercises might not have increased body core temperatures beyond a set threshold (≥38°C) to engage the thermoregulatory reflex. Further, it is unlikely that the exercises altered cardiac output, mean arterial pressure or heart rate to stimulate the baroreflex responses in the big arteries.\textsuperscript{9,61}

The underlying mechanisms demonstrated in skin blood flow and sensory perception thresholds obtained with exercise however appear to be complex and multifaceted.\textsuperscript{68} Apart from these three control mechanisms, personal factors and environmental factors have also been reported to alter skin responses. The distribution of glabrous skin is limited to the hands, feet, and faces, and is exquisitely sensitive to environmental temperature and emotional inputs. Even though the study was conducted in thermo-neutral environment in same subjects on same day to control the diurnal variations, we cannot address the issue of whether emotional inputs had any contribution to the observed findings.\textsuperscript{45,56} It has also been reported previously that glabrous skin has the capability of both static and dynamic auto-regulation.\textsuperscript{48} Hence, we can only presume that cutaneous auto-regulation might have contributed in some way to the observed findings.
The vasoconstrictor system in the palmar skin is the primary means of blood flow control through which exercise can exert any modifying effects.\textsuperscript{16, 44} The competition between thermoregulatory control of body temperature and the metabolic demands of exercise is also a competition between skin and the active skeletal muscle for the available cardiac output.\textsuperscript{44} There is no compromise or reduction in blood flow to the active muscles or to the blood pressure even in heat stress,\textsuperscript{52} but there is a limit to skin blood flow through redistribution or shunting blood towards the active tissues\textsuperscript{44} in such conditions. The limitation to skin blood flow also varies with the level and mode of exercise used.\textsuperscript{62} All these inferences lead us to a conclusion that the short term hand exercises used in this study were not sufficient to cause significant amount of variations in superficial palmar blood flow and sensory nerve function as compared to the values at rest. The findings of this study indicate that local hand exercise of either high or low intensity level (using theraballs of two different resistances) shows minimal systemic impact in individuals without injury or cardiac disease suggesting either is safe and does not affect superficial blood flow or sensory threshold. Therapists can apply this information in clinical practice as they can consider changes in superficial blood flow or reports of sensory disturbance with hand exercises to be abnormal. These should be investigated as they may indicate abnormal vascular, sensory or muscular function.

**Limitations and research recommendations:**

There are a number of limitations in the current study that may have affected the study findings and generalizability. Only one therapist provided the treatment and assessments, which meant that the evaluator was not blinded. However, both the measures were not under control of the therapist. The sensory threshold was determined by the participants and TiVi was not controlled by either the participant or the therapist so minimal bias was expected with respect to outcome evaluation. However, the TiVi system
while accurate is only able to measure superficial blood flow and was not a
direct measure of blood flow to the muscles or other deeper tissues. For the
sensory evaluation we used the rapid CPT assessment which has less
repetition than the full CPT protocol which involves a repeated force choice
protocol and included a site which records response from two nerves at
the same time. While this may have made our sensory measurements less
precise, it was deemed appropriate given we were looking for transient
changes and the forced choice protocol can be more time consuming and may
have lost the opportunity to see short term change. The participants performed
low intensity or the high intensity exercise during the tests using 2 pre-set
hand grip resistances and so there was no customization of resistance to the
individual’s strength. This meant that the exercise dosage varied across
individuals and may not have reached a high intensity for some. However,
since this approach is commonly used in clinical practice, it was selected for
its clinical relevance. The sensory perception thresholds were recorded from
the tip of ring fingers (dermatome supplied by C7 and C8), instead of
the treatment area in order to follow the recommended guidelines of the
manufacturer, and to avoid any unwanted motor point stimulation (muscle
contraction) and thus may not reflect sensory changes in the whole palmar
region. Furthermore, since the ring is innervated by both the median and
ulnar nerves differential effects in these nerves were not directly explored.
Real time measurements of skin blood flow over palmar area during the
exercise was not possible because of the continuous movement of fingers,
which was in turn blocking the view of images. This is considered a minimal
limitation since very transient effects are unlikely to have therapeutic value.
Due to small size of the exercise balls, the participants with long fingers
and big palms used only four fingers for gripping, leaving aside either
the thumb or little finger, leading to variable exercise performance in some.
However, this is considered a minor variation which was not under therapist
control.
This study indicates that a 5 min hand exercise had minimal impact on superficial blood flow or sensory threshold. Future exercise study is needed to explore the effects in patients with hand injuries and with comorbid health problems. Athletes and active individuals who participate in regular physical exercise may have different skin responses and this needs further investigation. It is possible that long-term hand exercise causes physiologic changes in vascularity or nerve function, and thus longer term effects of exercise programs should be explored. Finally, this exercise construct is only one form of exercise used in hand rehabilitation and other forms should also be tested. Knowledge about the short term and long term physiologic effects of hand exercise informs our understanding of the safety and therapeutic effects of exercise.

4.6 CONCLUSION

In conclusion, this study demonstrated a lack of short term effects on superficial palmar blood flow and sensory perception thresholds (A-beta and C fibres) with brief hand grip exercises. This is a non-invasive study and we deduced all relationships from the previous physiological findings. Even though the exact mechanisms behind these observations are unknown, there is a possibility that non-thermoregulatory reflexes and cutaneous auto-regulation in the palms might have led to the observed findings, and not the thermo-regulatory reflex control mechanism. Future studies should focus on assessing therapeutic effects of different modes of hand exercise commonly used in the clinical settings and apply the same in patient population.

4.7 REFERENCES


Tables and Figures:

Table 4.1: Participant demographic characteristics

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</table>

Table legends: M=mean; SD= Standard deviation; n = number of participants
Table 4.2: Summary of results for skin blood flow response in the palms.

<table>
<thead>
<tr>
<th>Gp</th>
<th>I</th>
<th>II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Intensity group</td>
<td>High intensity group</td>
</tr>
<tr>
<td>Tx</td>
<td>Control_L</td>
<td>Control_H</td>
</tr>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Bf</td>
<td>M:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI:</td>
<td></td>
</tr>
</tbody>
</table>

Table legends: Gp= groups; I = Low intensity group; II = High intensity group; Control_L = no exercise/rest in low intensity group; Control_H = no exercise/rest in high intensity group; † Low intensity = Pink ball/Low resistance - 25 rep with 30sec Rest, total 5min; ‡ High intensity = Black ball/High resistance - 12rep with 30sec Rest, total 5 min. Tx= treatment; Bf= Skin blood flow; M=mean; CI= 95% confidence interval; SD= standard deviation; CS = change scores; ES= Effect Size (pre -post/pooled SD); * significance level at p<0.05
Table 4.3: Summary of results for sensory perception thresholds at 2000Hz and 5Hz from ring finger.

<table>
<thead>
<tr>
<th>Gp</th>
<th>Low Intensity †</th>
<th>Control_L</th>
<th>High intensity ‡</th>
<th>Control_H</th>
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<tbody>
<tr>
<td>Tx</td>
<td>Before</td>
<td>After</td>
<td>CS</td>
<td>ES</td>
</tr>
<tr>
<td>Aβ</td>
<td>M: 8.6</td>
<td>M: 9.1</td>
<td>0.5</td>
<td>-0.08</td>
</tr>
<tr>
<td></td>
<td>SD: 1.95</td>
<td>SD: 3.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: (7.6-</td>
<td>CI: (7.2-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.5)</td>
<td>-10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>M: 13</td>
<td>M: 13.1</td>
<td>0.3</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>SD: 3.8</td>
<td>SD: 4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CI: (11-</td>
<td>CI: (10-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14)</td>
<td>15)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table legends: Gp= groups: I = Sequence in low intensity group; II = Sequence in high intensity group; Control_L = no exercise/rest in low intensity group; Control_H = no exercise/rest in high intensity group; † Low intensity = Pink ball/Low resistance - 25 rep with 30sec Rest, total 5min; ‡ High intensity = Black ball/High resistance - 12rep with 30sec Rest, total 5min; Tx= treatment; M=mean; CI= 95% confidence interval; SD= standard deviation; CS= change scores; ES= Effect Size (pre-post/pooled SD); * significance level at p<0.05; R-CPT = Ranged Current Perception Threshold test; Aβ= RCPT at 2000Hz; C =RCPT at 5Hz
Figure 4.1: Flow chart for the study design (Cross-over AB/BA):

Low Intensity gp

Exercise
Low-intensity
25 rep -30sec rest.
(5 min)

No
Exercise

High Intensity gp

Exercise
High-intensity
12 rep-30 sec rest.
(5 min)

No
Exercise

Pretest
TiVi, RCPT

Post-test
TiVi, RCPT

Post-test
TiVi, RCPT

Post-test
TiVi, RCPT

Figure legends: R= randomization; gp = group; 10 min= washout period; TiVi= tissue viability imager; rep= repetitions; sec. = seconds; RCPT= Range current perception threshold at 2000 Hz & 5 Hz.
Figure 4.2: Superficial palmar blood flow responses before and after exercise & control

Figure 4.3: Responses from sensory perception thresholds at 2000Hz before and after exercise & control
Figure 4.4: Responses from sensory perception thresholds at 5Hz before and after exercise and control.
Figure 4.5: i) TiVi images over the palmar region in High intensity group (rest followed by high intensity exercise) Images appear blue in beginning, if blood flow increases images appear yellow, orange or red on scale
Figure 4.5: ii) TiVi images over the palmar region in Low intensity group (low intensity exercise followed by rest)

Images appear blue in beginning, if blood flow increases images appear yellow, orange or red on scale
CHAPTER 5

General Discussion and Future Directions
Preamble to the chapter

This chapter revisits the key findings of the thesis and discusses the implications of these results on clinical practice. Limitations of the research along with future recommendations are also outlined.

5.1 Overview of this thesis

The overall theme in this thesis was to observe and report short term effects of thermal, ultrasound and exercise interventions on superficial blood flow and sensory perception thresholds (sPT for A-beta and C fibres) in the hands of healthy volunteers and patients with DRF with a focus on rehabilitation after immobilization (cast removal) in wrist fractures.

The specific objective of this thesis was in three parts. Firstly, to determine the effects of Immersion in cold water evaluation protocol on superficial blood flow, skin temperature and sensory perception thresholds at 2000 Hz (for A-beta fibres which detect touch and pressure) and 5 Hz (for C fibres which detect slow pain, temperature, and are post ganglionic sympathetic) in the injured and uninjured hands of patients with DRF, during 6th week after the cast removal. Secondly, to determine the effects of 3 MHz pulsed ultrasound and 1 MHz continuous ultrasound on superficial blood flow, skin temperature and sensory perception thresholds at 2000 Hz and at 5 Hz in the distal forearms of healthy volunteers. Thirdly, to determine the effects of low intensity and high intensity hand exercises on superficial palmar blood flow and sensory perception thresholds at 2000 Hz and 5 Hz in the hands of healthy volunteers.

The findings of this thesis are:

1. Through the first study we demonstrated that normal thermo-physiological responses such as ‘hunting reaction’ or cold induced vasodilation, digital
rewarming and unaltered C fibre activity can occur in both the injured and uninjured hands after ICE protocol. ICE was effective in reducing skin temperature and changing superficial blood flow and sPT’s at 2000 Hz in the fractured hand after cast removal. These findings indicate that minimal cutaneous vascular, sensory, sympathetic dysfunction or cold intolerance occurs in patients with closed reduction and casting with no obvious signs of other injuries/complications following a DRF. These findings also suggest that cold water immersion as applied in this study if used as therapeutic dosage, can induce some therapeutic effects associated with ‘hunting response’; like reducing pain and acute swelling, and might also induce a hypoalgesic effect; through its reductions in skin temperature and increases in sensory perception thresholds of large diameter, myelinated A beta fibres during the rehabilitation of DRF.

2. Through the second study, we demonstrated that small to moderate changes in skin blood flow, skin temperature and sensory nerve perceptions should be expected with brief exposure to US therapy. These findings also suggest a potential for ultrasound to modulate the pain pathway through alterations in C fibre perception thresholds (at 5 Hz). While our study does not provide an indication about a therapeutic dosage, it does suggest that 3 to 5 min applications may not be producing substantial superficial therapeutic effects. This would suggest that future studies looking at physiological effects of ultrasound on blood flow, temperature and sensory function should move towards investigating larger dosages and patient populations.

3. The third study found a lack of short term physiological changes in superficial palmar cutaneous blood flow and sensory perception thresholds following brief low intensity or high intensity hand exercise. It is presumed that the exercise protocol used in this study did not elicit any cutaneous thermoregulatory responses (no change in internal tissue temperature) but
might have stimulated non-thermoregulatory responses from the exercising muscle tissue (exercise pressor reflex and/or excess post exercise oxygen consumption).

5.2 What is already known on this subject?

1. A survey by Michlovitz et al.,\(^1\) and Bruder et al.,\(^2\) found that an exercise program and the use of heat or cold modalities were the most frequent interventions provided by therapists for the patients with DRF after cast removal.

2. According to the AAOS recommendations,\(^3\) ultrasound and/or ice are options for adjuvant treatments after distal radius fracture. There were only two randomized control trials in the literature that examined techniques of physical agents or electrotherapeutic modalities after DRF in adults.\(^4,5\) The findings in DRF\(^4\) suggest that cryotherapy in the form ice pack was beneficial and reduced pain and swelling up to 5 days when compared to pulsed electromagnetic therapy or sham.\(^4\)

3. An advice plus exercise program provided some additional benefits over no intervention for adults following distal radius fracture.\(^7\) These authors also proposed that review of patients at the time of, or near to, cast removal and again a few weeks later, provides physiotherapists with an opportunity to detect complications which might have been overlooked or have had delayed diagnosis.\(^7\)

4. There are also reports of complications from a large cohort study (275 patients) following DRF,\(^6\) like reflex sympathetic dystrophy (RSD) (20%), median nerve compression (22%), tendonitis or tenosynovitis (14%), and radial nerve compression (11%),\(^6\) which are often thought to be either missed or overlooked by the treating therapist.\(^7\) Injury to the peripheral
vasculature, defective vasoregulation, and nerve injury have been suggested as possible routes to cold intolerance.\textsuperscript{8,9} Cold intolerance was found in 38% of patients with hand fractures and this can be severely disabling for some patients.\textsuperscript{10}

5. Cryotherapy is used to reduce pain and swelling after DRF,\textsuperscript{1,4} but if an underlying neurovascular dysfunction exists such as reflex sympathetic dystrophy, or median nerve compression,\textsuperscript{11} then it would be detrimental for patients to continue treatments with cold modalities.

6. There was one randomized trial\textsuperscript{5} which looked at changes in range of motion (ROM) rather than pain or functional outcomes after the treatment of wrist with pulsed US. These authors found that low intensity pulsed US (5 min) over the dorsal aspect of fracture, did not improve the wrist ROM assessed at 2\textsuperscript{nd} and 8 weeks after cast removal when compared to the controls.\textsuperscript{5} In spite of the weak evidence, a survey by Michlovitz et al.,\textsuperscript{1} showed that over 50% of therapists opted for ultrasound and other adjunct modalities to treat patients during the rehabilitation of DRF.

7. We could not find any clear standard guidelines for US dosage in the literature.\textsuperscript{12}

8. There is also scarcity of RCT’s which have looked at the effects of different intensities of hand exercises in the healthy and DRF population.

9. A recent systematic review of 15 trials on the effectiveness of various rehabilitation techniques following DRF, managed conservatively or surgically (involving 746 adults) has concluded that, overall there is insufficient evidence to support the relative effectiveness of different interventions during the immobilization as well as mobilization phase after DRF.\textsuperscript{13}
5.3 What this thesis adds to knowledge base?

1. After an exposure to the ICE protocol, normal thermo-physiological responses such as ‘hunting reaction’ or ‘cold induced vasodilation,’ digital rewarming and unaltered C fibre activity can be expected in both the injured and uninjured hands of patients with DRF after cast removal. This also indicates the absence of abnormal neurovascular function after cold exposure in this uncomplicated patient group.

2. The thesis demonstrated across different constructs including exercise, sonation and thermal exposures that the TiVi system is a simple non-invasive method, able to capture data on superficial circulation. It was able to identify exposures that changed cutaneous circulation (cold and US) and one that did not (exercise). Similarly, infrared digital thermometer also captured changes in temperature across studies.

- As measured on the TiVi, the ICE protocol led to a significant increase in superficial blood flow (palm and distal forearm) along with a decrease in skin temperature (index and little fingers) immediately after immersion, and then showed a trend towards rewarming in fingers with the superficial blood flow reverting to their pre-immersion values by 10 min.
- There were significant reductions in superficial blood flow and skin temperatures over the treatment area after sonation with pulsed US (3 MHz, 1:4, 0.25W/cm², 5 min) and continuous US therapy (1 MHz, continuous, 0.8 W/cm², 3 min).
- Superficial palmar blood flow remained unaltered with the two types of hand exercises suggesting minimal impact of 5 min of hand exercises on the superficial skin blood flow.
3. The thesis has also demonstrated across studies that, the R-CPT test is able to capture sensory responses from ring finger (innervated by median and ulnar nerves) after exposure to exercise, ultrasound and cold. It was able to identify exposures that changed sensory perceptions (cold and US) and the ones that did not (exercise).

- The ICE protocol changed R-CPT responses at 2000Hz in the injured hand after DRF, suggesting that large diameter, myelinated A-beta nerve fibres are more responsive to cold application, and the C fibres have a negligible effect with cold immersion.\textsuperscript{14} These findings indicate normal cold response in the uncomplicated fractured hand and also suggest that, exposure to cold water immersion for a brief period can induce some therapeutic effects.

- The findings on R-CPT after two types of US showed that C fibres were more sensitive to US,\textsuperscript{15,16} than the A-beta fibres, suggesting their potential role in pain modulation via sensory inputs (temperature and pain) and possible contributions to blood flow changes via sympathetic neural pathways. Hence, the sensory and vascular changes observed with US therapy may have a beneficial effect on the injured tissue, and this needs further investigation in DRF population.

- Exercise had no effect on R-CPT scores at 2000 Hz or at 5 Hz. The lack of change in the C fibres (that carry sympathetic signals) is consistent with a lack of change in superficial palmar blood flow after the hand exercise, since the palmar skin is supplied only by sympathetic vasoconstrictor nerves. This is because of the anatomical variation in the palmar skin, which gets innervation from the sensory and sympathetic vasoconstrictor nerves, contrary to the hairy skin which also gets innervated by the sympathetic vasodilator nerves.\textsuperscript{17} Hence, any vasoconstriction or vasodilation in the palmar skin after the exercise
could have been attributed to either the stimulation or inhibition of sympathetic vasoconstrictor nerve fibres.

Therefore it can be presumed that, the changes observed in C fibres after US therapy in healthy volunteers, the vascular responses in ‘hunting reaction’ along with changes in skin temperature and A-beta function after an exposure to cold in DRF hands, may have a beneficial effect on swelling, pain modulation and tissue healing after fracture, which needs further investigation in this patient group.

5.4 Limitations:

1. This thesis forms only preliminary evidence since only short term effects were evaluated. Further, in two studies it was necessary to test people without a hand condition since normal responses had not been sufficiently delineated. This means that the implications for direct application in practice are limited.

2. While a cross-over design is efficient and we were able to find statistically significant changes in physiological effects, the small samples mean that uncommon vascular or sensory disorders, complications or atypical physiological effects were unlikely to be represented. Thus, the thesis findings apply to uncomplicated DRF cases treated with casting and may not apply where complications, pre-existing comorbidity or surgical intervention are present.

3. The vascular responses were tested with the TiVi system which only captures superficial blood flow and the extent to which this reflected the vascular responses in deeper tissues is unknown.

4. The clinical benefit of vascular and sensory changes on clinical outcomes is uncertain and was not addressed.
5. Healthy individuals were able to sit and wait for around 2 hours to complete each cross over trial (either US or exercise) on same day, but we do not know how patients would tolerate such protocols. Though Neurometer CPT has automatic double blind testing programs, before it displays one score (one reading), for one nerve fibre, the test has to be repeated multiple times (7-10 cycles) and the participants are required to be alert to give correct responses. For testing two nerve fibres in sequence, it takes more than 60 cycles to display the CPT scores. Hence, by the end of the trial majority of the healthy participants felt tired. Therefore, we do not know if patients could have tolerated such long hours (approx. 2 hours), if they had to undergo US or exercise protocol similar to the cross over trial used for healthy subjects. Testing could have been done on two different days, but the diurnal variations occurring in human body might have led to some variability in the skin blood flow and temperature responses. These practical issues affect how many different constructs or treatment variations can be assessed within one study.

6. Since we were unsure of the normal vascular and sensory responses to US and exercise, we tested people without hand pathology and did not measure their impact in the DRF population. These studies could have given us important information regarding patient responses to US therapy and exercise during their transition from immobilization phase to mobilization phase.

7. Sensory perception thresholds were recorded from the tip of ring fingers (dermatome supplied by C7 and C8), instead of the treatment area in order to follow the recommended guidelines of the manufacturer, and to avoid any unwanted motor point stimulation (muscle contraction) and thus may not reflect sensory changes in the complete area of application. Since the ring finger gets innervation from both the median and ulnar nerves, responses
may have been different in different fingers which are supplied by only one of these nerves. However, if changes occurred in either nerve, they should have measured in this finger.

8. The previous reports on CPT testing showed no difference between the responses from C fibres and A-delta fibres.\textsuperscript{18} Hence, to reduce response burden we decided to include two types of nerve fibres in this research; the large diameter myelinated A-beta fibres and the small diameter unmyelinated C nerve fibres. Inclusion of A-delta fibres could have given a better idea about the responses from all subtype of nerve fibres.

9. Real time measurements of skin blood flow and skin temperature over the treatment area during US therapy or hand exercises was not possible because of the continuous movement of transducer head and movement of fingers, which were in turn blocking the view of images. This is considered a minimal limitation since very transient effects are unlikely to have therapeutic value.

5.5 Implications of thesis findings on practice:

1. Tissue viability imaging system and Neurometer CPT/C device, are promising tools that can be used in Physiotherapy (PT) for the evaluation of sensory, sympathetic nerve responses (via C fibres) and cutaneous vascular responses noninvasively, during some of the important timelines in DRF rehabilitation or during the transition from immobilization to mobilization phase or after any other injury. These findings can also assist a PT to plan or modify physiotherapy treatment and thereby help to prevent complications (if any).

2. The treatment tested in this thesis did not have any adverse effects and hand exercise had inconsequential effect on sensory or vascular function suggesting that the interventions tested were safe.
3. Ultrasound and cryotherapy were potentially efficacious in changing skin blood flow, skin temperature and sensory function over the areas of application in the injured and uninjured hands suggesting possible clinical benefits in patients with different hand conditions.

4. The TiVi and Neurometer/CPT devices were feasible for use in clinical settings and provide information that complements clinical examination and special tests.

**5.6 Research recommendations:**

1. The two US doses (1MHz and 3 MHz) selected in this study were based on the empirical evidence and therapeutic principles of US therapy.\(^{19}\) There is a need to develop US therapy dosage guidelines for different disorders. Therefore, specific dosage trials which include longer application times and/or stronger dosages are needed to determine the threshold and range of short term physiologic effects. Longer term trials that investigate physiologic and clinical outcomes after typical treatment conditions are needed.

2. The two US dosages used in this study produced some clinical changes in people without hand pathology and may have more substantive effects in patients with DRF. Pain, swelling and deformity after DRF are reported to cause impairment and disability in these patients. Hence, clinical studies should assess short term and long term effects of US on patients with DRF and for specific indications like tendon adhesions/lack of glide or pain. These studies should include symptom and functional measures like, numeric pain rating scales and patient rated wrist and hand evaluation questionnaires along with biological measures like, Ti Vi, Neurometer and infrared thermometer.
3. Some complications after DRF are reported to have been overlooked or missed by therapists during rehabilitation. Hence, based on the type of injury, TiVi, skin temperature and Neurometer should be used to measure sensory and vascular responses at important timelines after DRF (after cast removal, 3 mon. and 6 mon. etc.). This will provide important insight into the development of any complications and help treatment providers in the early detection and secondary prevention.

4. It has also been reported that after hand fractures patients are more prone to develop cold intolerance. Hence, the brief 5 min ICE protocol has a double advantage; as an assessment tool to find out cold intolerance along with changes in skin temperature, sensory perceptions and vascular responses; and also as a physical agent modality to help with healing after cast removal in DRF. Hence, we recommend using 5 min of immersion in cold water as either a therapeutic dosage or to test vascular responses as described in the ICE. Future studies should address its long term effectiveness as an adjunct in hand rehabilitation and report changes in pain, swelling, range of motion and number days to return to work; or the prognostic value when used to assess patients.

5. Given the dosage of exercise had minimal circulatory or sensory impact, it can be considered safe for testing in patients and those with comorbid health conditions. Vascular adaptations to exercise training in the cutaneous vessels have been reported in studies. Hence, both short term and long term impacts of exercise training, using the strength or endurance type protocols should be tested in different subgroups of people with hand conditions using the TiVi and Neurometer.
5.7 References:


20. Traynor R, MacDermid JC. Immersion in cold-water evaluation (ICE) and self-reported cold intolerance are reliable but unrelated measures. Hand (N Y). 2008; 3(3):212-9.
Appendix 1A

Ethics approval for the thesis
Principal Investigator: Dr. Joy MacDermid  
File Number: 102884  
Review Level: Full Board  
Approved Local Adult Participants: 80  
Approved Local Minor Participants: 0  
Protocol Title: Short Term sensory and vascular responses to physical agent modalities and exercise in the hands of healthy volunteers and patients with Distal radius fracture  
Department & Institution: Schulich School of Medicine and Dentistry/ Surgery, Western University  
Sponsor:  
Ethics Approval Date: November 08, 2012  
Ethics Expiry Date: August 31, 2014

Documents Reviewed & Approved & Documents Received for Information:

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<th>Document Name</th>
<th>Comments</th>
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<tr>
<td>Western University Protocol</td>
<td>Including all instruments listed in section 8.1.</td>
<td></td>
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<tr>
<td>Letter of Information &amp; Consent</td>
<td>Healthy Volunteer</td>
<td>2012/10/12</td>
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<tr>
<td>Letter of Information &amp; Consent</td>
<td>DRF participant</td>
<td>2012/10/12</td>
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</tbody>
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This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICCH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000946.

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**Ethics Officer to Contact for Further Information**

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This is an official document. Please retain the original in your files.
Appendix 2 A

Screening and data collection form used for chapter 2
Cold water immersion study data collection form - DRF group ID:

- Name:
- Age:
- Gender: □ M □ F
- Occupation:
- Type of injury:
- Type of Treatment: □ ORIF □ Closed reduction
- Hand affected: □ Right □ Left
- Dominant Hand: □ Right □ Left

Screening DRF patients who Do not have the following:

- Recent injury or disease in neck and any upper extremity within the past year (2011)
- <18 or >65 yrs. of age
- Revision/second surgery
- Complex fracture/multiple fractures
- Had any treatment offered by any hospital for the same or other symptoms
- Heart disease
- Do you have cold sensitivity when exposed to cold environments, such as numbness tingling and burning pain in fingers? Or observed any colored or dark urine during winters? Or developed any rashes or bluish colored skin after touching ice?
- Autoimmune disorders (Systemic lupus erythematosis, Rheumatoid Arthritis etc.)
- Pregnancy
- Cancer/radiation within past 6 months
- Diabetes
- Have had any stroke or spine injury or any altered sensation in your limbs previously?
- Had any episodes of epilepsy or convulsions or fits previously?
- Have Skin Bruising/ Skin Infection/Open wound/bleeding disorders/skin rashes/redness
- Have any problems related to blood flow or circulation? Or taking any medicines like blood thinners or anticoagulants?
- Inability to understand instructions
• Deficits in sensation in the area to be treated (B/L Dermatome sensory test = )
• Decreased circulation in the area to be treated (B/L Digital patency test = )

Assess area to be treated:

• Sensory skin awareness test, using a pen or tooth pick and hot or cold to distinguish between sharp, dull, hot and cold sensation in the hand with eyes closed.

□ Normal □ Abnormal

• Cold reaction test: Before starting cold water immersion in DRF patients. The investigator rubs small piece of ice cube over the normal skin site for 2 min and checks for any adverse reactions of swelling or urticaria or bluish discoloration until 5 min later.

Any Impaired sensation? □ Yes □ No [If there is no abnormal response proceed to testing]
Testing and recording data:

<table>
<thead>
<tr>
<th>Hand 1</th>
<th>Pre Test</th>
<th>ICE</th>
<th>Post Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiVi</td>
<td>Aβ</td>
<td>C</td>
<td>temp</td>
</tr>
<tr>
<td>Index</td>
<td>little</td>
<td></td>
<td>TiVi</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Aβ</td>
</tr>
<tr>
<td></td>
<td>0min</td>
<td></td>
<td>1min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Switch to other hand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand 2</td>
</tr>
<tr>
<td>Pre Test</td>
</tr>
<tr>
<td>TiVi</td>
</tr>
<tr>
<td>Index</td>
</tr>
<tr>
<td>0min</td>
</tr>
<tr>
<td>1min</td>
</tr>
<tr>
<td>10min</td>
</tr>
</tbody>
</table>

*Stopped/paused at the end of cold water immersion or before 5 min?

☐ Yes ☐ No If yes, Reason: ________________

*other symptoms at the end of test:

- Any skin irritation-
- Pins and needles or tingling-
- Unusual skin color change(pale/blue) –
- Any other adverse reaction (Shivering/burning pain)
Appendix 3 A

Screening and data collection form used for chapter 3
Ultrasound study data collection form-Healthy volunteers

- Name
- Age
- Gender □M □F
- Occupation
- Dominant hand □R □L

Screening Healthy subjects who **Do not** have the following:

- Recent injury to neck, shoulder, elbow, wrist, or hand within the past year (2011)
- <18 or >50 yrs. of age
- Skin Bruising/ Skin Infection/Open wound.
- Deficits in sensation in the area to be treated (B/L Dermatome sensory test = )
- Decreased circulation in the area to be treated (B/L Digital patency test= )
- Neurovascular injuries
- Pregnancy
- Presence of a pacemaker/ monitoring device
- Malignancy/Cancer
- Hypertension/Cardiac failure
- Inability to understand instructions

Assess area to be treated:

- Sensory skin awareness test, using a **pen or tooth pick** to distinguish between sharp and dull sensation in the hand with eyes closed. □Normal □Abnormal
- Sensory discrimination test, over the area to be treated using, **2 test tubes** (1 hot and 1 cold) to distinguish between hot and cold with eyes closed. □Normal □Abnormal

**Any Impaired sensation?** □Yes □No [If there is no abnormal response proceed to testing]
Testing and recording data:

<table>
<thead>
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<th>Pre Test</th>
<th>US</th>
<th>Post Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand I</td>
<td>Tivi</td>
<td>Aβ</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3MHz</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tivi</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25 min washout period</td>
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</table>

<table>
<thead>
<tr>
<th>Cont. US group</th>
<th>Pre Test</th>
<th>No US</th>
<th>Post Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand 2</td>
<td>Tivi</td>
<td>Aβ</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>rest</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tivi</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25 min washout period</td>
</tr>
</tbody>
</table>

*Stopped/paused at end of Ultrasound therapy or before completion of therapy (Pulsed and Continuous)? □Yes □No

If yes, Reason: _________________
*other symptoms at the end of test:

- skin irritation/swelling/heat-
- Any Pain or discomfort -
- Any other adverse reaction-
Appendix 4 A

Screening and data collection form used for chapter 4
Exercise study data collection form- Healthy volunteers

- Name
- Age:
- Gender: □ M □ F
- Occupation:
- Dominant Hand: □Right □Left
- Does hand exercise: □Yes □No

Screening Healthy subjects who Do not have the following:

- No recent injury or disease at neck and upper extremity within the past year (2011)
- <18 or >50 yrs. of age
- Pregnancy/ menstruation
- Cancer
- Osteoporosis
- Dislocations
- Ligament tears/injuries
- Skin Bruising/ Skin Infection/Open wound/Swelling
- Neurovascular injuries
- Deficits in sensation in the area to be treated (B/L Dermatome sensory test = )
- Decreased circulation in the area to be treated (B/L Digital patency test= )
- Inability to understand instructions
- Open & close fist

Assess area to be treated:

- Sensory skin awareness test, using a pen or tooth pick to distinguish between sharp and dull sensation in the hand with eyes closed.
  □Normal □Abnormal

Any Impaired sensation? □Yes □No [If there is no abnormal response proceed to testing]
Testing and recording data:

<table>
<thead>
<tr>
<th>Low intensity group</th>
<th>Pre Test</th>
<th>Exe</th>
<th>Post Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand 1</td>
<td>Tivi</td>
<td>Aβ</td>
<td>C</td>
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</table>

10 min washout period

<table>
<thead>
<tr>
<th>High Intensity group</th>
<th>Pre Test</th>
<th>Rest</th>
<th>Post Test</th>
</tr>
</thead>
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<tr>
<td>Hand 2</td>
<td>Tivi</td>
<td>Aβ</td>
<td>C</td>
</tr>
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</table>

10 min washout period

<table>
<thead>
<tr>
<th>Hand 2</th>
<th>Pre Test</th>
<th>Exe</th>
<th>Post Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tivi</td>
<td>Aβ</td>
<td>C</td>
</tr>
</tbody>
</table>

*Stopped/paused at the end or before completion of exercise therapy or RPE more than 4-6 (Low intensity and High intensity exercise)? □ Yes □ No

If yes, Reason: _________________
*other symptoms at the end of test:

- Breathlessness
- Any Pain or discomfort
- Any other adverse reaction
Curriculum Vitae

Name: Shaguftha Sultana Shaik, PT, PhD.

Post-secondary education:

<table>
<thead>
<tr>
<th>Degree</th>
<th>Institution/Place</th>
<th>Department</th>
<th>Year</th>
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<tr>
<td>PhD</td>
<td>Western University, London, Canada</td>
<td>Physiotherapy (PT)</td>
<td>2009-2013</td>
</tr>
<tr>
<td>BA IS (c)</td>
<td>Islamic Online University, Doha, Qatar</td>
<td>Islamic studies</td>
<td>Since August 2011</td>
</tr>
<tr>
<td>MPT Cardiopulmonary</td>
<td>Jamia Hamdard New Delhi, India</td>
<td>Physiotherapy</td>
<td>2006-2008</td>
</tr>
<tr>
<td>BPT</td>
<td>Kakatiya College of Physiotherapy, Warangal, India</td>
<td>Physiotherapy</td>
<td>2000-2005</td>
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Related work experience in educator role:

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<th>Course name</th>
<th>Year</th>
<th>Teaching assistant/GRA</th>
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<tr>
<td>PT9526</td>
<td>Winter 2010</td>
<td>PT in Acute Care settings I</td>
</tr>
<tr>
<td>PT9510</td>
<td>Fall 2010</td>
<td>Professional practice in PT</td>
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<tr>
<td>PT9535</td>
<td>Fall 2010</td>
<td>PT in Rehab Settings II</td>
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**Related work experience in physiotherapy field:**

(Member of Indian Association of Physiotherapists, India)

<table>
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<tr>
<th>Role</th>
<th>Institute/organization, Place</th>
<th>Year</th>
</tr>
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<tr>
<td>Editorial board member (invited)</td>
<td>International journal of physiotherapy research &amp; practice.</td>
<td>Since August 2013</td>
</tr>
<tr>
<td>Physiotherapist (online consultant)</td>
<td>Association of Muslim Professionals, India.</td>
<td>Since August 2010</td>
</tr>
<tr>
<td>Physiotherapist</td>
<td>Shaphe Physiotherapy Clinic, New Delhi, India.</td>
<td>August 2006- July 2009</td>
</tr>
<tr>
<td>Physiotherapist</td>
<td>Alfa Diagnostics &amp; Shifa Clinic, Hyderabad, India.</td>
<td>October 2005- June 2006</td>
</tr>
<tr>
<td>Trainee PT (voluntary work)</td>
<td>Kakatiya Physio Care Centre, Warangal, India.</td>
<td>November 2004- September 2005</td>
</tr>
</tbody>
</table>
**Publications:**


Shaguftha SS, Nelima, Rajan G. Effects of different body positions on forced expiratory lung volumes in healthy volunteers. BPT research project available in the archives of NTR University of Health Sciences, Vijayawada, India, 2004.