EFFECTS OF OSTEOPATHIC TREATMENT ON LEG BLOOD FLOW AND SKIN TEMPERATURE IN CHRONIC SCI

THE EFFECTS OF OSTEOPATHIC TREATMENT ON COMMON FEMORAL ARTERY BLOOD FLOW AND SKIN TEMPERATURE IN SPINAL CORD INJURED AND ABLE-BODIED INDIVIDUALS

By

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ABSTRACT

Individuals with spinal cord injuries (SCI) are prone to significant alterations in vascular structure and function. These alterations can lead to many secondary complications, including an increased risk of mortality. This study was designed to examine the effects of osteopathic treatment on blood flow and skin temperature in the lower extremities of individuals with SCI. Previous research has shown that prolonged, electrically stimulated or assisted exercise results in increases to leg blood flow in SCI individuals while passive movement approaches result in minimal, or no, increases in leg blood flow. Pressure sores are a major secondary health complication in SCI individuals, and are associated with decreased skin blood flow, reduced healing potential and change in baseline and reactive skin temperature. A prime goal of osteopathic treatment is to alleviate restrictions in blood flow that may limit the capacity of the body to heal itself. There is, however, a lack of research examining the effects of osteopathic treatment in individuals with SCI. Thus, the goal of this study was to determine the acute effects of 3 different sessions of osteopathic treatment on mean leg blood flow (MLBF) in the left common femoral artery (CFA) and skin temperature at various sites on the lower limb of individuals with chronic SCI compared to able-bodied (AB) individuals. **Methods:** Nine individuals (eight male; age 44 ± 17.5 years) with a chronic SCI (C6-T12; AIS A-B; 3.7 ± 4.6 years post-injury) and six AB individuals (five male; 38.3 ± 9.7 years) participated in our study. The protocol consisted of 1familiarization and interview session of 40 minutes (Control) and 3 osteopathic treatment sessions at 7 day intervals, where our participants received osteopathic manual therapy (OMT) focusing on the cranium, abdomen and the lower extremities. Doppler ultrasound was used to determine the

diameter and mean blood velocity in the CFA before (Pre) and after (Post) each session. Skin temperatures were measured using skin thermistors at three different sites on the left leg of all participants. Change scores were calculated for each measure as post-treatment minus pre-treatment. **Results:** Two-way ANOVA statistical analysis revealed a between group difference in the maximal change in MLBF with SCI participants showing an increase in flow of 16±2 ml/min, and AB participants showing a decrease in flow of 25±2 ml/min ($p = 0.04$) over time for all conditions. There were no differences in absolute MLBF at baseline or delta MLBF between treatment days. There was also a main effect for group in the change in skin temperature at all sites with the magnitude of the reduction in temperature over time being smaller in individuals with SCI versus AB(left thigh: SCI, -0.5±0.2° C; AB, -1.2±0.2°C, $p<0.01$), (left calf: SCI, -0.2±0.2°C; AB -1.2± 0.3°C, $p<0.03$), (left foot: SCI, -0.1±0.4°C; AB, -1.8±0.4°C, $p<0.01$). **Conclusion:** All treatments (OMTs and Control) visit resulted in small increases in MLBF in the SCI group versus small decreases in the able-bodied group. All treatments resulted in decreases in skin temperature over time but the magnitude of these decreases were smaller in the SCI versus the AB group potentially indicating reduced skin temperature reactivity. Despite the lack of OMT specific treatment effects in comparison to the Control condition, the current findings emphasize the potential for different physiological responses to interventions in individuals with SCI compared to AB individuals.

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CHAPTER 1

1 LITERATURE REVIEW

1.1 *Spinal Cord Injury*

The effects of any paralysis resulting from a traumatic spinal cord injury (SCI) can be catastrophic to the injured individual (Weinberg & Solot, 1985). These effects are life altering in many different ways and limit the independence of the individual. In addition to the devastating nature of partial or complete paralysis, there are also secondary complications that arise, creating a future strain on the quality of life within these individuals. Many of these secondary complications are resultant effects, but can, in turn, cause many other problems.

It is the purpose of this thesis is to deal with aspects of the circulatory system within the lower extremity following SCI. The importance of the spinal cord to homeostasis is profound and with a SCI, many systems of the body can become impaired. The area of SCI research is continuing to advance and develop and there has been significant progress addressing the physical and psychological effects of SCI. The ultimate goal for research related to SCI focuses on the reestablishment of full neurological control below the level of the lesion. Until this goal is realized, however, research also continues to address other factors affecting individuals with a SCI, including the progression and development of secondary complications.

There are currently many different approaches pertaining to the care and treatment of individuals with SCI. These approaches cover many different aspects of life with an SCI and include psychological, social, economic and physical factors. Within the

physical element of rehabilitation, a significant amount of research continues. Some research continues to search for answers surrounding the ultimate goal of spinal cord repair while other research addresses other issues including secondary complications. The focus of the current research is on the effects of osteopathic treatment (OT) on blood flow in the lower extremity of individuals with chronic SCI and how this could potentially reduce secondary complications in SCI.

Those individuals who have sustained damage to the spinal cord within the cervical spine are labeled as tetraplegic, or quadriplegic, in that both the upper and lower extremities have been affected to some degree, respectively. Those individuals who have sustained an injury to the spinal cord below the cervical spine are then termed paraplegic and have use of their upper extremities, but may have significant impairment of the lower extremities, trunk, and pelvic organs. SCI can thus be labeled according to the level of the lesion and the resultant degree of damage. The injuries are listed as complete or incomplete, where an incomplete injury results in a partial preservation of motor and sensory functions above the level of the injury. A complete SCI is then, according to the International Standards Classifications of SCI, an absence of sensory and motor function in the lowest spinal segment (Maynard, Jr., Bracken, Creasey, Ditunno, Jr., Donovan, Ducker et al., 1997). These complete or incomplete injuries are then further subdivided by the American Spinal Injury Association (ASIA) within the ASIA Impairment Scale (AIS). According to the AIS, degree of impairment is categorized on an 'A' to 'E' scale where 'A' represents a complete sensory and motor function loss, 'B' to 'D' are varying degrees of incomplete damage, and 'E' is normal (Maynard et al., 1997).

Secondary complications resulting from SCI are widespread and include the development of pressure sores, urinary tract infections, diabetes, joint degeneration, respiratory complications and cardiovascular disorders (Johnson, Gerhart, McCray, Menconi, & Whiteneck, 1998; Ditor & Hicks, 2009). It was the purpose of the current research to focus on the cardiovascular system in chronic SCI and, in particular, regulation of blood flow and skin temperature in the lower extremities. In this section of the literature review, specific factors surrounding SCI including prevalence, mortality, secondary complications including pressure sore development, dysreflexia and the role of peripheral blood flow in secondary complications will be reviewed.

1.1.1 Etiology and Epidemiology

Statistics on SCI incidence rates taken from within Canada vary according to the reference (Ho, Wuermser, Priebe, Chiodo, Scelza & Kirshblum, 2007; International Campaign, 2004; Pickett, Campos-Benitez, Kellar & Duggal, 2006; Spinal Injury, 2006; Spinal Cord, 2008; Farry & Baxter, 2010). Reasons for these variances are widespread and include lack of, or, inaccurate reporting. With the potential discrepancies in reporting, the estimation of incidence and prevalence of SCI in Canada and worldwide can be quite difficult.

SCIs can be divided into two groups; traumatic SCI and non-traumatic SCI. Traumatic SCIs occur when the spinal cord is damaged as a result of an external physical impact. Non-traumatic SCIs occurs when a health condition such as disease, infection or a tumour damages the spinal cord. It is the non-traumatic SCI that creates greater challenges when estimating the prevalence and incidence of SCI. This type of SCI is, often, under-reported. In part, this is due to the fact that there is no specific standard or

consensus on what defines a non-traumatic SCI. As a result, there can be an absence of reporting for SCI. This, in turn, creates alterations in measures between studies and, ultimately, a lack of precision in estimations of incidence and prevalence (Rick Hansen Institiute, 2010).

The revised 2004 International Campaign for Cures of SCI Paralysis Global Summary of SCI states that there are approximately 27 injuries per million persons annually, which translates into 843 injuries per year in Canada (International Campaign, 2004). In total, based on this report, there were 30,000 Canadians living with a SCI within the country prior to 2004 (International Campaign, 2004). According to statistics taken from a Canadian Paraplegic Association Report in 2012, there are approximately 35 new cases per year per million persons(thespine.ca, 2012). Based on a current population within Canada of over 32,000,000 (Stats Canada), this translates into approximately 1,110 new cases of SCI per year. The Rick Hansen Institute currently estimates these totals to be higher. It is estimated that there are 1,785 new traumatic and 2,474 non-traumatic SCI each year. (Farry & Baxter, 2010). Regardless of the study, from 2004 to 2012, there has been a notable increase in the incidence of SCI in Canada.

According to the Rick Hansen Institute, the estimated prevalence of individuals within Canada currently living with an SCI is 85,556 persons (0.25% of the population). Of this total, it is estimated that 43,974 (51%) are the result of traumatic injuries and 41,581 (49%) are the result of non-traumatic incidences. Upon further analysis of these totals, it is estimated that 37,313 individuals (44%) are tetraplegic and 48,243 individuals (56%) are quadriplegic. (Farry & Baxter, 2010). Pickett and colleagues studied age-adjusted epidemiology within Ontario and found that, incidence rates were 41.79 per

million persons with values of 41.76, 50.87 and 3.37 in adults aged 15-64, adults aged 65+ and children, respectively (Pickett et al., 2006).

A SCI occurs most frequently in the third and fourth decade of life (The Journal of Spinal Cord Medicine, 2012; Spinal Cord Injury, 2010). Of these individuals, 80.8% are male (Spinal Cord Injury, 2010; thespine.ca, 2012). This number decreased only slightlysince 1980, where the percentage of males was 81.8% (Spinal Cord Injury, 2010). Regardless of the study or country, it can be seen that the incidence of SCI per year and per population is devastating, especially in the younger male population.

According to the SCI Information Network and the National SCI Database, the most prevalent neurological category is incomplete tetraplegia (38.3%), followed by complete paraplegia (22.9%), incomplete paraplegia (21.5%) and complete tetraplegia (16.9%), (Spinal Cord Injury, 2010). Pickett and colleagues found that complete SCI accounted for 35% of cases and of all reported cases 75% of these individuals had cervical cord injuries (Pickett et al., 2006). Not only are there a high number of individuals living with SCI in Canada, but these individuals are living with varying degrees of impairment.

The greatest cause of traumatic SCI is motor vehicle accidents (Spinal Cord, 2008; thespine.ca, 2012). The SCI Statistical Center states that, since 2005, 41.3% of all reported traumatic SCI were the result of motor vehicle accidents (Spinal Cord, 2008) while thespine.ca suggests that, in Canada, 35% of all SCI's are the result of motor vehicle accidents (thespine.ca, 2012). Other studies have found higher results. Yeo and colleagues identified this percentage to be even greater at 55% (Yeo, Walsh, Rutkowski, Soden, Craven & Middleton, 1998), while the International Campaign for Cures of SCI

Paralysis (International Campaign, 2004), reported that over 50% of all SCI were related to motor vehicle accidents in Canada, the United States and Australia. Improved vehicle safety and driver safety may account, in part, for lower values in more recent years. The second greatest cause for SCI now is falls. The SCI Statistical Center reports that falls account for 27.3% of SCI, (Spinal Cord, 2010). Ho and colleagues (Ho et al., 2007), and Pickett and colleagues (Pickett et al., 2006), have also found similar results with averages of 23.8% and 31%, respectively. In patients over 65 years, this average rises sharply to 63% (Pickett, 2006). In fact, falls now account for the greatest increase in cause of SCI (Ho et al., 2007, Spinal Cord Injury, 2010). In contrast, the percentage of SCI associated with acts of violence has decreased from the 1990's to present by approximately 10% (Ho et al., 2007, Spinal Cord Injury, 2010), while SCI associated with sport has declined by over 5% (Ho et al., 2007). These two causes however remain the third and fourth most common causes of SCI (Ho et al., 2007, Spinal Cord Injury, 2010).

1.1.2 Mortality

With many mechanisms of incidence of SCI, there is a significant potential for other traumatic injuries to occur coincident with the SCI. Mortality within the first 24 hours following a traumatic SCI is not uncommon. The ability for all systems within the body to accommodate and adapt to significant change is a critical factor in the initial and subsequent stages of survival after a traumatic SCI. Due to the effects of decreased or absent neurological function at various levels and within various systems, there is an increased overall stress placed on the human body. Statistics with regards to life expectancy of individuals with SCI are both alarming and encouraging. As modern science and technology advances, so does the life expectancy of all humans, including

those with SCI. However, the fact remains that, on average, the life expectancy of individuals with SCI remains lower than that of individuals without an SCI (Spinal Cord Injury, 2010). Frankel and colleagues stated in a study spanning five decades, "the general mortality rates of individuals with SCI exceed those of an age-matched non-disabled population" (Frankel, Coll, Charlifue, Whiteneck, Gardner, Jamous et al., 1998, pg.272).

Serious SCI alone can lead to a fatality. It is estimated that, within the United States alone, 4000 individuals with SCI die before reaching the hospital and another 1000 die during their hospitalization (Sekhon et al., 2001). Based on the mechanism of injury, there is an even greater potential for other areas of the body to be seriously damaged. It is estimated that 20% to 57% of persons with SCI have other significant injuries including brain injuries or major chest injuries (Sekhon et al., 2001). In fact, only 20% of SCI traumas are isolated incidences (Sekhon et al., 2001).

The second area to consider with regards to mortality is the vertebral level of injury. Higher cervical injuries can impair or ablate respiratory and cardiovascular controls centers. According to Sekhon and colleagues, individuals with lesions at levels of C1-C3 have a 6.6 times greater mortality rate than individuals with paraplegic injuries. Similarly, individuals with lesions at C4 or C5 and from C6-C8 had 2.5 and 1.5 times higher mortality rates than individuals with paraplegic injuries (Sekhon et al., 2001). The same authors also noted a higher mortality rate among individuals with traumatic SCI in the cervical spine where the prevalence of cervical SCI is lower than the actual percentage of newly diagnosed SCI within the cervical spine (Sekhon et al. 2001).

A third area to consider is the severity of the spinal cord lesion. Individuals with a complete SCI, (AIS A), have a higher mortality rate than those individuals with an incomplete injury (AIS B-D), (Frankel et al., 1998). More recent statistics are showing that fewer traumatic SCI are complete. Improved medical technology and emergency medical services have improved immobilization immediately after injury that reduces the potential for further injury (Sekhon et al., 2001). For complete SCI, the greatest neurological recovery occurs in those individuals with more cephalad injuries (Sekhon et al., 2001). It is promising to consider that the most significant of SCI show definite abilities to heal to certain degrees.

Over the past few decades, there has been a definite shift in the cause of mortality for individuals with SCI (DeVivo, Kartus, Stover, Rutt & Fine, 1989; Frankel et al., 1998; Spinal Cord, 2006). In the earlier years of spinal cord rehabilitation, urinary tract infection was the dominate cause of death (Frankel et al., 1998) while renal failure was also a key contributor to death within the SCI population (Sekhon et al., 2001). With advancements in care and medical treatments in urology, this area of mortality has now substantially decreased (Spinal Cord, 2006; Spinal Cord Injury Facts and Figures, 2012). There has now been a shift in the leading causes of death amongst those individuals who have survived past the initial one to two years post-trauma. More recent research indicates that respiratory complications and, more specifically, pneumonia, are the most frequent contributors to death after SCI (DeVivo et al., 1989; Frankel et al., 1998; Spinal Cord Injury 2010; Strauss, DeVivo, Paculdo & Shavelle, 2006; Yeo et al., 1998).

Other major causes of mortality within the SCI population are septicemia,

non-ischemic heart disease and external injuries, including suicide (Frankel et al., 1998; Sekhon et al., 2001; Spinal Cord Injury, 2010). Septicemia is often associated with the respiratory or urinary tract infections. Strauss and colleagues have noted that, over the last three decades, there has been a 40% decline in mortality during the first two years after injury (Strauss et al., 2006). At the same time, there has also been widespread research indicating that the life expectancies for individuals with SCI have also greatly improved (Frankel et al., 1998; Spinal Cord Injury, 2010; Yeo et al., 1998).

1.1.3 Secondary Complications

Any damage to the spinal cord will create a variety of repercussions throughout the body that can result from the loss of upper and lower extremity use or from other physiological factors. Regardless, these secondary complications such as pressure sore development, urinary tract infections, diabetes, decreased bone density, autonomic dysreflexia, bowel dysfunction and muscle atrophy can be, at times, extremely problematic for the individual and reduce the quality of life even further. These secondary complications have been summarized by Ditor and Hicks, 2009:

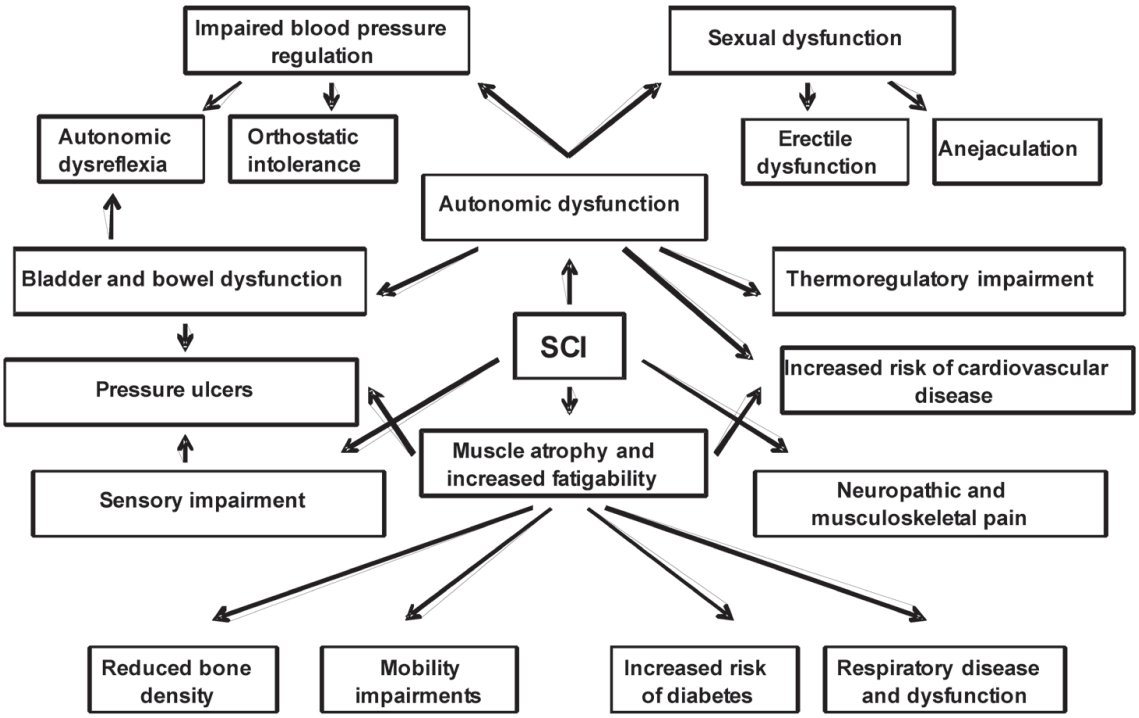


Figure 1 Relationships between secondary complications of SCI Ditor and Hicks, 2009.

1.1.4 Pressure Sores

According to Krause, pressure sores are considered to be one of the most devastating secondary complications of SCI (Krause et al., 1998). The potential for developing a pressure sore within the initial stages of acute care and rehabilitation for individuals with complete tetraplegia has been reported to be approximately 53% (Spinal Cord-Statistics, 2006). Because there is often a loss of sensation in addition to muscular paralysis, individuals with SCI are susceptible to the development and progression of pressure sores. These skin sores, or ulcers, can further progress into potentially fatal infections and result in loss of limb(s) due to medically necessary amputation of the lower extremities. Therefore, it is imperative to maintain constant care and vigilance in order to reduce or eliminate the potential for advanced pressure sores. An untreated sore can further progress to the point that surgery is required (Krause et al., 1998).

Pressure sores in individuals with SCI generally develop in areas of the body that have prolonged pressure. These areas are most frequently found in regions that are under pressure during sitting, as individuals with SCI spend the majority of their waking hours sitting in a wheelchair. The areas under increased pressure, therefore, include the sacral area, ischial tuberosities, the trochanters and the heels, (Ditor & Hicks, 2009).

1.1.5 Role of Blood Flow In Pressure Sore Development in SCI

As is the case with any injury in the body, increased blood flow to the area of injury, following the inflammatory stage, provides the area with oxygen, nutrients and flow to facilitate delivery of immune cells and factors required for optimal healing. When blood flow is decreased or restricted, healing can be reduced and healing time is generally increased. In the case of pressure sore development in SCI, blood flow in the area is already often reduced due to the associated reduction of input from the autonomic nervous system and the impairment of local control of blood flow. At the same time, research shows that decreased blood flow in the peripheral microcirculation may also be caused by peripheral alpha-adrenoceptor hyper-responsiveness (Teasell, Arnold, Kraissioukov & Delaney, 2000). It is this same hyper-responsiveness that is believed to cause the excessive pressor response in autonomic dysreflexia (Teasell et al., 2000).

In able-bodied individuals, Sanada and colleagues found that pressure sores in post-operative individuals developed as a result of changes in skin blood flow as opposed to the length of applied pressure to any particular area (Sanada et al., 1997). However, in individuals with SCI, prolonged pressure over lengthy periods of time occurs on a daily basis. As a result, these prolonged periods of pressure lead to an occlusion of blood flow

and, ultimately, reduced blood flow, edema and the development of a pressure sores (Ditor and Hicks, 2009).

Changes in resting systolic blood pressure have also been observed in chronic SCI and are linked to muscle atrophy (Mawson, Biundo, Neville, Linares, Winchester & Lopez, 1988). Research has shown that individuals with a resting systolic pressure below 100 mm Hg are at a higher risk of pressure sore development (Gosnell, 1973). At the same time, constant external pressure over a specific area will minimize or decrease superficial blood flow and lymphatic circulation in that particular area. Combined decreases in systolic pressure and local blood flow for both physiological (SCI-linked) and mechanical reasons result in decreased local supply of oxygen and nutrients to the skin tissue and cell necrosis (Krause et al., 1992).

1.1.6 Exercise and Blood Flow in SCI

Many different research groups have studied the effects of various interventions that might alter circulation in the paralyzed limbs of individuals with SCI, (Ter Woerds et al., 2006; Cotie, Guerts, Adams & MacDonald, 2010; Ballaz et al., 2007; Ditor & Hicks, 2009). In recent years, research has focused on active forms of treatment. Many of these forms involve movement and exercise and have demonstrated various effects on blood flow. Currently, one of the most effective means of actively increasing blood flow to the legs in SCI is through functional electrical stimulation (FES) of leg muscles. Many researchers have studied the effects of electrical muscular stimulation on blood flow and other arterial properties (Gerrits, de Haan, Sargeant, van Langen & Hopman, 2001; Hopman, Groothuis, Flendrie, Gerrits & Houtman, 2002; Olive, McCully & Dudley, 2002; Nash, Montalvo, Applegate, 1996; Ragnarsson, 1988; Thijssen, Ellenkamp, Smits

& Hopman, 2006). Each of the aforementioned studies used electrically stimulated cycling as the method of muscle activation, with the quadriceps being stimulated in each study and, in one study, the hamstrings and gluteal muscles were also stimulated in one, as well. The stimulation protocols varied in frequency and duration, with time periods of stimulation training ranging from two to six weeks, where each week consisted of two to three training sessions. Although each of these studies measured various aspects and factors affecting blood flow, a resultant acute increase in blood flow within the common femoral artery was found in all studies upon stimulation. The observed increases in leg blood flow were then hypothesized to create further positive effects on various properties of the artery, thus creating even greater improvements in blood flow along with other benefits. For example, increased cross-sectional area of the artery (Gerrits et al., 2001; Thijssen et al, 2006), decreased vascular resistance (Hopman et al., 2002), increased muscle mass and improved vascular response to ischemia and normalization of flow-mediated dilation (FMD) (Thijssen et al., 2006).

A second form of exercise that has been more recently studied for its effects in SCI is body- weight supported treadmill training (BWSTT). BWSTT allows the SCI individual to walk with assistance using a support harness bearing various degrees of the subjects' body weight. At this point, BWSTT does not appear to have as significant of an effect on blood flow as does FES. In one study performed by Ditor and colleagues, no exercise-induced changes were found in femoral artery cross-sectional area or blood flow after four months of BWSTT, with three to four training sessions per week (Ditor, MacDonald, Kamath, Bugaresti, Adams & McCartney, 2005) despite a significant increase in femoral artery compliance.

A third form of exercise that has been examined for a potential impact in leg blood flow in SCI is passive exercise including passive leg movements and passive cycling. The results of research surrounding this form of exercise are less conclusive. Muraki and colleagues found that passive leg cycle exercise in able bodied inviduals increased stroke volume and cardiac output and resulted in a delayed increase in venous return from the muscles (Muraki, Ehara & Yamasaki, 2000). However, in another study involving passive cycling, Ter Woerds and colleagues found that this form of exercise did not alter peripheral arterial circulation in individuals with SCI (Ter Woerds, De Groot, van Kuppevelt & Hopman, 2006).

To this point, previous research has addressed the exercise, movement or stimulation of the lower extremities to try and affect blood flow. Other studies, however, have focused on exercise using the upper extremities and the potential effects of this exercise on blood flow in the lower extremity. Muraki and colleagues found no increases in skin blood flux of the lower extremity after maximal arm-cranking exercise in SCI individuals, (Muraki, Yamasaki, Ehara, Kikuchi & Seki, 1996). In an earlier study by the same group, arm-cranking exercise resulted in increases in skin blood flow in the lower extremity in individuals with SCI below the level of L1 while no changes were observed in individuals with SCI at T12 or above (Muraki, Yamasaki, Ishii, Kikuchi & Seki, 1995).

1.1.7 Skin Temperature and SCI

The effects of altered large conduit artery blood flow can have an effect on skin temperature. Skin ulcers, or pressure sores, have been found to be directly affected by alterations in local blood flow in able-bodied and SCI individuals (Cotie et al., 2010;

Ditor & Hicks, 2009; Sandana et al., 1997). As increased pressure is applied to the skin, the tissue hydrostatic pressure rises above the arterial pressure and skin blood flow becomes occluded. Reactive hyperemia occurs following the release of pressure in order to reoxygenate tissues and flush vasodilator metabolites from the tissues (Petrofsky, 2012). Sandana and colleagues found that the body's inability to increase blood flow in response to prolonged pressure in specific areas could contribute to the development of pressure sores (Sandana et al., 1997). After examining able-bodied individuals undergoing lengthy surgical procedures, it was found that the individuals who did not develop pressure sores had a 500% increase in mean blood flow at the sacral or iliac prominences, depending on whether the individuals were supine or prone lying, scompared to those individuals that showed a decrease in blood flow and the subsequent development of pressure ulcers (Sandana et al., 1997).

With the introduction of a physiological stimulus, such as heat or exercise, skin temperature reactivity can provide information about the regulatory capacity of the microcirculation, (Cotie et al., 2010). Cotie and colleagues studied the effects of BWSTT and tilt-table standing training (TTS) on leg blood flow, resting skin temperature and reactivity skin temperature in individuals with SCI. Their results showed a decrease in resting skin temperature at several sites after either training method, but no changes in resting blood flow. From these results, the researchers emphasized the need for measurement of microvascular blood flow in order to detect small changes in skin temperature that may not be detected by bulk blood flow measures taken from the femoral artery. Another study led by Ek and colleagues noted that impairment in the ability to increase skin blood flow in response to a heat stimulus could be a factor in the

development of pressure sores, (Ek et al., 1984). At the same time, other research has suggested that an increase in local skin temperature leads to a greater susceptibility of pressure sores. Braden and Bergstrom found that, with a 1ºC increase in resting skin temperature, there was a 10% increase in tissue metabolism and subsequent increase in the susceptibility to ischemic injury (Braden & Bergstrom, 1987). Regardless of the resulting change in resting and reactive skin temperature, research has shown that pressure sores can result from these changes in skin temperature in, both, able-bodied and individuals with SCI.

1.1.6 Autonomic Dysreflexia

Autonomic dysreflexia (AD) is a condition that is the result of noxious stimulation introduced to certain areas of the body below the level of the spinal cord lesion (Mathias & Frankel, 1999). AD is a reflexive reaction in response to the causes listed in Table 1 that triggers a pressor response resulting in a sudden rise in blood pressure. In response to an increased blood pressure, there is a reactionary decrease in heart rate. This decrease in heart rate is a result of a baroreceptor reflex initiated within the sinoaortic region. This baroreceptor reflex causes a vagal response that then leads to a decrease in the heart rate. However, the compensatory decrease in heart rate may be temporarily preceded by rise in heart rate (Mathias & Frankel, 1999). This brief rise may be the result of sympathetic stimulation of the heart via spinal cardiac reflexes. As mentioned, this rise in heart rate is only temporary until the sinoaortic baroreceptor reflex stimulates a drop in heart rate.

Particular areas that may elicit a dyreflexic response with stimulation include the pelvic and abdominal viscera, skin and skeletal muscle. A more complete list of these causes can be found in Table 1.

Abdominal or pelvic visceral stimulation
Ureter
Calculus
Urinary bladder
Distension by blocked catheter or discoordinated bladder
Infection
Irritation by calculus, catheter, or bladder washout
Rectum and anus
Enemas
Faecal retention
Anal fissure
Gastrointestinal organs
Gastric dilatation
Gastric ulceration
Cholecystitis or cholelithiasis
Uterus
Contraction during pregnancy
Menstruation, occasionally
Cutaneous stimulation
Pressure sores
Infected ingrowing toenails
Burns
Skeletal muscle spasms
Especially in limbs with contractures
Miscellaneous
Intrathecal neostigmine
Electroejaculatory procedures
Ejaculation
Vaginal dilatation
Urethra—insertion of catheter or abscess
Fractures of bones

Table 1: Causes of Autonomic Dysreflexia from Mathias, 1999, pg. 503

Signs and symptoms of AD, as well as other causes and treatment reminders can be found in Appendix D. One particular area of importance that must be noted is that of the urinary bladder. Specific stimulation of the bladder can create a dysreflexic response. This stimulation can come through different forms, whether it is distension created by a partial blockage in a catheter or discoordinated bladder, infection, or irritation (Mathias & Frankel, 1999). The specific area must be considered during the osteopathic treatment of individuals with SCI. It was an intention within the methodology of treatment in this

study to address areas surrounding the bladder. As a result, specific and close attention was made to the signs and symptoms of AD. There are many clinical manifestations that can result from AD that must be monitored during osteopathic treatment. These manifestations can be found in Table 2.

Manifestations of Autonomic Dysreflexia
Paraesthesiae in neck, shoulders, and arms
Fullness in head
Hot ears
Throbbing headache, especially in the occipital and frontal regions
Tightness in chest and dyspnoea
Hypertension and bradycardia
Occasionally cardiac dysrythmias
Pupillary dilatation
Above lesion—pallor initially, followed by flushing of face and neck and sweating in areas above and around the lesion
Below lesion—cold peripheries; piloerection
Contraction of urinary bladder and large bowel[a]
Penile erection and seminal fluid emission[a]

[a]May occur as part of the 'mass reflex'.

Table 2: Manifestations of Autonomic Dysreflexia

These conditions listed in Table 2 must not only be considered and monitored throughout this study, but must also be closely monitored by all health care professionals when addressing individuals with SCI. If AD is not addressed or monitored, not only will the listed clinical manifestations proceed, but also further detrimental factors may result. These include myocardial failure, further neurological deficits and in the worst-case scenario, death (Mathias & Frankel, 1999).

The significance of AD is related to the health of the individual. Typically, most individuals with SCI are susceptible to this condition. Individuals with complete lesions

within the cervical cord are all potentially at risk. In contrast, certain individuals with incomplete lesions may be at a decreased risk. It has been found that individuals with specific, intact descending spinal pathways may be void of the risk of AD (Curt, Weinhardt & Gietz, 1996). Certain skin blood flow responses within the hands and feet can indicate the integrity of sympathetic cholinergic pathways. If these pathways remain intact, specific skin responses will be present and the risk of AD is much less (Curt et al., 1996).

For individuals who have dysreflexic responses, it is imperative to determine and eliminate the cause of this response. For example, a blockage in a urinary catheter will result in accumulation of urine, creating increased pressure within the bladder and can cause dysreflexia. If increased external pressure, via clothing or even during osteopathic treatment, over areas on or surrounding the bladder are creating responses, then this, too, must be eliminated. A dysreflexic response must also be treated in a way that will decrease blood pressure. This can often be addressed by performing a heads up tilt, which causes venous pooling, breaking the dysreflexic circuit. As a result, there will be an initial reduction in blood pressure and the immediate risk, in most cases, will be eliminated.

1.2 Osteopathic Treatment

Osteopathic medicine, founded by Andrew Taylor Still in 1874 (Still, 1902), is an alternative form of health care that emphasizes the relationships between the structure and function of the body and is grounded in the concept that the body has an ability to heal itself. Osteopathic treatment involves diagnosis on the basis of palpation, comprehensive history and conventional diagnostics. A hallmark of osteopathic

treatment is manual therapy and manual manipulation. In osteopathic treatment, body structures are manually manipulated to increase blood flow and, thereby, increase healing (DiGiovanna et al, 1997). Currently, very little osteopathic literature exists related to research that has been performed on individuals with SCI.

It has been previously reported that osteopathic treatment is successful in the treatment of low back pain (Andersson et al, 1999) and in patients with coronary artery disease (Rogers, 1976), hypertension (Spiegel et al, 2003) and peripheral arterial disease (Lombardini et al., 2009). More recently, Arienti and colleagues reported that osteopathic treatment is effective in controlling pain in SCI individuals (Arienti et al. 2011). Although modern medicine continues to report on various treatment procedures for individuals with SCI, minimal research has being reported from an osteopathic standpoint.

Within the field of Osteopathy, "…it is a cardinal principle that blood flow must be free; that if it be not so, disease results" (Hazard, 1931; pg. 57). This statement was ultimately derived from A.T. Still's principle that "*the rule of artery and vein is universal in all living beings"* (Still, 1902). By achieving increased blood flow within the lower extremities of individuals with SCI, the risk of many secondary complications could potentially be reduced. Blood flow is dependent on many intrinsic and extrinsic factors, many of which are under neurological control. In the partial or complete absence of neurological control, as with individuals with a SCI, blood flow can be significantly altered or diminished. This reduction of blood flow in paralyzed limbs can also elicit a further negative impact on the nervous tissue by decreasing blood supply to the nervous tissue itself. This statement not only emphasizes the importance of circulation, nervous

tissue and their interdependence, it also supports the second main principle of osteopathy, the concept of self-regulation.

The second basic principle of osteopathic medicine is that in the healthy organism, the body is capable of self-healing and health maintenance (Gevitz, 2006). However, the concept of self-regulation becomes severely jeopardized when the function of certain tissues or systems are impaired or eliminated. In the case of a SCI, the reduction or ablation of neurological control below the level of the lesion severely impairs the body's ability to control blood flow and ultimately the ability to self-regulate.

The third osteopathic principle is the principle of structure (McConnell, 1951). If the spinal cord is damaged, all living tissues that are supplied by this structure will have impaired function. The relevance of a structurally disrupted spinal cord, from an osteopathic standpoint, is critical to the function of the entire physiological being. These three principles form a significant portion of the overall philosophy behind the osteopathic approach. While the rule of the artery is a critical principle relating to this current research, the subsequent two principles also relate to the study design and interpretation of results.

A central theory of osteopathic treatment includes consideration of the regulation of the central nervous system (CNS), including the autonomic nervous system (ANS). Osteopathic treatment is also designed to consider the concept that tissues and systems will have improvements in their function with effective treatment and potentially allow for improved local control. At the same time, with a significant disruption of the CNS and ANS as occurs with SCI, osteopathic treatment of individuals with SCI may have a

greater impact on blood flow through alteration of local control factors and the tissues directly surrounding the associated vessels.

One critical factor that must be considered with regards to osteopathic treatment of individuals with SCI is the fact that these individuals spend the majority of their waking hours sitting in a wheelchair. As a result, structures within the abdomen and pelvis, including blood vessels, are under constant compression. This compression can not only restrict blood passing through the vessels on route to further destinations, but it can also restrict blood flow as it passes through and supplies structures within the abdomen. If blood flow is restricted within the abdomen, pooling could result. This blood pooling can then create more pressure within the abdomen, resulting in the potential for further obstructions of vasculature.

Within the lower extremity, blood flow can be impaired in many different areas and this must be considered in osteopathic treatment. Initially, because there is little or no movement within the lower extremity, venous return will be significantly impacted. Because the only consistent form of muscle contraction in the limbs below the level of the lesion comes through spasticity, pooling of blood within the veins is much more common. Muscles within the lower extremity must be reduced of tension through osteopathic treatment, where possible, in order to reduce the potential increase in pressure placed on the arterial supply. Spasticity within the lower extremities is very common and, in some individuals, very frequent (Edgar, 1992). Although frequent muscle spasms can be alarming or irritating, they also provide significant benefits. Without neural control in the lower extremity, controlled muscle contraction is not possible. Therefore, uncontrolled muscle spasm, or spasticity, is often the only means by which to maintain

any muscle tone. Additionally, these muscle spasms also have other benefits with respect to blood flow. For example, venous return is aided through the contraction of muscles within the lower extremities. Spasticity and muscle spasm are, also, often the only way bones of the lower extremities are stressed. Unfortunately, demineralization within the SCI population is a constant problem facing these individuals (Jones et al, 2002). The potential for fractures throughout the body, especially within the lower extremity, is very high. Therefore, muscle spasms are the only way to stress chronically unloaded bones within the lower extremity. These potential benefits of spasticity and an associated increase in muscle tension must be considered when treating the individuals with SCI. Although one goal of osteopathic treatment of SCI would be to reduce any tension or pressure on the blood vessels that may be constrictive in nature, it is of equal importance to maintain enough tension on these vessels to assist with the transport of blood, especially within the venous system.

For many of the individuals with SCI, various levels of pooling and swelling can be found within the ankle and foot (Nash, Montalvo & Applegate, 1996, Wecht et al, 2005). Obviously, with the force of gravity, blood will pool at the lowest, most inferior aspect of the body when upright. Once again, the fact that these individuals sit in a wheelchair for a large percentage of each day, blood will move to and pool in the feet. Many individuals with SCI who experience more severe cases of blood pooling within the feet often attempt to combat this problem with compression stockings. This creates a definite challenge for individuals with minimal movement, at best, within the upper extremity since it can be extremely difficult to put on a restrictive stocking.

A central osteopathic treatment principle is that the flow of arterial and venous blood is critical to maintain a homeostatic state within the entire body (Hazzard, 1931). Any restrictions of this blood flow can certainly impair homeostasis and, as a result, have a critical effect on one of the main principles of osteopathy where the body is a self-regulatory mechanism. This previous description of suggested regions and tissues to treat is extensive but not necessarily exhaustive as there are a significant number of structures that must be considered with regards to anatomical structures affecting blood flow. At the same time, justification of osteopathic treatment for secondary complications resulting from SCI is quite evident. Many of these secondary complications can be very serious and interventions that can reduce or alleviate these problems are critical. Finally, individuals with SCI face increased challenges on a daily basis and one goal of osteopathic treatment is to address some of these challenges.

1.3 Leg Blood Flow

Previous research has found significant decreases of vessel diameter and overall blood flow within the common femoral artery of the individuals with SCI (Wecht, de Meersman, Weir, Baumann & Grimm, 2004; DeGroot, Van Kuppevelt, Pons, Snoek, Van Der Woude & Hopman, 2003). In fact, DeGroot and colleagues found a 30% reduction in diameter and a 30% reduction in blood flow in the femoral artery within 6 weeks following injury (DeGroot et al., 2003). Research has also focused on the reasons for this decreased blood flow (Stoner, Manning, Van Hiel, Groves, Ripley, Palardy et al., 2005, Wecht et al., 2004; Olive, McCully & Dudley, 2002; Hopman, Groothuis, Flendrie, Gerrite & Houtman, 2002) and it has been suggested that the amount to which blood flow

is affected in the lower extremity is dependent upon the level and severity of the spinal cord segment involved (Wecht et al., 2004).

1.3.1 Blood Flow Control

Blood flow is under constant regulation and control by several different systems and many factors within the human body. These systems all come together to affect and aid in the functioning of the cardiovascular system. In order to accomplish this monumental task, these systems respond to afferent feedback from different tissues throughout the body as a means of maintaining a homeostatisis.

Blood has many critical functions as it passes through the arterial and venous systems. These functions include oxygen transport to all tissues, the transport of nutrients to all tissues, the transport of hormones throughout the system, the removal of metabolic waste, the removal of carbon dioxide from the tissues, and the removal of hydrogen ions from the tissues (Guyton & Hall, 2000). With a chronic impairment of blood flow to any area of the body, a decrease in oxygen and nutrient supply combined with the decreased removal of metabolic waste can lead to gradual cell death.

One of the major principles of the human body and, more specifically, the circulatory system, is the ability of each tissue to control local blood flow based on its own metabolic needs (Guyton & Hall, 2000; Hopman et al., 2002). Through this control, precise amounts of blood perfuse all tissues continuously, based on the requirements at each particular moment. As a result, blood flow can be regulated in a much more effective and efficient manner. At the same time, this efficiency is further increased by these local control mechanisms and their ability to control this blood flow in either a rapid manner via a slow, long-term regulation (Guyton & Hall, 2000). The major factor

controlling blood flow throughout the body is the central nervous system (CNS) and, more specifically, the autonomic nervous system (ANS). However, there are factors and substances that have a significant and primary role in the control of local blood flow.

Due to the significant effect that a SCI has on the CNS and, ultimately the ANS, global control of blood flow can be drastically affected or altered (Schmid, Huonker, Barturen, Stahl, Schmidt-Truckass, Kanig et al., 1998). As a result, the body must adapt and rely on other compensatory mechanisms to control local blood flow. There are many substances and factors that assist in the local control of blood flow. This control is based on the body's requirement for oxygen or the metabolic needs of all tissues. Changes in either of these factors will elicit a specific response. Through local control of blood flow, the body is able to send blood to areas with a greater need and shunt it away from areas requiring less blood at that particular instant. This allows for maximal efficiency of the cardiovascular system. Local blood flow is controlled according to metabolic needs on an acute basis and also on a long-term basis (Guyton & Hall, 2000).

Local control of blood flow is believed to occur through the stimulation of chemoreceptors within the vessels. These chemoreceptors within the vessels monitor the presence and alterations of specific metabolites. When these chemoreceptors detect the presence of specific metabolites within the blood, they will produce specific responses within the blood vessels and body. Vasodilation occurs in response to an increase in metabolic requirements or a decrease in available oxygen. Thus, contraction must result in the release of a vasodilator substance from the tissues and cause vasodilation. Another process which might be responsible for acute increases in blood flow is the response to a lack of oxygen or other nutrients within local tissues and smooth muscle fibers of the

local blood vessels. As a result, these blood vessels dilate in order increase oxygen and nutrient supply to the local tissues (Guyton & Hall, 2000). Another factor that controls, or affects, the flow of blood locally, is the actual physical characteristics of the blood vessels themselves.

1.3.2 Autonomic Failure in Hormonal and Humoral Control

As previously described, hormones and other substances can play a critical role in the control of blood flow. While certain substances can create vasoconstriction sufficient enough to significantly alter circulation and blood pressure, other substances can create the opposite effects by stimulating vasodilation. Some of these substances are released from tissues or organs in response to local metabolic needs and situations. Most of these substances can, therefore, create an effect regardless of overriding neurological signals that may be signaling for vasoconstriction. However, the release of some substances is under the specific control of neural stimulation. As a result, reduction or elimination of neurological control can have a profound impact on blood flow.

Two major substances that are affected by SCI and the associated reduction or elimination of neurological control are epinephrine and norepinephrine. Because these hormones are released by the adrenal glands in response to stimulation from the preganglionic sympathetic neurons, there can be a significant alteration in blood flow control with SCI (Schmid et al., 1998). Alterations in blood flow can be more prominent in individuals who have sustained a recent SCI and are still in a state of spinal shock. As time progresses and these individuals move out of this spinal shock, the body becomes more sensitive to smaller amounts of these hormones. The organs, which were once innervated by neurological tissue, now rely on chemical changes and adaptations in order

to release these two hormones (Guyton & Hall, 2000). At the same time, epinephrine and norepinehrine travelling within the plasma now have a greater effect on the effector organs because the sensitivity to these substances increases.

1.3.3 The Heart and Blood Flow Regulation

With regards to blood flow, stimulation of the sympathetic nevous system (SNS) has a significant impact through a variety of different mechanisms. Through activation of the SNS, blood flow can be increased in specific areas or tissues of the body and reduced simultaneously in others.

Another one of the major means through which blood flow is affected by SNS stimulation is via the heart rate. Sympathetic stimulation of the heart causes an increase in heart rate and contractility and thus a subsequent increase in blood flow. At the same time, an increase in sympathetic stimulation will cause vasoconstriction of most blood vessels within the body. This will then create a resistance to flow and, ultimately, an increase in blood pressure (Guyton & Hall, 2000). Through SNS-mediated vasoconstriction, blood flow can be reduced to certain areas or tissues of the body while increased to other tissues. An example of this occurs during exercise where blood flow to specific organs and viscera is reduced while, at the same time, a subsequent increase in blood flow to skeletal muscle occurs in order to meet the increased metabolic demands.

The final pathways for sympathetic and vagal control of the cardiovascular system from the CNS come from the preganglionic neurons. The sympathetic neurons are localized within the intermediolateral cell column of the thoracic and upper lumbar spinal cord (Mathias & Frankel, 1999). Vasomotor neurons are distributed throughout the length of the spinal cord, but sympathetic neurons related to cardiac activity are

located within the upper thoracic ganglia and upper thoracic segments of the spinal cord. More specifically, sympathetic control originates at levels from T1-T4 (Mathias & Frankel, 1999; Wang, 2000). As a result, SCI within the cervical spine has a significant impact on the sympathetic supply to circulation and, ultimately, the heart.

Vagal preganglionic neurons control the heart come from the ventrolateral aspect of the medulla oblongata and the dorsal vagal nucleus (Mathias, 1999). Therefore, because vagal control comes from control centers above the level of a high cervical SCI and pass caudally via the vagus nerve outside of the spinal cord, parasympathetic control of the heart often remains intact after SCI. As a result, control of the heart rate from the ANS after a SCI falls mainly under a resultant altered function of the parasympathetic system (Wang, Huang, Lin, Hwang, Chan, Lai et al., 2000). When there is a required need for increased circulation due to metabolic or oxygen requirements, parasympathetic stimulation is withdrawn. Once these metabolic needs are satisfied, the parasympathetic system will once again activate accordingly and bring the heart rate back to normal values as required.

1.3.4 The Blood Vessels and Blood Flow

It is quite apparent that, although there are many factors affecting blood flow, the blood vessels have a substantial impact on blood flow. There are many factors within these blood vessels that can both encourage or impede blood flow. Therefore, regardless of the previous factors that have been discussed that influence blood flow, if blood is unable to pass through a vessel without restriction, these other factors become secondary.

Individuals with SCI have the potential to have definite and numerous alterations in the characteristics of their blood vessels, particularly in the paralyzed limbs.

The most obvious factor of a blood vessel that will affect circulation is the actual diameter of the vessel, or the size of the lumen. By studying individuals who are very active, individuals who are sedentary and individuals with SCI, differences in many factors, including luminal size can be distinguished. Research has shown a 60% decrease in the luminal size of the femoral artery in individuals with SCI compared to their sedentary counterparts and a 70% decrease in size compared to active individuals (Schmidt-Truckass et al., 2000). To a lesser degree, DeGroot et al. have found similar results, where luminal size of the femoral artery showed a 30% decrease when comparing individuals with SCI to their able-bodied counterparts (DeGroot et al., 2003). At the same time, this study also showed a 30% decrease in blood flow. These differences between the three groups provides a definite indication that blood flow, especially in the lower extremity, is significantly reduced in individuals with SCI as indicated by luminal size.

Specific reasons behind the reduction in conduit artery luminal diameter in paralyzed limbs are still unclear, but several explanations have been brought forth. One specific hypothesis is that the reduction in diameter is due primarily to inactivity (DeGroot et al., 2003). Similar to muscle atrophy within inactive muscle, the blood vessels, including the femoral artery, will decrease in size as a result of inactivity. If the surrounding musculature has atrophied, there is a decreased requirement for oxygen and other nutrients provided by the arteries. As a result, there will be decreased activity within the arteries and vessels. This will, ultimately, lead to a decrease in luminal size

through vessel atrophy. This is a significant factor when addressing blood flow in the lower extremity. It also emphasizes the positive effect that even occasional uncontrolled muscle contractions associated with spasticity can have since spasticity creates muscle contractions, which then creates a need for increased leg blood flow.

Another factor that has been identified as being important in the regulation of the structure of blood vessels is the wall shear rate, or shear stress. The wall shear rate represents the frictional force of the blood on the endothelial layer of the blood vessel and is directly related to blood flow velocity. This endothelial layer is the innermost layer of the blood vessel and is in direct contact with the blood flowing through it. For individuals with SCI, the conduit artery shear rate in the paralyzed limbs almost doubles (DeGroot et al, 2003; Schmidt-Truckass et al., 2000). It is hypothesized that the body attempts to adapt to this significant increase by altering the blood vessel structure. One way to do this would be to increase the size of the lumen. However, as previously mentioned, in individuals with SCI, the exact opposite occurs since luminal size decreases. It appears, though, that any luminal size is somewhat dependent on the endothelium. Due to denervation, this endothelium becomes less effective and the shear rate escalates. At the same time, this denervation causes decreased stimulation for the walls of the arteries to constrict. This has been shown to result in stiffening of the arterial wall due to an increase of collagen content within the vessel walls (Schmidt-Truckass et al., 2000). As a result, this increased shear rate causes a physiological change within the vessel that leads to a decrease in blood flow velocity. From a research standpoint, if treatment can increase blood flow within the lower extremity, shear stress would initially

be further increased, but a resultant vasodilation might then occur, thereby reducing shear stress over time.

A third factor related to local blood flow is vascular compliance. "Arterial compliance refers to the degree to which its internal diameter may deform in response to alterations in intravascular pressure, and is related to the elastic properties of the vessel wall." (Ditor, 2003). Without elastic properties, the vessel is unable to adapt and change shape according to blood volume and pressure within the vessel. The reduction in elastic properties can then decrease the effectiveness of the arterial baroreceptors that are affected by stretch within some vessel walls. Because these baroreceptors stimulated less despite alterations in pressure, increased loads are then placed on the heart and coronary perfusion is decreased. From this fact alone, it is apparent that these vascular changes are very significant in the overall health of the individual with SCI.

1.4 Overall Objectives

The overall objective of this research was to examine the effects of osteopathic treatment on lower limb blood flow and skin temperature in the lower extremity of individuals with SCI compared to able-bodied individuals. Measures were analyzed across time (pre to post treatment) and treatments (control, treatment 1, treatment 2 and treatment 3).

1.5 Hypotheses

1) Osteopathic treatment will acutely increase blood flow in the lower extremity of individuals with chronic SCI.
2) Osteopathic treatment will acutely increase skin temperatures in the lower extremity of individuals with chronic SCI.

3) Osteopathic treatment will result in greater increases in blood flow and skin temperatures in the lower extremity of individuals with SCI compared to able-bodied individuals.

2 CHAPTER 2

The Acute Responses of Leg Blood Flow and Skin Temperature in Chronic SCI are not different between Osteopathic Treatment and Time Control.

2.1 Introduction

The effects of paralysis resulting from a traumatic spinal cord injury (SCI) can be catastrophic to the injured individual (Weinberg & Solot, 1985). These effects are certainly life altering in many different ways and limit the independence of the individual. In addition to the devastating nature of partial or complete paralysis, there are also secondary complications that arise which can create a future strain on the quality of life for individuals with an SCI. Many of these secondary complications of SCI are resultant effects, but will, in turn, cause many other problems.

Previous research has found significant reductions in vessel diameter and overall blood flow in the common femoral artery of individuals with SCI (Wecht, de Meersman, Weir, Baumann & Grimm, 2004; DeGroot, Van Kuppevelt, Pons, Snoek, Van Der Woude & Hopman, 2003). In fact, DeGroot and colleagues found a 30% reduction in diameter and a 30% reduction in resting blood flow in the femoral artery within 6 weeks following injury (DeGroot et al., 2003). The amount to which lower limb blood flow is reduced has been shown to be dependent upon the level and severity of the spinal cord segment involved (Wecht et al., 2004). Other vascular adaptations to chronic SCI included reduced peripheral capillarization, (Chilibeck et al., 1999) and impaired skin microcirculation (Nicotra et al., 2005) below the level of the lesion. Potential impacts of these changes in vascular structure and function with SCI include reduced healing

potential, increased susceptibility to pressure sore development and ineffective responses to a variety of stimuli designed to increase muscle and bone mass and health.

A variety of rehabilitative techniques have been previously examined for their potential to acutely increase lower limb blood flow in SCI. Functional electrical stimulation results in acute increases in femoral artery blood flow (Scremin et al., 1998) while reports on the effects of passive leg cycling are conflicting with reports of both acute increases (Ballaz et al., 2007) or no change (Ter Woerds et al., 2006) in lower limb blood flow in individuals with SCI.

Both resting skin temperature and the change in skin temperature in response to a physiological challenge provide useful information about the regulatory capacity of skin blood flow. Previous research has demonstrated that reduced skin temperature reactivity exists in SCI (Nicotra et al., 2005) and may be an predisposing factor in pressure sore development (Ek et al., 1984 and Sanada et al., 1997). Research in our lab has demonstrated that both body weight supported treadmill exercise and tilt table standing in individuals with chronic SCI result in acute increases in skin temperature but no change in lower limb blood flow and that longer term BWSTT resulted in decreases in resting lower limb skin temperature (Cotie et al., 2010). Using laser Doppler for cutaneous blood flow assessments, Van Duijnhoven and colleagues determined that SCI individuals demonstrated impaired skin vasodilation both above and below the lesion in response to local heating in comparison to able-bodied controls and that these responses were not altered in the SCI group with 8 weeks of functional electrical stimulated exercise training (Van Duijnhoven et al., 2009).

Osteopathic manipulative therapy (OMT) is one aspect of oseteopathic medicine (Still 1902). A primary goal of OMT is to identify and address maladaptive alterations in the regulation of blood flow. Treatment protocols include manipulations of bones, muscles, and connective as well as soft tissues in order to improve blood flow and enable the body to heal injuries. The use of OMT in SCI is founded on the same principles as OMT treatment for any other patient group, however to date the efficacy of OMT in chronic SCI has only addressed the area of pain control (Arienti et al, 2010). Previous research has, however, demonstrated positive effects of OMT in persons suffering from low back pain (Andersson et al., 19990, peripheral arterial disease (Lombardini et al., 2009), coronary artery disease (Rogers & Rogers, 1976) and hypertension (Spiegel et al., 2003). One proposed mechanism of action is that osteopathic treatment results in release of nitric oxide, resultant vasodilation and increased blood flow (Salamon et al., 2004).

The primary purpose of this study was to determine the effects of osteopathic treatment on lower limb blood flow and skin temperature in individuals with chronic SCI. We hypothesized that OMT would result in acute increases in leg blood flow and skin temperature in individuals with chronic SCI while AB individuals would not experience any acute changes to similar treatment as they were not being treated for specific restrictions in blood flow.

2.2 Methods

2.2.1 Study Design

This study employed a factorial, repeated measures treatment design. One group was made up of nine individuals with SCI and included both tetraplegic and paraplegic SCI individuals. The other group was made up of six able-bodied individuals (AB). Blood

flow and skin temperature measures of the lower extremity were collected before (Pre) and after (Post) each intervention (Control, Treatment 1, Treatment 2, and Treatment 3). The change from pre- to post-intervention values were determined. All testing was performed within the Vascular Dynamics Lab at McMaster University. Approval to carry out the research was granted by the Research Ethics Board of Hamilton Health Sciences (Appendix C).

2.2.2 Participants

The SCI group included both tetraplegics and paraplegics with chronic complete or incomplete SCI. The SCI sample group was made up of five tetraplegics and four paraplegics having SCI as a result of acute trauma, there was one female and eight males with a mean age of 48.5 $\pm$ years. The youngest individual was 23 years and the oldest individual was 67 years at the time of testing. The mean length of time from injury to the commencement of testing was 12.5 years, with the shortest duration being six months post-injury and the longest being 21 years. There were 4 subjects with complete injuries and 5 subjects with incomplete injuries. In reference to the ASIA Impairment Scale (AIS), 4 of these subjects were graded as AIS A, 2 subjects were AIS B and 3 subjects were AIS C.

The able-bodied group consisted of 1 female and 5 females with a mean age of 37.5 ± years. The youngest individual was 25 years of age and the oldest individual was 51 years of age.

2.2.3 Inclusion and Exclusion Criteria

This research included individuals who had had their SCI for longer than six months. This eliminated individuals who were still in a transient state of spinal shock

and undergoing vascular adaptations. This research sample included tetraplegic and paraplegic individuals with a SCI located within the cervical or thoracic spine who were all wheelchair dependent; males and females between the ages of twenty-three to sixty-seven years; and individuals with complete and incomplete spinal cord lesions graded as AIS A-D. Prior to participating, all individuals gave their written informed consent to participate. We excluded individuals in either group with pre-existing cardiovascular conditions. Therefore, individuals with any heart pathology that could be irritated with treatment or whose condition could skew results were excluded. Also, SCI individuals who had documented difficulties with autonomic dysreflexia were excluded for safety reasons.

2.2.4 Dependent and Independent Variables

The primary dependent variables of interest were femoral artery blood flow, which is calculated as a product of mean femoral artery diameter and mean femoral artery blood velocity, and lower limb skin temperature measures. The independent variable was the treatment (Control, Treatment 1, Treatment 2 and Treatment 3) that was performed on each individual.

The dependent variable of femoral artery blood flow was measured within the femoral artery of the left leg, 2-4 cm proximal to the bifurcation that divides the common femoral artery into the superficial femoral artery and the profunda femoris arteries using the Doppler ultrasonography. The key variables being measured were arterial diameter and mean blood velocity. The dependent variable of skin temperature was measured in the left lower limb at three different locations, including the thigh, lower leg and foot. Initial measurements were made after fifteen minutes of supine rest following transfer to

the examination and treatment table. A second measurement was taken five minutes after the cessation of osteopathic treatment (Treatment 1, 2 or 3) or time control (Control).

2.2.5 Procedures

For each individual, the study involved four sessions. Where possible, these sessions were held seven days apart and standardized to the same time of the day in order to reduce variation due to circadian changes in blood flow or skin temperature. Prior to each session, the individual was instructed not to consume caffeine or any other stimulant that might alter hemodynamic responses. The individual was also asked to avoid nicotine on the day of testing. Finally, each individual was asked to empty their bladder or catheter bag prior to testing in order to reduce the potential for any dysreflexic responses. All procedures or treatments were performed within the Vascular Dynamics Lab associated with the Department of Kinesiology at McMaster University. In a further attempt to control for variability in blood flow and skin temperature responses, the room temperature of the lab was kept constant at 24 degrees Celsius.

Each session began with a fifteen minute adaptation period of supine rest. This period of rest allowed for acclimatization, instrumentation and a resultant stabilization of heart rate and blood pressure. Following this rest period, initial measurements of arterial diameter and mean blood velocity were taken from the common femoral artery of the left leg. Data for blood flow, arterial diameter and blood velocity was collected using an imaging Doppler ultrasound unit (GE Vingmed System FiVe, Horten, Norway). A ten MHz probe in both B-mode and pulse wave Doppler at an angle of isonation between 60-68 degrees was used. The B-mode measures brightness to obtain a cross-sectional diameter of the artery while the pulse wave Doppler measures were used to determine

blood flow velocity. Mean blood flow (MBF) in the common femoral artery was calculated as follows:

$$MBF = \pi (\text{average diameter}/2)^2 \times \text{average blood velocity} \times 60 \text{ seconds}$$

Simultaneous measures of skin temperatures were obtained at three points in the left lower extremity using the skin thermistors and the SmartReader Plus 8-Channel Data Logger and TrendReader Standard 2 software. Three thermistors were placed on the anterior surface of the thigh 7 inches below the anterior superior iliac spine of the pelvis, at the anteromedial border of the lower leg at a level 6 inches below the apex of the patella and a third placed on the dorsum of the foot at the mid-shaft of the third metatarsal.

In the initial assessment (Control), the individual underwent a forty-five minute verbal assessment and interview. This initial visit established a baseline for each individual in that measurements were taken but no physical treatments were performed. The subsequent three visits involved hands-on osteopathic manual treatments (OMT) lasting from fifty to sixty minutes in duration with efforts made to maintain an equal length of time for each of the four visits. The initial verbal assessment, consisted of a series of questions surrounding the subjects' past and current health. For the SCI group, questions regarding the causes and events leading up to the SCI were also presented. The initial assessment was consistent with a regular osteopathic verbal assessment, or history. The initial hands-on treatment occurred not less than seven days after the initial verbal assessment. Osteopathic techniques that were used as part of the treatments are described in Appendix E.

2.2.6 Diameter Analysis

B-mode ultrasound images of the CFA were obtained at the beginning of each measurement time point at a sample rate of 11 frames per second. The arterial diameter was measured later over a total of three heart cycles in both systolic and diastolic states using electronic calipers internally calibrated to the ultrasound. Two video clips of 3 heart cycles each were obtained at each time point. All images were visually inspected to ensure measurements and were determined at a constant region of the common femoral artery within each subject. Arterial diameter measures were taken from the leading edge of the artery to the opposing side, while excluding the endothelial layer on either side of the arterial walls. These diameter values were then averaged to gain a mean systolic and mean diastolic value for each time point. Mean arterial diameter was calculated as :

Mean Arterial Diameter = 2/3 Diastolic + 1/3 Systolic.

a) b)

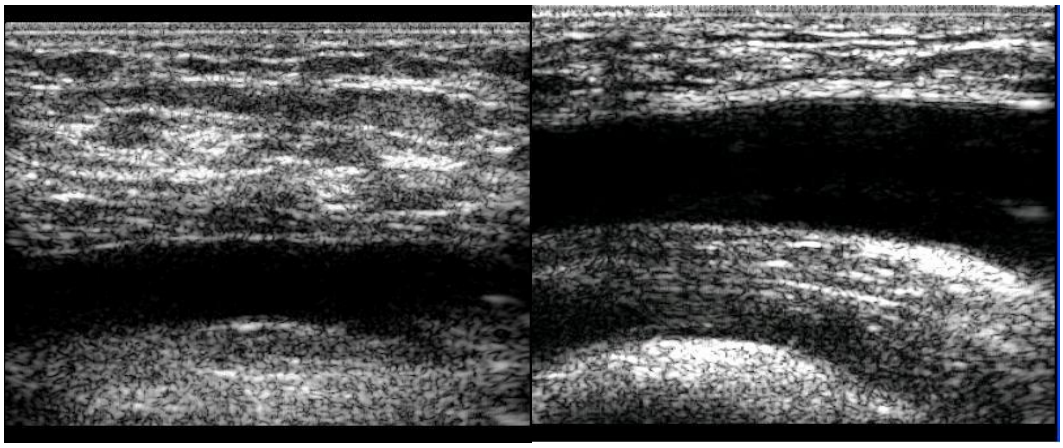


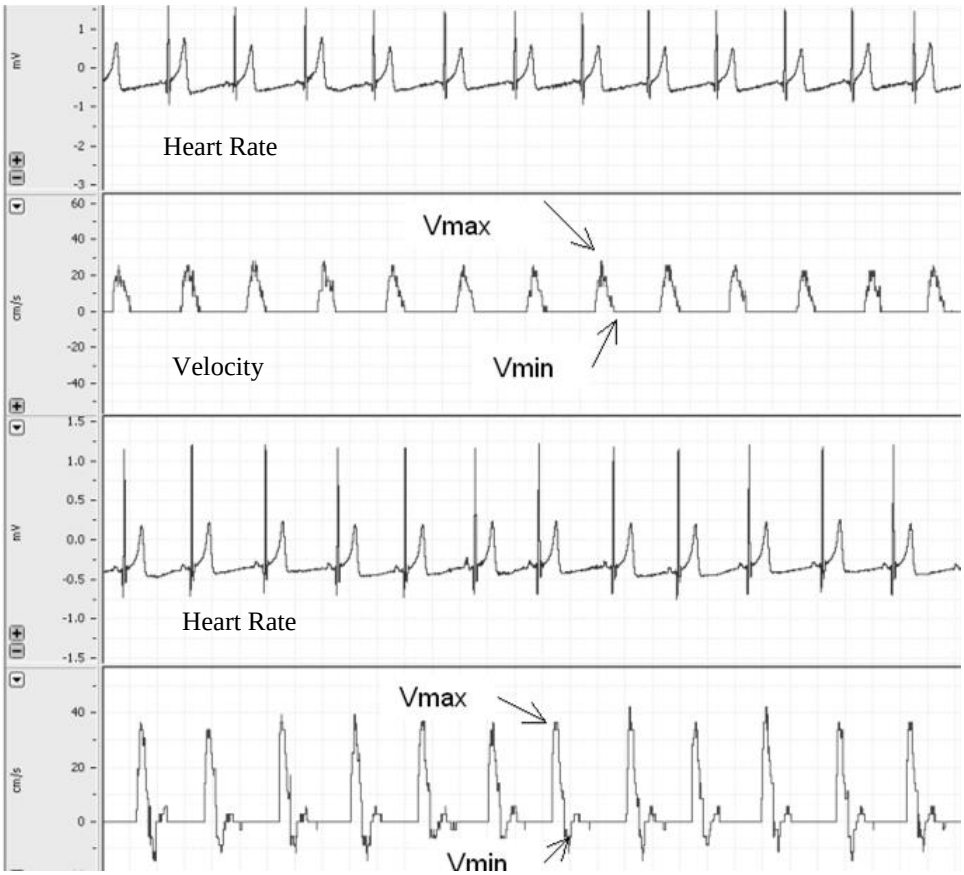
Figure 2 Actual image of femoral artery from B-mode Doppler ultrasound (Vascular Dynamics Lab, McMaster University). Image: a) SCI participant, b) AB participant.

2.2.7 Blood Velocity Analysis

Mean common femoral artery blood velocity was determined from the same region of the ultrasound image as the vessel diameter using pulse wave Doppler ultrasound. The frequency signal from the ultrasound was continuously exported to an external spectral analyzer that used a fast-Fourier transform to convert this signal to an intensity weighted power spectrum (model Neurovision 500M TCD, Multigon Industries, Yonkers, USA). This weighted signal was then sampled at 100Hz to obtain continuous tracings of the voltage representing the mean blood velocity simultaneous to the heart rate and stored offline using a digital data collection system (Powerlab) and later analyzed with the program Labchart 6. At the same time, the angle of isonation was recorded for each measure and used to convert the velocity signal from volts to centimeters per second based on previous calibration of the velocity measurement system. In this particular study, the angles were maintained between 60-68 degrees. Blood velocities were obtained for a minimum of 30 seconds at each time point and then averaged. The vessel diameter and blood flow velocity were then used to calculate mean leg blood flow according to:

Mean Leg Blood Flow = π(average diameter/2)^2 x average blood velocity x 60 seconds/min.

(a)



(b)

Figure 3 Raw data of the heart rate and blood velocity patterns in Labchart 6 of an: a) SCI individual and b) an able-bodied individual.

2.2.8 Skin Temperature Measurements

Skin temperature data was originally obtained from a typical graph (Figure 4) of temperature data gathered over 5 minutes at each data collection time point.

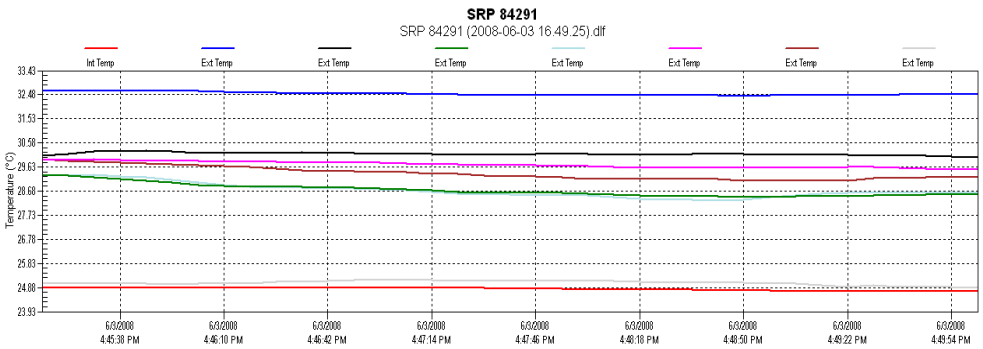


Figure 4 Typical Skin Temperature Data Graph

The data was then converted into a Microsoft Office Excel CSV Spreadsheet. In this form, a smaller sample of temperature values (i.e. 1 minute) from each channel was taken from the original sample (5 minutes) and averaged to produce a mean temperature, per data collection site, for each time period.

2.2.9 Suggested Osteopathic Treatment

Due to the extensive nature of many SCIs, there are a significant number of factors and systems that require attention during osteopathic treatment. Because each individual responds differently to his or her injury, both psychologically and physiologically, a set treatment plan was difficult to predict and establish. At the same time, because primary and secondary complications are highly dependent upon the level and severity of injury, many different problems between and within each individual were expected. As a result, the focus on methodology and treatment plan, obviously, varied from individual to individual. A tentative protocol for the treatment of the SCI individuals was established and followed for the AB participants to ensure consistency. In doing so, specific guidelines could be followed in order to ensure that all systems were addressed while maintaining consistency between participants.

The general plan for treatment included:

Day 1 – Initial Verbal Evaluation

Day 2 – Treatment 1 - cranial

Core Link – structures within the core link

- scar tissue from surgeries within the cervical spine
- sacrum, C0-C1, sphenobasilar joint, sphenoethmoidal joint
- falx cerebri, tentorium cerebelli, straight sinus – cranial dura
- sacrum/occiput – spinal dura
- diaphragm - thoracic

Day 3 – Treatment 2 - abdominal

Abdomen/Pelvis – addressing the viscera within the pelvis and abdomen

ie. mesentery, kidneys, colon, uterus/prostate, liver

- addressing the musculature within the pelvis and abdomen
- pelvic diaphragm

Day 4 – Treatment 4 – Lower extremity

- iliac fascia
- lower extremity – interosseous membrane
  - fibula and tibia
  - femoral artery
- addressing the lateral fascial chain
- temporal bones, occiput, OM Suture – cranial diaphragm
- balance 3 diaphragms

2.2.10 Statistical Analysis

Baseline values (Pre) for SCI and AB groups were compared using a 2-way repeated measures ANOVA with 4 levels of the within factor (treatment day) and 2 levels of the between factor (group). Change scores were calculated for all variables as Post-Pre values on each treatment day. A 2-way repeated measures ANOVA was then used to determine the effect of the intervention (Control, Treatment 1, Treatment 2, Treatment 3) and group (SCI, AB) on the change scores in each variable (femoral artery diameter, mean blood velocity, and mean blood flow, heart rate, systolic blood pressure, diastolic blood pressure, and skin temperature at 3 sites) using commercially available software (Sigmastat 3.10, Systat Software Inc., San Jose CA, USA). When a significant F ratio was observed, Tukey's Honestly Significant Difference (HSD) post hoc tests were used in further analysis. A p value of less than or equal to 0.05 was considered to be significant for all variables. All values are represented as a mean $\pm$ standard error of the mean (SEM). Statistical Analysis Reports for all variables can be found in Appendix D.

2.3 Results

2.3.1 Program Compliance

The compliance rate [(number of sessions completed/number of scheduled sessions) x 100)] of the 15 participants that initially entered the study was 100%. In the SCI group, only one individual experienced a mild autonomic dysreflexic response towards the end of the third visit (Treatment 2) as a result of a full bladder. Once this subject's bladder was emptied, all signs and symptoms of dysreflexia abated. No other secondary complications arose during the study. One individual was just recovering from

a pressure sore in the lower sacral region and required extra padding placed under the right side of their lower back. This did not affect the treatment in any way.

2.3.1 Baseline differences between SCI and AB

There were no treatment effects observed on the baseline values of any of the variables assessed in either group, however there were some group differences in baseline values (**Table 3**). Baseline mean diameter of the femoral artery was smaller for SCI participants (6.4±0.4 mm) than for AB participants (9.0±0.5 mm) [$F(1,13) = 14.926$, $p = 0.002$]. As well, baseline mean blood velocity was higher for SCI participants (6.59 ±0.70 cm/sec) than for AB participants (3.68±0.86 cm/sec) [$F(1,13) = 6.928$, $p = 0.02$]. There were no measurable differences in baseline femoral artery blood flow, heart rate, systolic or diastolic blood pressure ($p>0.05$) between the SCI and AB participants. There were no differences in baseline left thigh and left foot ($p>0.05$) skin temperature between groups. However, baseline left calf skin temperatures were lower for SCI participants (29.2±0.5ºC) than for AB participants (31.2±0.6 ºC) [$F(1,13) = 7.674$, $p = 0.016$].

Table 3: Baseline (Prex) cardiovascular and skin temperature data on each treatment day.

Variable	SCI (n=9)				AB (n=5)			
	C	T1	T2	T3	C	T1	T2	T3
Diam (mm)	6.1±0.5	6.4±0.4	6.5±0.4	6.5±0.4	8.9±0.6	9.5±0.5	8.8±0.5	8.9±0.5
MBV (cm/sec)	5.58±1.06	7.61±1.14	6.13±0.94	7.03±1.55	4.22±1.23	3.58±0.98	3.36±0.42	3.58±0.87
MBF (ml/min)	87±12	146±27	119±20	131±29	149±32	137±19	116±6	129±37
HR (bpm)	66±4	66±3	70±3	65±3	59±2	61±3	61±3	58±3
SBP (mmHg)	123±7*	124±7*	124±7*	117±5*	116±2	120±1	113±3	114±1
DBP (mmHg)	73±5*	73±5*	72±5*	69±6*	69±2	69±3	68±2	68±2
SkTthigh(°C)	30.6±1.1	31.4±0.5	31.6±0.4	31.4±0.5	32.6±0.3	31.3±0.6	31.3±1.3	32.4±0.4
SkTCalf(°C)	28.6±1.0	29.2±.05	29.0±0.7	30.2±0.5	31.2±0.2	31.0±0.3	31.2±0.2	31.5±0.1
SkTFoot(°C)	28.3±1.2	29.3±0.9	30.1±0.6	30.4±0.7	30.4±0.5	30.1±0.5	30.5±0.4	30.3±0.5

SCI, spinal cord injured participant; AB, able-bodied participant; Diam, femoral artery mean diameter; MBV, femoral artery mean blood velocity; MBF, femoral artery mean blood flow; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; Skthigh, left thigh skin temperature; SkTCalf, left calf skin temperature; SkTFoot, left foot skin temperature. All means ± SE. * n=6

2.3.2 Common Femoral Artery Changes over time

Overall the interventions (control or any treatment) resulted in minimal changes in hemodynamic characteristics of the femoral artery. There was, however a significant group by treatment interaction for mean femoral artery diameter [$F(3,39) = 4.911$; $p < 0.005$]. Within controls the change in diameter on the control day was lower than after Treatment 3 and within Treatment 3 the change in diameter (post-pre) was lower in SCI compared to AB (**Figure 5**). There was a significant main effect for group in the mean change in blood velocity with mean blood velocity increasing over time in SCI (0.76 ± 0.90cm/s and decreasing over time in AB (-0.71 ± 0.46 cm/s) [$F(1,13) = 5.88$, $p = 0.031$] across all days (**Figure 6**).

There were no differences in the Post-Pre treatment change in MBF between different days, however, there was a significant main effect for group such that across all days SCI participants demonstrated an increase in flow of 16.3 ± 2 ml/ min, while flow decreased by 25 ± 2 ml/ min [$F(1,13) = 5.283$; $p = 0.04$] in AB (**Figure 7**).

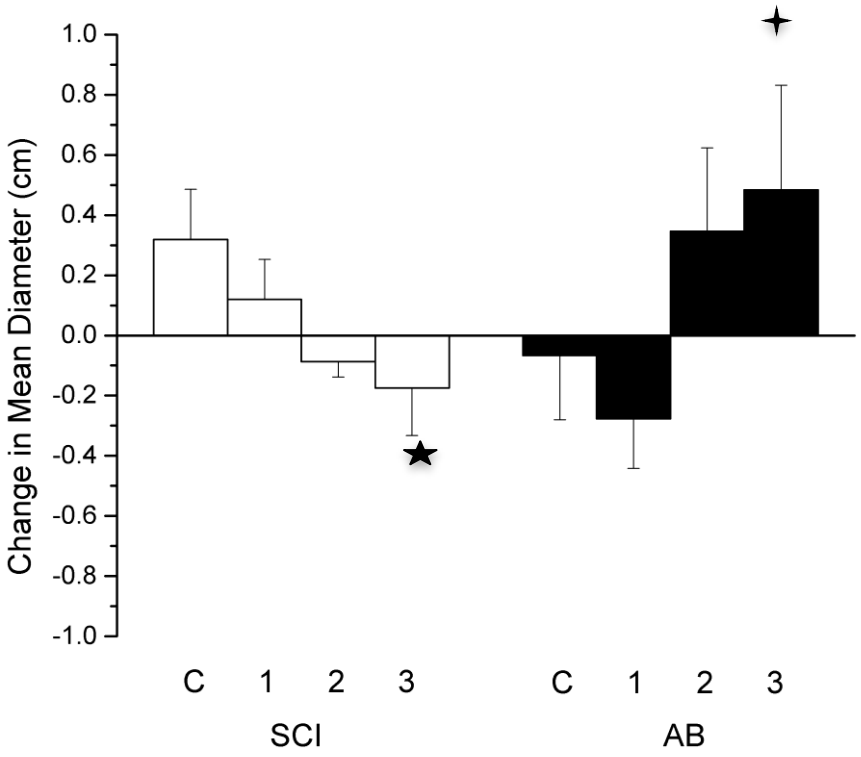


Figure 5 Change (Post-Pre) in femoral artery mean diameter of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3).Values are means ± SE. ⋆ different from AB. + different from Control.

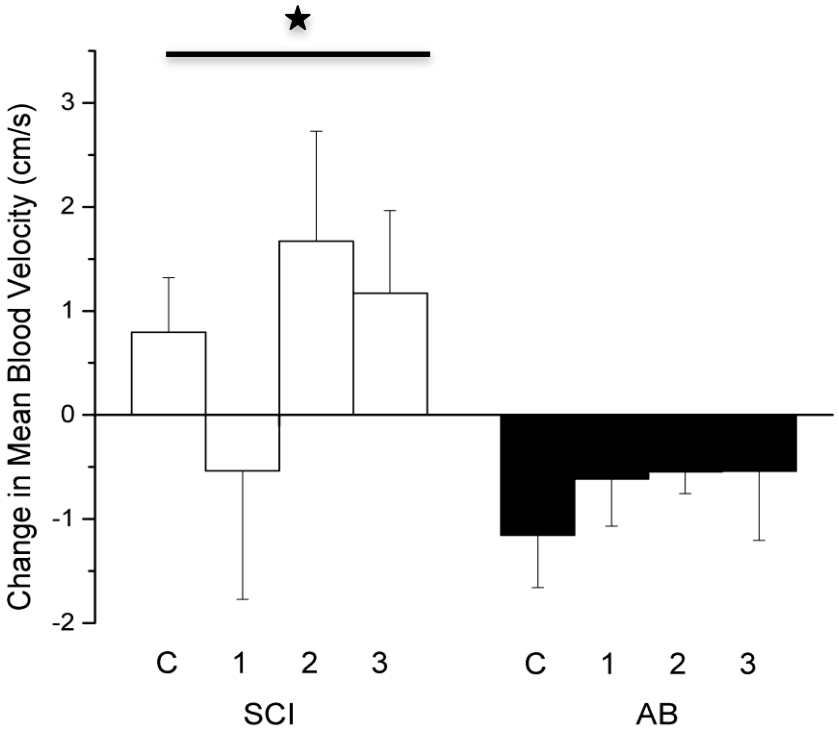


Figure 6 Change (Post-Pre) in femoral artery mean blood velocity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3). Values are means ± SE. ⋆ indicates different from AB.

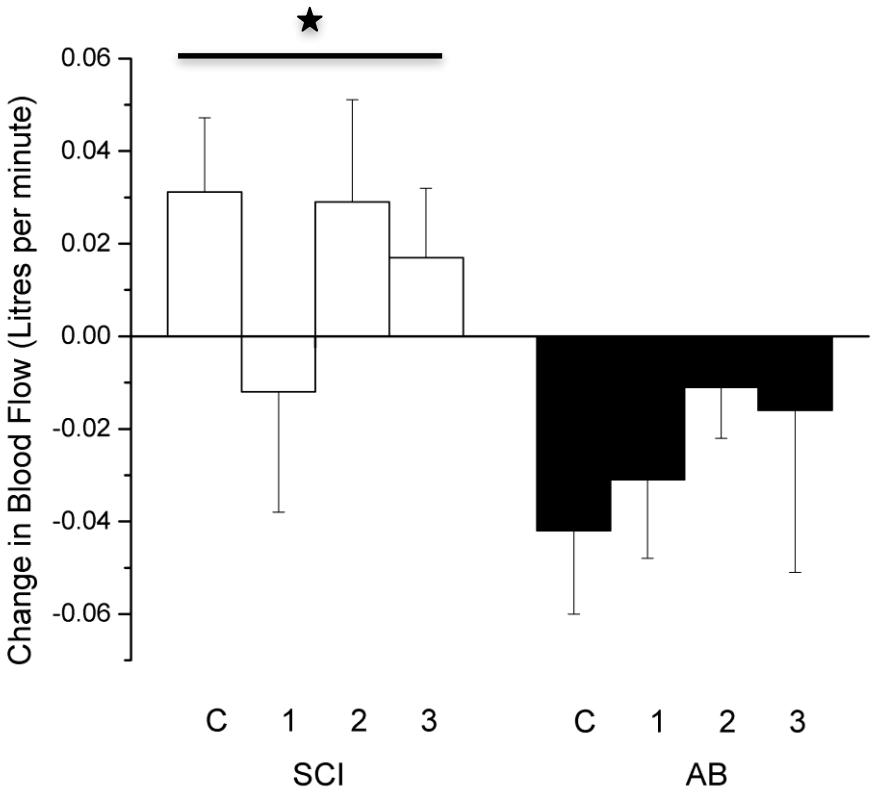


Figure 7 Change (Post-Pre) in femoral artery mean blood flow of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3).. Values are means ± SE. ⋆ indicates different from AB.

2.3.3 Cardiovascular Hemodynamics

The treatment-induced change in heart rate was not different between groups. There was a significant main effect of treatment on the change in heart rate [$F(3,39) = 3.511$, $p = 0.02$] with larger decreases in heart rate observed after Treatment 1 and 2 compared to control (**Figure 8**).

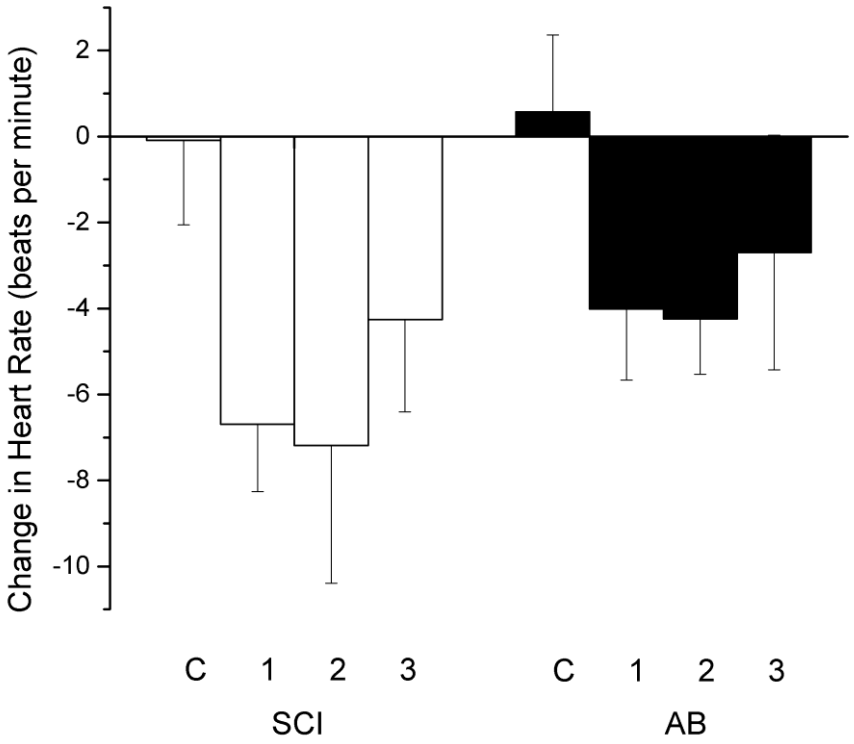


Figure 8 Change (Post-Pre) in heart rate in the lower extremity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3).. Values are means ± SE.

We observed a main effect for group in the change in systolic blood pressure with larger increases with treatment in SCI compared to AB [$F(1,10) = 7.173$, $p = 0.023$] (**Figure 9**). However, analysis revealed that this response was driven by an outlier in the

data that was more than 2 standard deviations from the mean. When this data point was removed there were no significant group or treatment effects for the change in systolic blood pressure or diastolic blood pressure.

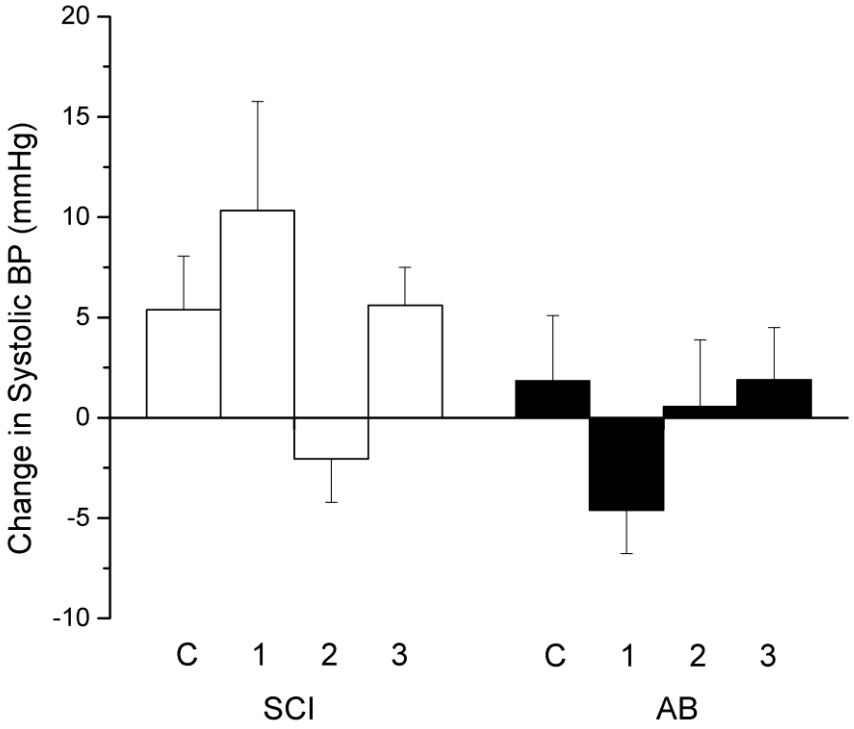


Figure 9 Change (Post-Pre) in systolic blood pressure in the lower extremity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3). Values are means ± SE.

2.3.6 Skin Temperature

The general finding with respect to skin temperature was that all interventions, treatment and control days, resulted in small, but significant cooling, of the lower extremity and that the change in temperature over time was greater in AB versus SCI participants. The skin temperature of the left thigh cooled less over time in SCI (-0.5 $\pm$ 0.1 ºC) versus AB (-1.2 $\pm$0.2 ºC) participants [$F(1,13) = 9.379$, $p<0.01$] (**Figure 10**). This data was analyzed with the removal of one data point from the second treatment (third visit) in the AB group. This point showed a 6.1ºC increase in value from pre to post 0 which was

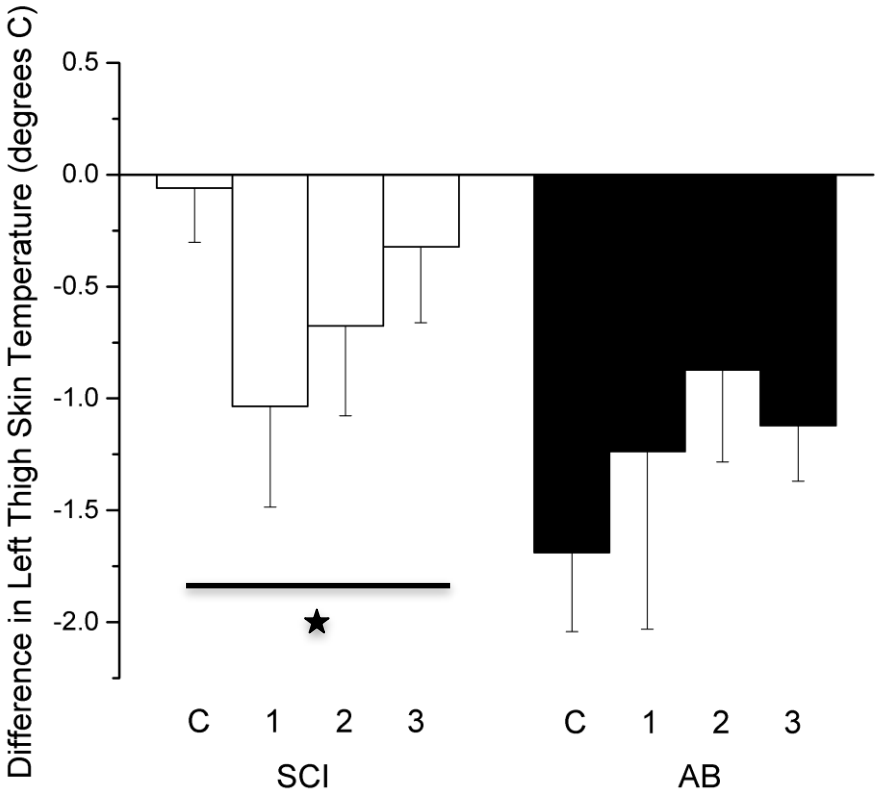


Figure 10 Change (Post-Pre) in left thigh skin temperature in the lower extremity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3). Values are means $\pm$ SE. ⋆ indicates different from AB.

greater than two standard deviations from the mean (SD =3.0 ºC) and therefore determined to be an outlier.

There was a change in skin temperature of the left calf in SCI (-0.2 ± 0.2 ºC) versus AB (-1.1 ± 0.3 ºC) participants [F (1,13) = 6.155, p<0.03] across all days (**Figure 11**). It must be noted that this data was analyzed with the removal of one data point from the second treatment (third visit) in the SCI group. This point showed a 5.0ºC increase in value from pre to post which was greater than two standard deviations (SD =1.8 ºC) from the mean.

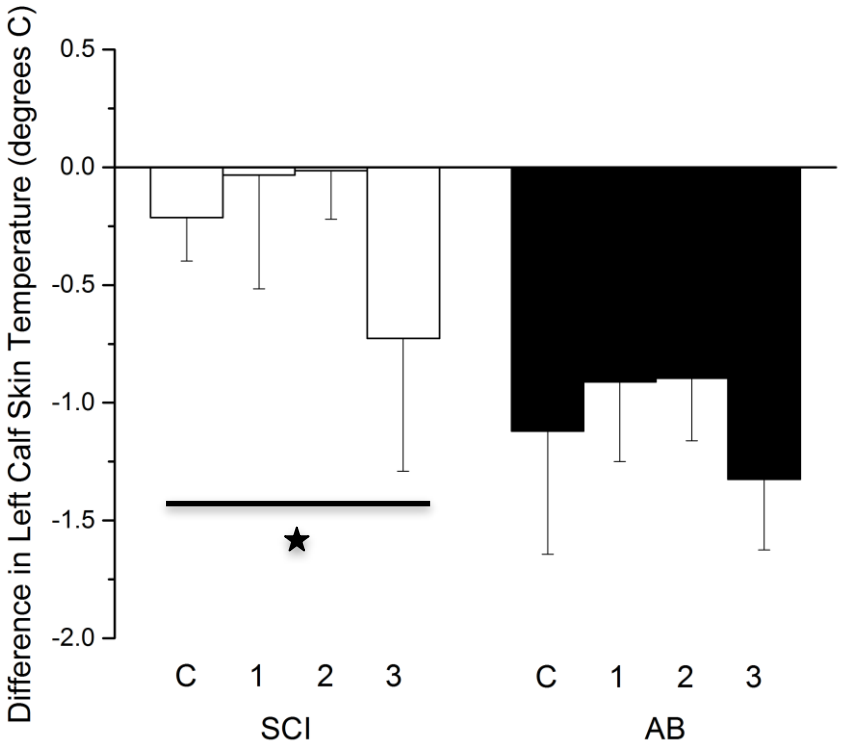


Figure 11 Change (Post-Pre) in left calf skin temperature in the lower extremity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3). Values are means ± SE. ⋆ indicates different from AB.

There was a main effect observed for the change in skin temperature of the left foot between the SCI and AB such that the magnitude of decrease over time was smaller in SCI (-0.1 ± 0.4 ºC) compared to AB (mean = -1.8 ± 0.4 ºC) participants [$F(1,13) = 8.995$, $p<0.01$] (**Figure 12**).

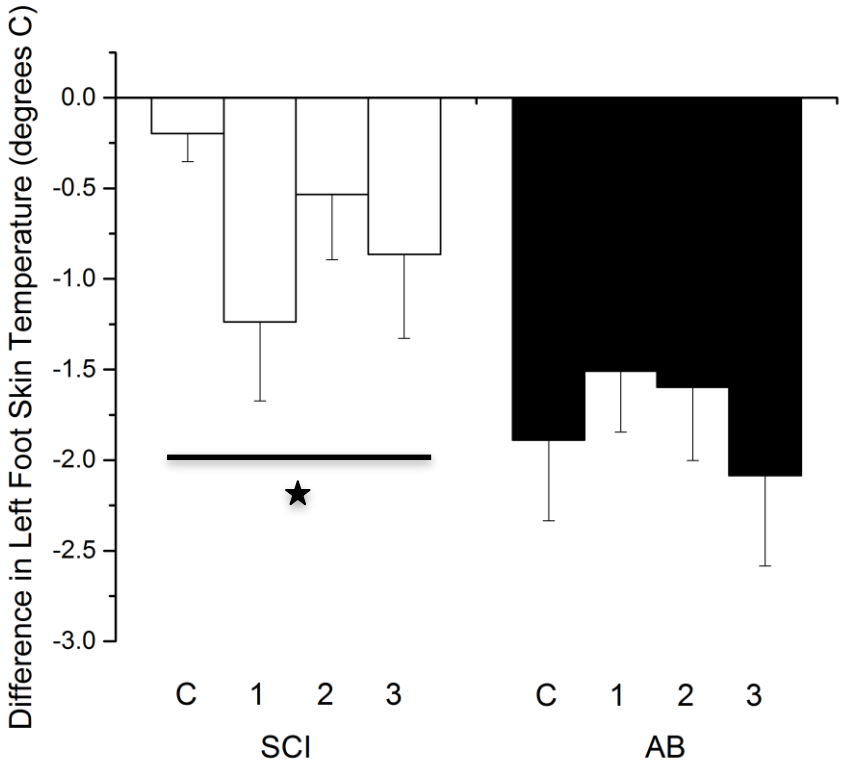


Figure 12 Change (Post-Pre) in left foot skin temperature in the lower extremity of SCI and able-bodied individuals with treatment (C: Control, 1: Treatment 1, 2: Treatment 2, 3: Treatment 3). Values are means ± SE. ⋆ indicates different from AB.

2.4 Discussion

Contrary to our hypothesis, we found no increases in blood flow or skin temperature occurring as a result of any of the osteopathic treatments in comparison to the timed control condition in either SCI or AB participants. Despite the lack of OMT-specific effects on femoral artery blood flow we did find that in both SCI and AB individuals Treatments 1 and 2 (cranial and abdominal treatments) resulted in decreases in HR in comparison to the Control condition. SCI individuals also demonstrated smaller decreases in skin temperature over time on all treatment days compared to AB, confirming previous findings of less skin temperature reactivity to physiologic stimuli in individuals with SCI. Although there were no OMT-specific leg hemodynamic effects in individuals with SCI, it is promising that small increases in leg blood flow were observed in comparison to the small decreases in leg blood flow observed in our AB participants. These increases in leg blood flow were likely due to alterations in mean blood velocity rather than acute changes in femoral artery diameter and occurred in the face of decreased HR and no change in blood pressure, thereby indicating a local blood flow regulating mechanism. Together these findings emphasize the potential for chronic increases in resting leg blood flow with an increased number of osteopathic treatments for individuals with SCI. In addition to these objective findings, specific subjective findings were also noted by different participants within this research project that justify the positive potential of osteopathic treatments in SCI.

The complete or incomplete loss of neurological control associated with a SCI is profound. Beyond the immediate and subsequent increased risk of mortality (Sekhon et al., 2001; Frankel et al., 1998), the devastating neurological impairments present, in most cases, is the greatest concern for every affected individual. In the subsequent weeks

following an SCI, however, major changes begin to occur within all tissues, systems and, ultimately, throughout the entire body as a result of the neurological impairment. These other reactions, or secondary complications, can become as much, or even more significant with regards to the individual's overall health (Johnson et al., 1998). To reverse, even in part, any of these complications after the alteration of neurological control is extremely challenging and can often take a prolonged period of time, however, there is certainly a great potential to eliminate or reduce some of the affiliated secondary complications that are associated with SCI. The purpose of this research was to examine the effects of osteopathic treatment, in comparison to a control visit, on blood flow and skin temperature in the lower extremity of individuals with SCI and an AB comparison group. With OMT induced acute increases in blood flow and skin temperature in the lower extremity, we proposed that the potential for other secondary complications, such as pressure sore development and progression could be reduced. We are unable, however, to distinguish if the positive increases in leg blood flow observed were simply a result of the period of supine rest or associated with the osteopathic treatment itself.

2.4.1 Leg Blood Flow

It has previously been established that passive leg movement results in increases in lower limb blood flow in AB individuals (Trinity et al., 2011). Interestingly, leg blood flow increases observed with passive leg exercise in AB participants was 2 fold higher when the exercise was performed in the upright compared to the supine position. In individuals with SCI, the impact of passive leg movement on leg blood flow are not as definitive with previous research identifying both increases (Ter Woerds et al., 2006) or no change (Ballaz et al., 2007) in leg blood flow with passive leg movement. In the

current study, in which all OMTs were performed in the supine position, we found no OMT specific changes in leg blood flow in either group. The focus of the OMT treatment was, however, not passive limb movement but tissue manipulation, and this may explain the lack of OMT specific changes in our study.

Previous research has identified that OMT results in release of endothelial anandamide and nitric oxide synthase with the potential to increase blood flow through the nitric oxide mediated vasodilation (McPartland et al., 2008). Pervious research by Hopman and colleagues has demonstrated that individuals with SCI retain preserved NO mediated endothelium dependent dilation in the femoral artery (deGroot et al., 2004) and preserved contribution of NO to baseline leg vascular tone (Bleeker et al., 2005). Based on this research indicating preserved lower limb NO vasodilatory pathways, we hypothesized that the OMT would result in elevated NO stimulated vasodilation and therefore increased blood flow versus the control condition in both SCI and AB groups. We further hypothesized that as the people with SCI may have more blood flow restrictions prior to treatment, they would have greater increases in flow with OMT. It may be that the magnitude of the NO stimulated vasodilatation was not sufficient to be detected with our study design and our blood flow measurement techniques. It is possible that the supine treatment position limited leg blood flow increases in our study or that the specific OMTs used in this study did not result in vasodilation and subsequent increased blood flow of the femoral artery.

2.4.2 Skin Temperature

We further hypothesized that because the OMTs used in this study were developed specifically to address tissue restrictions and lesions in the SCI group, while

the AB group presented with no specific complaints, the treatments would stimulate greater increases in leg blood flow and skin temperature in the SCI group. We found that despite small increases in leg blood flow in the SCI group, there were decreases in skin temperature over time with both control and OMT days and the magnitude of the change in skin temperature was smaller in people with SCI in comparison to the AB group. Possible reasons for the observed decreases rather than increases in skin temperature are that the 15minute acclimatization period was insufficient to reach a stable baseline and that skin temperature was still adjusting to the laboratory temperature throughout the testing sessions. Despite the direction of the skin temperature changes, our findings of smaller changes in skin temperature in people with SCI compared to AB are supported by previous research identifying decreased skin temperature and skin blood flow reactivity in individuals with SCI (Noortje et al., 2009; Cotie et al., 2010; Van Duijnhoven et al., 2009). Despite this reduced response it is possible that with repeated OMT treatment, adaptations would occur to improve reactivity in SCI over time.

2.4.3 Baseline Changes Within and Between Groups

Evaluating the baseline measures within and between groups allows for an analysis of day to day repeatability and baseline comparisons of our groups. There were no differences in the within group pre-intervention measures between days. As a result, it was concluded that any post-intervention (treatment) changes were the result of the treatment and not due to changes in the baseline values over time. These findings also indicate that, upon consideration of the OMTs, there were no lasting effects from the previous treatments. From a therapeutic standpoint, the researchers recognize that, given the severity of an SCI and the prolonged lengths of time post-injury (12.5 years in this

study), an early treatment carryover effect would be unlikely. Certainly, further research with regards to the minimum number of osteopathic treatments that might be required to obtain a prolonged treatment effect would be of benefit.

Evaluating the baseline measures between groups did highlight some group differences. It is of interest to note that certain pre-treatment differences between groups followed the expected or predicted norms, based on previous research, while other values did not. The mean femoral artery diameter was smaller in the SCI group when compared to the AB group. A significant amount of literature examining arterial diameter within the SCI population notes similar findings (Ditor & Hicks, 2009; Ditor et al., 2005; Schmidt-Truckass et al., 2000; Olive et al., 2000). Baseline femoral artery mean blood velocity was higher in SCI versus AB and these divergent diameter and velocity group effects account for the finding of no group difference in baseline leg blood flow.

Previous research has found chronic SCI results in significant decreases in blood flow within the femoral artery (Ter Woerds et al., 2006; Ditor et al., 2005; Hopman et al., 2002). Other measures which did not demonstrate significant differences between the SCI and AB groups include heart rate, systolic blood pressure, diastolic blood pressure and skin temperatures within the left thigh and foot. Left calf skin temperature was slightly, but significantly, lower in the SCI group. Cotie and colleagues (2010), found lower resting skin temperatures in four points of the lower extremity of the SCI group after BWSTT, and therefore this skin temperature group difference may be associated with the training status of our participants with SCI.

2.4.4 Osteopathic Treatment Considerations

In holding with the principles and methodology of osteopathy, each individual in the current study was treated in safe and effective manner. As the research and treatment progressed, it became apparent that many areas and tissues within each individual with a SCI were affected in similar manners. These areas included the core link as well as abdominal vitality, and pressures within the regions of the cranium, thorax and abdomen/pelvis. Although certain aspects of each treatment varied slightly according to each individual's presentation, many other tissues and systems were treated in similar manners. In order to gain insight into the effectiveness of specific treatments and techniques, we took effort to maintain continuity of treatment between individuals. As a result, each intervention and treatment was designed in such a way so as to maintain research specificity between subjects while accommodating for the variability and individuality of affected tissues between each participant.

With regards to treatment, the potential for autonomic dysreflexia was considered and monitored throughout each treatment. Because stimulation of certain tissues, regions or organs can elicit dysreflexic responses, constant recognition of this potential was prevalent. Subject awareness of symptoms associated with the early onset of dysreflexia helped to provide feedback prior to the development of any significant problems. Increased risk for potential dysreflexic responses was also previously determined for each subject through the initial verbal assessment. Visceral treatments performed below the level of the lesion were continually monitored through patient feedback. Individuals with SCI have specific early recognizable warning signs when potential dysreflexic reactions or responses have been initiated. Through verbal communication with the researcher, testing was altered or discontinued until all signs and symptoms indicating dysreflexia

had ceased. At the onset of this study, it was emphasized that each subject should empty their bladder prior to all treatment interventions in order to decrease the potential of dysreflexic responses resulting from issues of the bladder.

In this study, one specific, yet minor, dysreflexic response occurred as the result of a full bladder. Prior to this particular treatment, the individual had consumed a significant amount of water in order to combat extremely warm weather, and did not empty their bladder prior to the commencement of treatment. The mild feeling of illness began towards the end of the session and, upon bladder emptying, these symptoms quickly disappeared.

Each individual within this study had a surgical repair of the displaced vertebral fracture(s) and had some form of internal fixation of the affected vertebra(e). The scarring was extensive in each individual and, depending on the surgical procedure used, this scarring was either in the anterior or posterior aspect of the cervical region. One significant effect of this scarring was the extensive adhesions and tension created within the superficial, middle and deep layers of the cervical fascia. These tensions created a subsequent pull onto the pharyngobasilar fascia and into the dura. This tension was fremarkable in each subject and required specific and focused treatment. This fascia was treated for each individual in the first treatment when the core link, cranial lesions and cervical lesions were addressed. Another area requiring specific attention was the vertebral fracture(s). Compactions within the healed vertebra(e) were also addressed.

With the prolonged removal of neurological supply to any structure or tissue, complete or partial, these structures, tissues and affiliated regions lose a significant amount of vitality. In order to restore some of this vitality, increased amounts of time

and energy were required and channeled towards these structures in order to create a therapeutic effect. As a result, time availability for other regions was limited. Ultimately, these areas might have benefitted from further time and attention. In recognizing that osteopathic treatments often have profound and immediate effects in able-bodied individuals (Stefano et al., 2006; Crow & Gorodinsky, 2009; Arienti et al, 2011), it must be recognized and appreciated that the treatment and restoration of position, mobility and vitality will require significantly greater lengths of time to create an effect within the individuals with SCI. Restrictions of time limited the areas and tissues that could be treated in full in the 3 OMT days in the current study and although many structures were in lesion, to varying degrees, time did not allow for the complete treatment in all tissues.

The initial visit of each individual focused on the general assessment of the tissues and the systems. From these assessments, lesions of greater significance were addressed. In following the osteopathic methodology, compactions and intraosseous lesions were addressed first. According to the Canadian College of Osteopathy Methodology, (Canadian College of Osteopathy, 2005), following the treatment of compactions, treatment would focus on non-physiological lesions without respect to the axis. However, because any type of osteopathic adjustment or impulse is contraindicated for SCI, this type of technique was not performed. Upon consideration of the osteopathic principle 'The rule of the artery is absolute,' focus also centered around the entire fluidic system and, in particular, the femoral artery. Not only were direct techniques on the femoral artery performed, but also, techniques on lesioned structures surrounding the artery were conducted.

In addition to the vascular fluids, it was also an objective of the OMT to address the flow of cerebrospinal fluid (CSF) in all subjects. In order to reach and address the CSF within the spinal cord during treatment, one must first affect the dura. This dura is a key aspect of the core link, as it helps to form a link between the cranium and the sacrum. Certainly, some of the most profound effects of osteopathic treatment within this research occurred as a result of dural treatment. From a subjective standpoint, certain individuals commented on the positive effects that the first treatment (second visit) had on overall energy levels. Although questionnaires and subjective findings were not used as measuring tools in this particular research, the comments made around this initial treatment justified the use of osteopathic treatments on individuals with SCI.

2.4.5 Limitations

There are many challenges and limitations that can occur when working with a special population, including the SCI population. The most significant problem for this particular study proved to be the recruitment of participants. In order to gain approval from the Hamilton Health Sciences Research Ethics Board, recruiting was only to be done based on the use of a recruiting flyer. Within the population that became aware of the study, many other challenges were also presented. In several instances, individuals with SCI were not interested in participation. Within this group, each individual had legitimate reasons that were given, including transportation and freedom of time. Although the area within which this study occurred provides accessible transportation to the disabled, wait times and travel times can be quite lengthy. Other reasons for refraining from participation included previous participation in many other SCI studies. Regardless of the reasons behind non-participation, the decision of each individual was

respected. At the same time, it created a greater awareness as to how many obstacles and challenges these individuals face every day.

Another challenge of this research surrounded the methodology. More specifically, difficulties in maintaining a seven-day schedule between each session became a challenge. Although these situations were infrequent, the main contributing factor was that of inclimate weather conditions. In the winter, excessive snow created transportation problems and, as a result, sessions had to be delayed. At the same time, excessive heat in the summer months also posed a problem. Because individuals with SCI can have significant challenges with heat control due to a decreased ability to sweat, occasions arose where sessions had to be rescheduled. One final consideration that delayed sessions was the fact that other life issues occurred that forced the delay of particular sessions. However, in all situations, the next subsequent session was not delayed by more than an extra seven days.

Certainly, research presents many challenges and obstacles that can lead to critical problems in some situations and positive breakthroughs in other situations. Although recruiting was a significant problem in this research, one of the greater challenges became the crossing of traditional osteopathic treatments with traditional scientific research. In scientific research, the more each study establishes consistency and continuity within its methodologies, the more a proven hypothesis will be accepted. In contrast, osteopathy has established a strong reputation due to its unique and individual approach to the evaluation and treatment of each individual. Although there is an established methodology that is to be followed, where more significant lesions affecting global vitality should be addressed prior to the correction of minor lesions, it is

imperative for an osteopathic approach to establish and maintain individualism throughout each treatment. Therefore, treatments must vary between subjects if they are to be effective. In order to address health within the true osteopathic approach, treatments will vary between every individual. As a result, it is very difficult to proceed with an approach that would resemble a classical scientific model of research with consistent, if not exact, interventions for each subject. Hence, the challenge of this 'scientifically osteopathic' research. Keeping this in mind, it was, at times, a challenge to ensure that each session was an osteopathic treatment as opposed to a session of osteopathic techniques. While maintaining a true osteopathic approach, it was also necessary to follow a guided approach that would eliminate or reduce scientific scrutiny. This was further challenged by the constant awareness that the results of each treatment were being measured. In true osteopathy, focus does not waiver from the individual in front of the osteopath. This research, therefore, created a challenge from which the researcher developed and established stronger grounding mechanisms.

Another significant limitation surrounding osteopathic methodology and the treatments of SCI's was that of vertebral osteoarticular lesions. From an ethical and medical standpoint, absolutely no osteoarticular adjustments were to be performed on the vertebral column or any other joint within the body. With a reduction in bone density and an accompanying risk for potential fractures (Giangregario et al., 2005), any osteoarticular adjustment was and always should be strongly contraindicated within the SCI population. This point can be strongly supported by the experiences of one particular subject within this study. Since the occurrence of an SCI over twelve years ago, this particular individual has sustained two tibial fractures on separate occasions and fractures

of the transverse processes of L2-4 on another occasion. For this reason, adjustments of any joint within individuals with SCIs are unsafe and unethical. With significant reductions in the methods available to align the vertebral column, it made the treatment of the spine within these subjects very difficult. With the inability to generate any muscle contractions, true muscle energy techniques were also not appropriate, or possible, for this population. The main method of vertebral normalization was through the use of indirect osteopathic techniques (Nicholas & Nicholas, 2011). The problem which arose from the use of these techniques was the positioning of the subject. With no muscular control or input, it was difficult to place them in sitting or sidelying in order to apply any techniques on areas other than the cervical spine. Without a true and risk-free method of aligning the spine, the methodology of osteopathy was difficult to follow. At the same time, having a vertebral column out of line can certainly cause other problems as well. The potential for spinal segmental facilitation, as described by Patterson, could affect a variety of structures, which include the muscles and viscera (Patterson, 1976). Without normalizing these vertebrae, certain individuals with SCI could develop segmental facilitation in the regions where spinal reflexes might be present. However due to pain, lack of stability or current/previous fractures in the area, normalizations of specific vertebrae were not always possible. This is another reason as to potential benefits of a longer treatment protocol, where additional time could be taken to correct these lesions.

Other scientific methodological limitations of our research include our small sample size, the relatively short acclimatization period to the testing environment and lack of direct measures of skin blood flow or nitric oxide metabolism. There is a

possibility that with more participants in each group we may have observed treatment specific changes in some of the variables of interest.

2.4.6 Future Considerations

In the future, it would certainly be helpful to have access to more research surrounding osteopathy and SCI. The current research provides a stepping stone for further research addressing the effects of OMT in individuals with SCI. Due to the broad realm of issues and problems afflicting those individuals with SCI, many avenues of research can be approached in the future. Certainly, one strong recommendation would be to conduct a research project that examines the effects of specific osteopathic treatments or techniques over a prolonged period of time. SCI has a profound effect on all aspects of the human body. Positive effects of any treatment may be observed on a greater scale if treatments were to take place over a much longer time period. This, in itself, could be the focus of one study, where the time required to effect beneficial changes through treatment are measured. Although each individual is different and responsive adaptations vary between these individuals, measuring the time or number of treatments required to cause a significant and prolonged effect could provide other osteopaths with a very important example or idea as to what a time frame for positive results might be.

Another potential approach would be to study the effects of specific techniques on particular measures throughout the treatment. This may also provide insight into what osteopathic treatments or techniques might be more beneficial to the individuals with SCI. This current research used one type of intervention, osteopathic treatment, and its effect on blood flow and skin temperature. It might also be of benefit to study the

combination of various interventions within one study. It would be interesting to analyze the effects of osteopathic treatment immediately followed by exercise, such as the body-weight supported treadmill, on blood flow and skin temperature in the lower extremity. As mentioned much earlier, individuals with SCI withstand many subsequent secondary complications to various extremes. Research focused on the reduction or elimination of any one of these complications would be beneficial and well received.

Certainly, the comparative effects of osteopathic treatment between tetraplegics, paraplegics and able-bodied on various outcomes is beneficial. It would also be of interest to compare these effects within the SCI population of different neurological classifications. In other words, examining the effects of osteopathic treatment in SCI individuals with similar vertebral levels of different severities according to the AIS classification scale would also be a valuable study. This would provide further insight into the potential of osteopathy amongst SCI individuals with varying neurological severity. This would also provide the osteopathic profession with potential outcomes of treatment amongst individuals with SCI of various severities.

Another extremely important and critical study would be to study the effects of osteopathy after various onsets of injury. It would be very interesting to note if these treatments would be more effective if the onset were closer to the date of injury, or if this may have no bearing on overall results. Based on the lesions and tensions that have been felt and discovered by this particular investigator, time between injury and the onset of treatment could be critical. As with any lesion in any individual, able-bodied or otherwise, the longer it remains untreated, the greater and more profound the resultant

effects are on the local and global tissues. Therefore, within reason, quicker access to treatment might prove to be more beneficial within the SCI population.

Each subject within this study was, previously, unaware of osteopathy prior to their participation in the study. Therefore, more SCI treatment and rehabilitation centers must be made aware of osteopathy and the potential benefits of this treatment. Within today's medical community, the best way to draw positive awareness to osteopathy and the treatment of SCI is through research.

Based on the feedback provided from the subjects within this research, it would also be of further benefit to develop a distinct and recognizable questionnaire to the individuals with SCI when participating in osteopathic research. Through a specific questionnaire, many subjective, yet positive, effects could be established if consistencies were noted between individuals.

The possibilities and areas for research surrounding osteopathy and SCI are numerous. The vast potentials of research can definitely exceed objective findings. At the same time, these potentials can direct future research within the SCI population. The potential positive benefits that can result from osteopathic treatments within the SCI population are significant for both the SCI population and the practitioner.

2.4.7 Conclusions

This current research examined the effects of osteopathic treatment on blood flow and skin temperature in the lower extremity of individuals with SCI and able-bodied individuals. The individuals with SCI demonstrated a greater increase in blood flow over time with treatment and control conditions than the able-bodied individuals. At the same time, smaller increases in lower extremity skin temperatures were found in the

individuals with SCI when compared to the able-bodied individuals. These findings support the hypothesis that people with SCI have reduced lower extremity skin temperature reactivity in comparison to AB individuals and that osteopathic treatment may be one mechanism to acutely increase femoral artery blood flow. Further research is required to determine if longer term osteopathic treatment would result in beneficial effects in terms of lower extremity blood flow and skin temperature in this population.

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4 APPENDICES

4.1 APPENDIX A – Standard Neurological Classification of Spinal Cord Injury

Patient Name _____

Examiner Name _____ Date/Time of Exam_____

STANDARD NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

ISCOS

MOTOR

KEY MUSCLES (scoring on reverse side)

	R	L	
C5			Elbow flexors
C6			Wrist extensors
C7			Elbow extensors
C8			Finger flexors (distal phalanx of middle finger)
T1			Finger abductors (little finger)
UPPER LIMB TOTAL (MAXIMUM)		+	=
	(25)	(25)	(50)

Comments:

L2			Hip flexors
L3			Knee extensors
L4			Ankle dorsiflexors
L5			Long toe extensors
S1			Ankle plantar flexors

Voluntary anal contraction (Yes/No)

LOWER LIMB TOTAL (MAXIMUM) + = (50)

SENSORY

KEY SENSORY POINTS

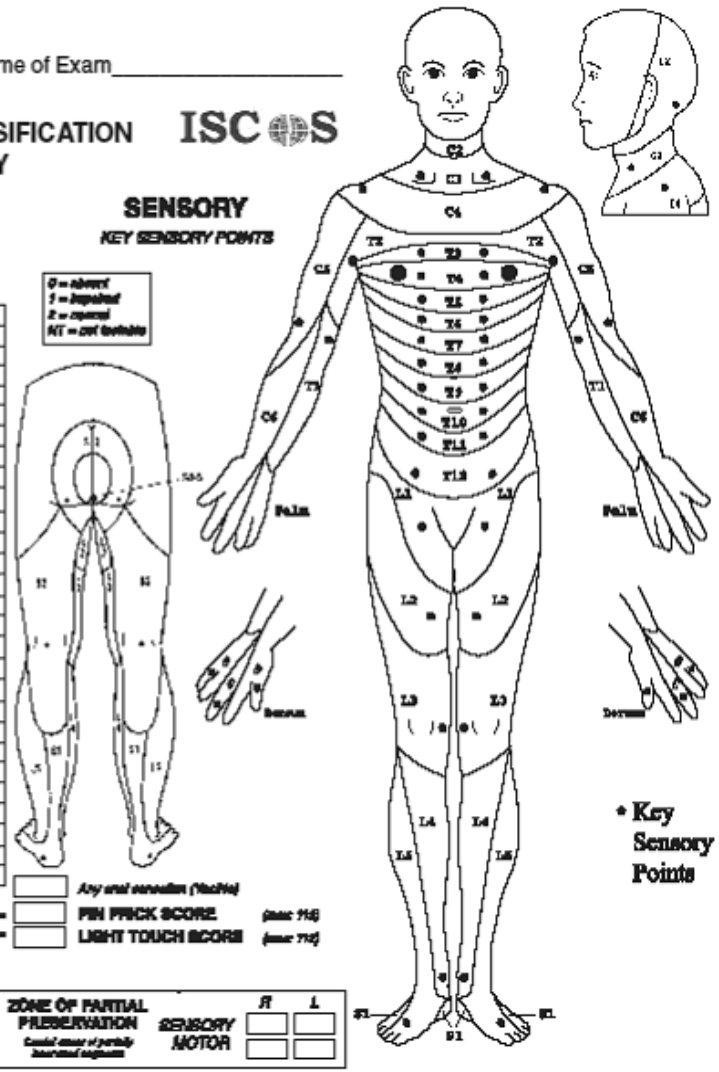
0 = absent
1 = impaired
2 = normal
NT = not testable

	LIGHT TOUCH R	LIGHT TOUCH L	PIN PRICK R	PIN PRICK L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				
TOTALS (MAXIMUM)	+ (56)	+ (56)	+ (56)	+ (56)

Any anal sensation (Yes/No)

PIN PRICK SCORE (max: 112) =

LIGHT TOUCH SCORE (max: 112) =



NEUROLOGICAL LEVEL	SENSORY R	SENSORY L	COMPLETE OR INCOMPLETE?	ZONE OF PARTIAL PRESERVATION	SENSORY R	SENSORY L
The most caudal segment with normal function	MOTOR		ASIA IMPAIRMENT SCALE	Caudal extent of partially innervated segments	MOTOR	

This form may be copied freely but should not be altered without permission from the American Spinal Injury Association.

REV 02/04

4.2 Appendix B – ASIA Impairment Scale

MUSCLE GRADING

0 total paralysis

1 palpable or visible contraction

2 active movement, full range of motion, gravity eliminated

3 active movement, full range of motion, against gravity

4 active movement, full range of motion, against gravity and provides some resistance

5 active movement, full range of motion, against gravity and provides normal resistance

5* muscle able to exert, in examiner's judgement, sufficient resistance to be considered normal if identifiable inhibiting factors were not present

NT not testable. Patient unable to reliably exert effort or muscle unavailable for testing due to factors such as immobilization, pain on effort or contracture.

ASIA IMPAIRMENT SCALE

☐ **A = Complete**: No motor or sensory function is preserved in the sacral segments S4-S5.

☐ **B = Incomplete:** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.

☐ **C = Incomplete:** Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.

☐ **D = Incomplete:** Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.

☐ **E = Normal:** Motor and sensory function are normal.

CLINICAL SYNDROMES (OPTIONAL)

☐ Central Cord
☐ Brown-Sequard
☐ Anterior Cord
☐ Conus Medullaris
☐ Cauda Equina

STEPS IN CLASSIFICATION

The following order is recommended in determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
2. Determine motor levels for right and left sides.
   Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level.
3. Determine the single neurological level.
   This is the lowest segment where motor and sensory function is normal on both sides, and is the most cephalad of the sensory and motor levels determined in steps 1 and 2.
4. Determine whether the injury is Complete or Incomplete (sacral sparing).
   If voluntary anal contraction = **No** *AND all S4-5 sensory scores* = **0** *AND any anal sensation* = **No**, *then injury is COMPLETE. Otherwise injury is incomplete.*
5. Determine ASIA Impairment Scale (AIS) Grade:

   Is injury Complete?
   NO → If **YES**, AIS=A Record ZPP (For ZPP record lowest dermatome or myotome on each side with some (non-zero score) preservation)

   Is injury motor incomplete?
   YES → If **NO**, AIS=B (Yes=voluntary anal contraction OR motor function more than three levels below the motor level on a given side.)

   Are at least half of the key muscles below the (single) neurological level graded 3 or better?
   NO → AIS=C
   YES → AIS=D

If sensation and motor function is normal in all segments, AIS=E
Note: AIS E is used in follow up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact; the ASIA Impairment Scale does not apply)

4.3 Appendix C: REB Letter of Approval

Hamilton Health Sciences

RESEARCH ETHICS BOARD

McMaster University

REB Office, 1057 Main St. W., Hamilton, ON L8S 1B7
Telephone: 905-521-2100, Ext. 42013
Fax: 905-577-8379

June 14, 2006

PROJECT NUMBER: **05-427**

PROJECT TITLE: The effects of osteopathic treatment on blood flow in the lower extremities of individuals with spinal cord injuries

PRINCIPAL INVESTIGATOR: **Dr. M. MacDonald**

This will acknowledge receipt of your letter dated June 8, 2006 which enclosed the revised Participant Information Sheet and Consent Form, version dated March 2006 along with the revised recruitment flyer for the above-named study. These issues were raised by the Research Ethics Board at their meeting held on December 20, 2005. Based on this additional information, we wish to advise your study has been given ***final*** approval from the full REB. The submission, including the Participant Information Sheet and Consent Form, version dated March 2006 and the recruitment flyer was found to be acceptable on both ethical and scientific grounds. ***Please note*** attached you will find the Information Sheet/Consent form with the REB approval affixed; all consent forms and recruitment materials used in this study must be copies of the attached materials.

We are pleased to issue final approval for the above-named study for a period of 12 months from the date of the REB meeting—December 20, 2005. Continuation beyond that date will require further review and renewal of REB approval. Any changes or amendments to the protocol or consent form must be approved by the Research Ethics Board.

We wish to advise the Research Ethics Board operates in compliance with ICH Good Clinical Practice Guidelines and the Tri-Council Policy Statement.

Investigators in the Project should be aware that they are responsible for ensuring that a complete consent form is inserted in the patient's health record. In the case of invasive or otherwise risky research, the investigator might consider the advisability of keeping personal copies.

A condition of approval is that the physician most responsible for the care of the patient is informed that the patient has agreed to enter the study. Any failure to meet this condition means that Research Ethics Board approval for the project has been withdrawn.

PLEASE QUOTE THE ABOVE-REFERENCED PROJECT NUMBER ON ALL FUTURE CORRESPONDENCE

Sincerely,

S. Salama

for F. Jack Holland, MD, FRCP, FRCP(C)
Chair, Research Ethics Board

4.3.1 PARTICIPANT INFORMATION SHEET

The effects of osteopathic treatment on leg blood flow

in individuals with spinal cord injury

You are invited to participate in a research study conducted by:

- David Murray, Athletic Therapist, Department of Athletics and Recreation, McMaster University; Student, Canadian College of Osteopathy
- Dr. Audrey Hicks, Professor, Department of Kinesiology, McMaster University
- Dr. Maureen MacDonald, Assistant Professor, Department of Kinesiology, McMaster University

This study is funded in part by:

- The National Science and Engineering Research Council (NSERC)

You are being invited to participate in this research study because you have a spinal cord injury.

In order to decide whether or not you want to be a part of this research study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the research study, which will be discussed with you. Once you understand the study, you will be asked to sign this form if you wish to participate. Please take your time to make your decision. Feel free to discuss it with your friends and family, or your family physician.

WHY IS THIS RESEARCH BEING DONE?

This research is being done because spinal cord injuries often results in a decrease in blood flow and skin temperature in the legs. This decrease in blood flow can then cause many other problems including pressure sores and weakening of bones. Finding ways to increase blood flow and skin temperature in people with spinal cord injury should decrease the number and severity of these other problems and create a possible increase in the quality of life. At the same time, by creating a further awareness of spinal cord injury within the field of osteopathy, further research may be done and, as a result, further benefits may be found. While it is the aim of this study to increase blood flow and skin temperature in the legs, there are no certainties.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to:

1. Determine the effects of osteopathic treatment on leg blood flow and skin temperature in people with spinal cord injury.
2. Determine if different parts or aspects of each treatment is more effective than other parts of the treatment.

WHAT IS AN OSTEOPATHIC TREATMENT?

Osteopathy is a type of therapy that is entirely based on the use of hands to treat specific physicalproblems within an individual. This hands-on therapy is used to create a balance between and within many of the systems of the body. These systems would include the musculoskeletal, cardiovascular, nervous and digestive systems. By creating this balance, painful areas within the body could possibly be eliminated. When using an osteopathic treatment, the therapist's hands are always on the body of the individual being treated. Most of the hand placements on the patient are very light and should not create any discomfort or pain. The individual may, at times, feel warmth in the areas being treated as specific areas being treated release their tensions. However, no pain should be noticed. Areas that will be touched may include the head, the neck, the abdomen and the upper and lower leg. It is the hope of this study to create a measurable increase in blood flow in the legs, but because past research has few studies dealing with the effects of osteopathic treatments on individuals with spinal cord injuries, improvements can not be guaranteed.

WHAT WILL MY RESPONSIBILITIES BE IF I TAKE PART IN THE STUDY?

If you volunteer to participate in this study, we will ask you to do the following things, in this order:

1. Obtain a doctor's approval for participation in this study.
2. Come to McMaster University for an initial information and verbal assessment visit. The study will be explained to you and you will then have your initial resting blood flow and skin temperature measured.
3. Asked a series of questions pertaining your injury and your overall health
4. Placed on a comfortable treatment table where your initial leg blood flow and skin temperature will be measured in the left groin area. This will all be done while lying supine (on your back).
5. Retested for blood flow and skin temperature in the leg -- this completes the initial assessment and is expected to take ~ 1hour and 15minutes.

6. The next 3 visits will all follow the same pattern, with only the types of techniques changing for each visit.
7. Each visit will commence with a measure of resting leg blood flow blood and skin temperature.
8. Treatment will then begin, lasting for ~45minutes. Each treatment will involve hands-on actions that will be gentle and should not produce any pain. These different actions will cover different areas of the body including: the head, the neck, the abdomen and the legs. Once again, these treatments should be pain free and are performed while you are fully dressed.
9. At the end of the treatment, another resting leg blood flow and skin temperature measure will be taken.
10. This study will take place over a period of ~6 weeks, with 3 weeks between the initial assessment visit and the first treatment visit and then 1 week between each treatment visit.

In total, you will:

- take part in one information/verbal assessment session (~ 1 hour and 15 minutes)
- take part in 3 sessions of osteopathic treatment (~ 45 minutes/session)
- have your leg blood flow and skin temperature measured before and after each session (~ 30 minutes/session)

Measuring leg blood flow:

- Each assessment will take approximately 30 minutes.
- You will be asked to avoid products that contain nicotine (cigarettes, chewing tobacco) for 2 hours before the test.
- A machine called an echo-Doppler ultrasound will be used to measure your blood flow. You will be laying down, very still, for the test. A hand-held probe will be moved lightly over the skin above a blood vessel in the area of your upper thigh. The probe sends and receives sound waves that bounce off solid objects, including blood cells. A clear, water-based conducting gel will be applied to the skin over the area being examined to help with the transmission of the sound waves. Information from the reflected sound waves will be processed by a computer to provide graphs or pictures that represent the flow of blood through blood vessels. This information will be stored on a computer for analysis.
- The leg blood flow will be measured in one leg only and that leg will be exposed in the groin area in order to be assessed.
- This procedure poses no physical risk to you because the sound waves produced by the probe are harmless.
- If you have feeling in your groin area, you might find that the conducting gel feels cool.
- Skin temperature will be measured at the same time over six different sites

on the leg by the placement of temperature sensors on the skin. These should cause no discomfort.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Osteopathic treatment is a complete hands-on type of therapy. It is non-invasive and should not create any pain during the treatment. At times, mild discomfort may be felt due to increased pressure of the therapist's hands during specific treatment, but this discomfort will disappear when the hands are removed.
Blood flow measurements are not expected to cause any pain. If you have feeling in your legs, the ultrasound gel might feel cold when it is applied to your skin. By making sure that the skin is always adequately coated with ultrasound gel, we will prevent the uncommon risk for a minor burning sensation that can occur if there is insufficient gel. There is the possibility that some minor skin irritation might occur as a result of the ultrasound gel, but this is extremely uncommon and, if it occurs, clears up within a few days. The blood flow measurement test mentioned above does not have any known risks. Skin temperature measurement should not cause any pain or discomfort and has no known risks.

You will be required to travel to McMaster University for all assessment and treatment sessions. The payment provided for participation in this study is intended to help reimburse you for the financial costs associated with your travel and parking for this study.

If you choose to take part in this study, you will be told about any new information which might affect your willingness to continue to participate in this research.

HOW MANY PEOPLE WILL BE IN THIS STUDY?

In total, 15 people will be taking part in this study.

WHAT ARE THE POSSIBLE BENEFITS FOR ME AND/OR FOR SOCIETY?

We cannot promise any personal benefits to you from your participation in this study. However, possible benefits include increased blood flow to your legs, which may result in warmer legs and a decreased risk for pressure sores. In addition, your participation may help other people with spinal cord injury in the future, because you would be helping to increase knowledge about how osteopathic treatment could positively affect the consequences of spinal cord injury.

IF I DO NOT WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

It is important for you to know that you can choose not to take part in the study. Choosing not to participate in this study will in no way affect your medical care or treatment.

WHAT INFORMATION WILL BE KEPT PRIVATE?

Your data will not be shared with anyone except with your consent or as required by law. All personal information such as your name, address, phone number, and physician's name will be removed from the data and will be replaced with a number. A list linking the number with your name will be kept in a secure place, separate from your file. The data, with identifying information removed, will be securely stored in a locked office in the research laboratory.

If the results of the study are published, your name will not be used and no information that discloses your identity will be released or published without your specific consent to the disclosure.

CAN PARTICIPATION IN THE STUDY END EARLY?

If you volunteer to be in this study, you may withdraw at any time and this will in no way affect the quality of care you receive. You have the option of removing your data from the study. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise which warrant doing so.

WILL I BE PAID TO PARTICIPATE IN THIS STUDY?

If you agree to take part, we will reimburse you for the costs of parking and/or transportation for study-related expenses. In the event that you cannot complete the requirements of the study, you will receive a pro-rated amount at the rate of $6.00 per assessment or treatment session attended.

WILL THERE BE ANY COSTS?

Your participation in this research project may involve additional costs to you for travel to and parking at McMaster University. The payment provided for participation in this study is intended to help reimburse you for financial costs associated with your travel and parking for this study.

WHAT HAPPENS IF I HAVE A RESEARCH-RELATED INJURY?

If you sign this consent form it does not mean that you waive any legal rights you may have under the law, nor does it mean that you are releasing the

investigator(s), institution(s) and/or sponsor(s) from their legal and professional responsibilities.

IF I HAVE ANY QUESTIONS OR PROBLEMS, WHOM CAN I CALL?

If you have any questions about the research now or later, or if you think you have a research-related injury, please contact David Murray (905-525-9140, extension 23575), Dr. Audrey Hicks (905-525-9140, extension 24643) or Dr. Maureen MacDonald (905-525-9140, extension 23580). If you have any questions regarding your rights as a research participant, you may contact Hamilton Health Sciences Patient Relations Specialist at 905-521-2100, ext. 75240.

CONSENT STATEMENT

SIGNATURE OF THE RESEARCH PARTICIPANT/LEGALLY-AUTHORIZED REPRESENTATIVE

I have read the preceding information thoroughly. I have had the opportunity to ask questions, and all of my questions have been answered to my satisfaction. I agree to participate in this study. I understand that I will receive a signed copy of this form.

_____
Name of Participant

_____
Name of Legally Authorized Representative (if applicable)

_____ _____
Signature of Participant or Legally Authorized Representative Date

Consent form administered and explained in person by:

_____
Name and title

_____ _____
Signature Date

SIGNATURE OF INVESTIGATOR:

In my judgement, the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent to participate in this research study.

_____ _____
Signature of Investigator Date

4.4 Raw Data

subject	time	treatment	group	Flow (L/min)	Diam (mm)	MBV (cm/sec)	HR (bpm)	SBP (mmHg)	DBP (mmHg)	ST-lt thigh (°C)	ST-lt calf (°C)	ST-lt foot (°C)
1	1	1	1	0.144	10.8	2.60	65	118	67	31.8	30.1	30.5
2	1	1	1	0.067	8.2	2.11	57	123	69	33.1	31.5	29.8
3	1	1	1	0.191	10.4	3.74	56	122	64	32.6	30.9	29.5
4	1	1	1	0.284	7.7	10.26	61	118	77	32.9	31.7	32.5
5	1	1	1	0.126	8.6	3.57	59	109	74	31.5	31.6	30.2
6	1	1	1	0.085	7.8	3.00	53	109	62	33.8	31.3	29.6
1	1	2	1	0.124	11.3	2.06	60	124	70	32.7	31.9	32.1
2	1	2	1	0.121	9.5	2.82	48	120	66	31.8	31.1	31.0
3	1	2	1	0.138	9.8	3.06	65	119	59	33.1	31.4	29.4
4	1	2	1	0.225	7.5	8.43	68	115	69	30.7	31.1	30.1
5	1	2	1	0.084	8.9	2.22	60	119	79	29.4	30.0	28.4
6	1	2	1	0.132	9.9	2.87	62	119	69	30.4	30.8	29.5
1	1	3	1	0.132	10.9	2.37	62	121	71	32.8	31.2	31.9
2	1	3	1	0.113	8.0	3.72	49	116	68	32.4	31.1	29.7
3	1	3	1	0.125	9.5	2.93	60	122	63	33.1	31.1	30.4
4	1	3	1	0.121	7.0	5.24	67	105	64	25.3	30.4	29.2
5	1	3	1	0.090	8.4	2.74	71	109	76	30.9	31.5	31.5
6	1	3	1	0.115	8.8	3.15	61	106	65	33.6	31.8	30.2
1	1	4	1	0.056	10.8	1.01	58	114	71	32.2	31.5	30.2
2	1	4	1	0.089	8.6	2.59	51	115	68	32.6	31.1	31.6
3	1	4	1	0.305	9.8	6.68	65	117	60	32.4	31.1	29.5
4	1	4	1	0.135	7.2	5.53	65	111	68	31.6	31.7	31.2
5	1	4	1	0.116	8.7	3.28	60	112	77	31.4	31.7	31.0
6	1	4	1	0.076	8.3	2.36	50	118	66	33.9	32.0	28.6
1	2	1	1	0.102	11.1	1.76	72	123	68	30.7	29.6	29.9
2	2	1	1	0.091	9.1	2.36	52	116	71	31.8	31.0	28.8
3	2	1	1	0.163	10.1	3.40	58	131	67	32.0	31.4	28.4
4	2	1	1	0.175	7.3	6.90	64	114	72	30.1	28.5	29.3
5	2	1	1	0.075	8.3	2.34	60	121	80	29.8	30.3	27.7
6	2	1	1	0.040	7.3	1.62	50	104	63	31.2	29.6	26.8
1	2	2	1	0.101	11.3	1.69	59	112	68	30.9	31.5	31.8

2	2	2	1	0.058	9.2	1.45	48	109	66	31.7	31.2	28.3
3	2	2	1	0.104	10.0	2.20	57	119	61	30.7	29.5	28.2
4	2	2	1	0.135	6.8	6.21	67	114	68	29.6	29.9	28.0
5	2	2	1	0.096	8.9	2.58	57	117	81	28.4	29.7	27.1
6	2	2	1	0.143	9.1	3.66	52	118	67	29.3	29.0	28.1
1	2	3	1	0.089	11.3	1.49	55	112	69	30.6	30.1	29.7
2	2	3	1	0.116	9.1	2.95	47	115	71	31.7	30.8	27.1
3	2	3	1	0.080	8.8	2.19	51	115	60	32.2	30.3	28.7
4	2	3	1	0.119	7.8	4.17	62	114	69	31.4	30.3	28.6
5	2	3	1	0.088	8.2	2.78	70	109	72	31.3	29.7	29.3
6	2	3	1	0.139	9.4	3.29	58	118	67	32.6	30.4	30.0
1	2	4	1	0.070	12.4	0.98	52	123	70	31.5	29.9	28.9
2	2	4	1	0.100	8.9	2.65	47	119	72	31.4	30.2	27.2
3	2	4	1	0.137	9.7	3.09	54	118	60	30.7	31.1	28.2
4	2	4	1	0.124	7.1	5.28	61	104	70	31.4	29.8	29.2
5	2	4	1	0.085	8.4	2.57	64	120	83	30.3	29.8	28.5
6	2	4	1	0.165	9.8	3.65	56	115	68	32.2	30.3	27.5
7	1	1	2	0.068	3.8	10.12	66			32.6	32.8	32.5
8	1	1	2	0.058	5.4	4.22	61			23.1	23.3	22.5
9	1	1	2	0.067	5.6	4.52	48			30.9	25.5	24.9
10	1	1	2	0.063	5.4	4.50	57	108	64	32.1	29.9	31.8
11	1	1	2	0.110	8.1	3.56	68	133	78	28.9	29.6	28.8
12	1	1	2	0.068	7.3	2.71	65	133	83	32.7	27.4	25.0
13	1	1	2	0.103	8.3	3.18	71	149	92	32.1	29.4	29.2
14	1	1	2	0.080	5.5	5.65	77	111	63	29.1	27.3	28.4
15	1	1	2	0.167	5.5	11.75	83	103	60	34.0	32.5	32.3
7	1	2	2	0.084	4.5	8.85	67			33.2	30.3	31.1
8	1	2	2	0.068	5.5	4.71	58			31.6	28.5	30.4
9	1	2	2	0.160	5.6	10.82	63			30.3	26.8	25.9
10	1	2	2	0.098	5.7	6.32	54	110	61	31.4	30.9	31.4
11	1	2	2	0.203	8.3	6.23	79	126	73	30.2	29.4	29.3
12	1	2	2	0.291	6.8	13.41	61	143	90	32.7	28.5	24.8
13	1	2	2	0.101	8.5	2.98	76	140	85	31.1	28.9	29.0
14	1	2	2	0.071	5.6	4.89	73	127	69	29.1	28.5	29.5
15	1	2	2	0.237	7.0	10.29	60	97	58	33.1	31.1	32.6
7	1	3	2	0.058	4.0	7.89	79			32.4	28.2	29.1

8	1	3	2	0.088	5.7	5.72	70			32.4	27.7	29.9
9	1	3	2	0.215	6.4	11.21	75			33.2	24.8	33.1
10	1	3	2	0.075	6.5	3.73	50	106	62	31.7	31.0	31.4
11	1	3	2	0.087	8.1	2.83	79	121	73	29.2	29.5	29.0
12	1	3	2	0.059	6.6	2.83	60	146	84	32.7	29.5	26.9
13	1	3	2	0.177	8.3	5.42	76	139	87	31.2	29.1	29.5
14	1	3	2	0.128	5.7	8.34	70	131	66	31.4	29.3	29.9
15	1	3	2	0.185	7.4	7.18	70	103	58	29.8	31.5	32.2
7	1	4	2	0.083	4.9	7.21	60			31.8	30.6	30.9
8	1	4	2	0.106	6.0	6.24	61			32.7	30.4	31.2
9	1	4	2	0.072	5.5	5.06	51			30.2	28.6	29.3
10	1	4	2	0.158	6.6	7.75	53	115	63	31.7	32.5	33.3
11	1	4	2	0.072	8.6	2.09	74	117	70	29.5	29.3	27.1
12	1	4	2	0.348	6.3	18.36	67	134	86	33.7	29.7	28.5
13	1	4	2	0.117	8.7	3.30	69	131	86	31.6	30.4	30.1
14	1	4	2	0.097	5.6	6.44	70	118	60	30.0	28.1	30.4
15	1	4	2	0.125	6.2	6.82	76	91	52	31.6	32.2	32.7
7	2	1	2	0.146	4.9	12.81	80			31.6	32.3	32.0
8	2	1	2	0.069	5.6	4.62	62					
9	2	1	2	0.094	5.9	5.75	41			30.0	25.6	24.2
10	2	1	2	0.041	5.6	2.73	58	123	70	32.2	30.5	32.1
11	2	1	2	0.095	8.0	3.19	64	130	82	28.2	28.6	28.5
12	2	1	2	0.134	7.1	5.58	64	144	78	33.5	26.7	24.2
13	2	1	2	0.120	8.2	3.78	71	153	107	32.5	29.6	29.5
14	2	1	2	0.077	5.7	5.09	76	117	72	29.3	27.2	28.2
15	2	1	2	0.288	6.6	13.84	79	103	63	34.5	32.1	32.6
7	2	2	2	0.083	4.8	7.59	65			33.5	31.3	29.2
8	2	2	2	0.063	5.5	4.42	56			33.1	31.4	29.4
9	2	2	2	0.277	5.9	17.03	50			29.1	24.8	24.3
10	2	2	2	0.072	6.5	3.65	49	109	62	30.0	31.0	31.4
11	2	2	2	0.094	7.7	3.38	66	125	74	28.2	28.8	27.6
12	2	2	2	0.150	6.9	6.61	60	150	88	31.8	27.9	24.5
13	2	2	2	0.070	8.2	2.20	70	175	90	28.3	27.4	24.9
14	2	2	2	0.121	5.6	8.08	61	139	82	28.7	28.6	29.6
15	2	2	2	0.278	7.4	10.70	54	106	64	30.8	31.5	32.1
7	2	3	2	0.051	3.8	7.51	65			30.8	27.6	26.4

8	2	3	2	0.120	5.8	7.65	63			31.3	27.9	30.9
9	2	3	2	0.199	6.4	10.41	50			31.1	29.8	32.0
10	2	3	2	0.103	6.4	5.39	56	111	62	31.1	30.2	30.5
11	2	3	2	0.088	8.2	2.77	68	123	74	31.3	29.9	29.4
12	2	3	2	0.195	6.2	10.64	57	136	82	31.8	29.0	26.4
13	2	3	2	0.107	8.3	3.27	72	135	74	31.3	29.9	29.4
14	2	3	2	0.153	5.8	9.81	76	124	66	30.2	29.9	30.3
15	2	3	2	0.313	7.2	12.71	60	104	56	29.0	31.2	31.0
7	2	4	2	0.098	4.8	8.89	63			30.7	28.3	27.3
8	2	4	2	0.108	6.1	6.08	53			32.0	31.8	30.6
9	2	4	2	0.077	5.9	4.66	44			29.6	27.7	27.3
10	2	4	2	0.099	6.4	5.16	62	125	69	30.2	30.8	31.4
11	2	4	2	0.061	7.3	2.44	68	124	71	30.0	29.0	27.9
12	2	4	2	0.400	6.0	23.72	61	141	78	34.2	29.7	28.6
13	2	4	2	0.202	8.6	5.73	67	138	85	30.9	31.0	29.6
14	2	4	2	0.095	5.5	6.63	57	115	63	31.7	28.8	30.6
15	2	4	2	0.193	6.3	10.48	67	96	57	30.5	28.2	32.5

4.5 Appendix D: Statistical Analysis Reports

4.5.1 Mean Diameter Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:25:19 PM

Data source: Mean Diameter Data in combined.JNB

General Linear Model

Dependent Variable: mean diameter mm

Equal Variance Test: Passed (P = 0.347)

Source of Variation	DF	SS	MS	F	P
group	1	100.129	100.129	14.926	0.002
subject(group)	13	87.207	6.708		
treatment	3	1.453	0.484	2.610	0.065
group x treatment	3	1.676	0.559	3.012	0.042
Residual	39	7.234	0.185		
Total	59	197.527	3.348		

Main effects cannot be properly interpreted if significant interaction is determined. This is because the size of a factor's effect depends upon the level of the other factor.

The effect of different levels of group depends on what level of treatment is present. There is a statistically significant interaction between group and treatment. (P = 0.042)

Power of performed test with alpha = 0.0500: for group : 0.944
Power of performed test with alpha = 0.0500: for treatment : 0.381
Power of performed test with alpha = 0.0500: for group x treatment : 0.469

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	9.014	0.529
2.000	6.377	0.432

Least square means for treatment :

Group	Mean

1.000 7.504
2.000 7.943
3.000 7.642
4.000 7.692
Std Err of LS Mean = 0.355

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	8.915	0.550
1.000 x 2.000	9.492	0.550
1.000 x 3.000	8.761	0.550
1.000 x 4.000	8.888	0.550
2.000 x 1.000	6.093	0.449
2.000 x 2.000	6.395	0.449
2.000 x 3.000	6.523	0.449
2.000 x 4.000	6.497	0.449

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	Diff of Means	p	q	P	P<0.050
1.000 vs. 2.000	2.637	2	5.464	0.002	Yes

Comparisons for factor: **treatment**

Comparison	Diff of Means	p	q	P	P<0.050
2.000 vs. 1.000	0.439	4	3.870	0.044	Yes
2.000 vs. 3.000	0.301	4	2.651	0.256	No
2.000 vs. 4.000	0.251	4	2.211	0.411	Do Not Test
4.000 vs. 1.000	0.188	4	1.659	0.647	No
4.000 vs. 3.000	0.0499	4	0.440	0.989	Do Not Test
3.000 vs. 1.000	0.138	4	1.219	0.824	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 3.000	0.731	4	4.155	0.027	Yes
2.000 vs. 4.000	0.604	4	3.435	0.088	No
2.000 vs. 1.000	0.577	4	3.283	0.111	Do Not Test
1.000 vs. 3.000	0.153	4	0.872	0.926	No
1.000 vs. 4.000	0.0269	4	0.153	1.000	Do Not Test
4.000 vs. 3.000	0.127	4	0.720	0.957	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	Diff of Means	p	q	P	P<0.05
3.000 vs. 1.000	0.430	4	2.996	0.165	No
3.000 vs. 2.000	0.129	4	0.897	0.920	Do Not Test
3.000 vs. 4.000	0.0267	4	0.186	0.999	Do Not Test
4.000 vs. 1.000	0.403	4	2.810	0.210	Do Not Test
4.000 vs. 2.000	0.102	4	0.711	0.958	Do Not Test
2.000 vs. 1.000	0.301	4	2.099	0.457	Do Not Test

Comparisons for factor: **group within 1**

Comparison	Diff of Means	p	q	P	P<0.05
1.000 vs. 2.000	2.821	2	5.618	0.001	Yes

Comparisons for factor: **group within 2**

Comparison	Diff of Means	p	q	P	P<0.05
1.000 vs. 2.000	3.097	2	6.167	<0.001	Yes

Comparisons for factor: **group within 3**

Comparison	Diff of Means	p	q	P	P<0.05
1.000 vs. 2.000	2.238	2	4.456	0.007	Yes

Comparisons for factor: **group within 4**

Comparison	Diff of Means	p	q	P	P<0.05
1.000 vs. 2.000	2.391	2	4.761	0.004	Yes

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.2 Mean Blood Velocity Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:23:47 PM

Data source: MBV Combined Data in combined.JNB

General Linear Model

Dependent Variable: MBV

Equal Variance Test: Passed (P = 0.193)

Source of Variation	DF	SS	MS	F	P
group	1	121.544	121.544	6.928	0.021
subject(group)	13	228.071	17.544		
treatment	3	6.469	2.156	0.296	0.828
group x treatment	3	14.266	4.755	0.653	0.586
Residual	39	284.225	7.288		
Total	59	658.525	11.161		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.021). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.828).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.586)

Power of performed test with alpha = 0.0500: for group : 0.615
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**
1.000	3.682	0.855
2.000	6.587	0.698

Least square means for treatment :

Group	**Mean**
1.000	4.897
2.000	5.594
3.000	4.743
4.000	5.303

Std Err of LS Mean = 0.827

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	4.215	1.281
1.000 x 2.000	3.578	1.281
1.000 x 3.000	3.358	1.281
1.000 x 4.000	3.575	1.281
2.000 x 1.000	5.580	1.046
2.000 x 2.000	7.610	1.046
2.000 x 3.000	6.127	1.046
2.000 x 4.000	7.030	1.046

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
2.000 vs. 1.000	2.905	2	3.722	0.021	Yes

Comparisons for factor: **treatment**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**

2.000 vs. 3.000	0.851	4	1.197	0.832	No
2.000 vs. 1.000	0.697	4	0.979	0.899	Do Not Test
2.000 vs. 4.000	0.292	4	0.410	0.991	Do Not Test
4.000 vs. 3.000	0.560	4	0.787	0.944	Do Not Test
4.000 vs. 1.000	0.405	4	0.569	0.978	Do Not Test
1.000 vs. 3.000	0.155	4	0.217	0.999	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 3.000	0.857	4	0.777	0.946	No
1.000 vs. 4.000	0.640	4	0.580	0.976	Do Not Test
1.000 vs. 2.000	0.637	4	0.578	0.977	Do Not Test
2.000 vs. 3.000	0.220	4	0.199	0.999	Do Not Test
2.000 vs. 4.000	0.00292	4	0.00265	1.000	Do Not Test
4.000 vs. 3.000	0.217	4	0.197	0.999	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	2.030	4	2.256	0.393	No
2.000 vs. 3.000	1.483	4	1.648	0.652	Do Not Test
2.000 vs. 4.000	0.580	4	0.645	0.968	Do Not Test
4.000 vs. 1.000	1.450	4	1.611	0.668	Do Not Test
4.000 vs. 3.000	0.903	4	1.003	0.893	Do Not Test
3.000 vs. 1.000	0.547	4	0.608	0.973	Do Not Test

Comparisons for factor: **group within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	1.365	2	1.167	0.414	No

Comparisons for factor: **group within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	4.032	2	3.447	0.019	Yes

Comparisons for factor: **group within 3**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	2.769	2	2.367	0.102	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	3.455	2	2.953	0.043	Yes

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.3 Baseline Blood Flow Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 2:02:51 PM

Data source: Blood Flow Combined in pre_test1.snb.JNB

General Linear Model

Dependent Variable: bloodflow

Equal Variance Test: Passed (P = 0.762)

Source of Variation	DF	SS	MS	F	P
group	1	0.00216	0.00216	0.298	0.595
subject(group)	13	0.0945	0.00727		
treatment	3	0.00566	0.00189	0.526	0.667
group x treatment	3	0.0122	0.00406	1.132	0.348
Residual	39	0.140	0.00359		
Total	59	0.257	0.00436		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.595).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.667).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.348)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.0708

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	0.133	0.0174
2.000	0.121	0.0142

Least square means for treatment :

Group	Mean
1.000	0.118
2.000	0.142

3.000 0.117
4.000 0.130
Std Err of LS Mean = 0.0177

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	0.149	0.0274
1.000 x 2.000	0.137	0.0274
1.000 x 3.000	0.116	0.0274
1.000 x 4.000	0.129	0.0274
2.000 x 1.000	0.0870	0.0224
2.000 x 2.000	0.146	0.0224
2.000 x 3.000	0.119	0.0224
2.000 x 4.000	0.131	0.0224

4.5.4 Heart Rate Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:24:55 PM

Data source: HR Data in combined.JNB

General Linear Model

Dependent Variable: HR b/min

Equal Variance Test: Passed (P = 0.350)

Source of Variation	DF	SS	MS	F	P
group	1	678.194	678.194	3.948	0.068
subject(group)	13	2232.890	171.761		
treatment	3	142.600	47.533	1.347	0.273
group x treatment	3	25.334	8.445	0.239	0.868
Residual	39	1376.203	35.287		
Total	59	4477.899	75.897		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.068).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.273).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.868)

Power of performed test with alpha = 0.0500: for group : 0.344
Power of performed test with alpha = 0.0500: for treatment : 0.109
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	59.799	2.675
2.000	66.662	2.184

Least square means for treatment :

Group	Mean
1.000	62.539
2.000	63.158
3.000	65.748
4.000	61.476

Std Err of LS Mean = 2.195

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	58.778	3.401
1.000 x 2.000	60.608	3.401
1.000 x 3.000	61.440	3.401
1.000 x 4.000	58.369	3.401
2.000 x 1.000	66.299	2.777
2.000 x 2.000	65.708	2.777
2.000 x 3.000	70.057	2.777
2.000 x 4.000	64.583	2.777

4.5.5 Systolic Blood Pressure Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:25:49 PM

Data source: Systolic BP Data in combined.JNB

Balanced Design

Dependent Variable: systolic BP

Equal Variance Test: Failed (P < 0.050)

Source of Variation	DF	SS	MS	F	P
group	1	460.454	460.454	0.834	0.383

subject(group)	10	5520.731	552.073		
treatment	3	199.833	66.611	2.197	0.109
group x treatment	3	114.343	38.114	1.257	0.307
Residual	30	909.491	30.316		
Total	47	7204.852	153.295		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.383).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.109).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.307)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.280
Power of performed test with alpha = 0.0500: for group x treatment : 0.0915

Least square means for group :

Group	**Mean**
1.000	115.931
2.000	122.125

Std Err of LS Mean = 4.796

Least square means for treatment :

Group	**Mean**
1.000	119.694
2.000	121.667
3.000	118.750
4.000	116.000

Std Err of LS Mean = 3.660

Least square means for group x treatment :

Group	**Mean**
1.000 x 1.000	116.444
1.000 x 2.000	119.500
1.000 x 3.000	113.222
1.000 x 4.000	114.556
2.000 x 1.000	122.944
2.000 x 2.000	123.833
2.000 x 3.000	124.278
2.000 x 4.000	117.444

Std Err of LS Mean = 5.176

4.5.6 Diastolic Blood Pressure Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:26:12 PM

Data source: Diastolic BPData in combined.JNB

Balanced Design

Dependent Variable: diastolic BP

Equal Variance Test: Passed (P = 0.121)

Source of Variation	DF	SS	MS	F	P
group	1	133.333	133.333	0.366	0.559
subject(group)	10	3643.907	364.391		
treatment	3	31.500	10.500	1.155	0.343
group x treatment	3	22.019	7.340	0.808	0.500
Residual	30	272.648	9.088		
Total	47	4103.407	87.307		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.559).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.343).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.500)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.0741
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Least square means for group :

Group	Mean
1.000	68.444
2.000	71.778

Std Err of LS Mean = 3.897

Least square means for treatment :

Group	Mean
1.000	71.056
2.000	70.639
3.000	69.806
4.000	68.944

Std Err of LS Mean = 2.856

Least square means for group x treatment :

Group	Mean

1.000 x 1.000 68.889
1.000 x 2.000 68.611
1.000 x 3.000 67.833
1.000 x 4.000 68.444
2.000 x 1.000 73.222
2.000 x 2.000 72.667
2.000 x 3.000 71.778
2.000 x 4.000 69.444
Std Err of LS Mean = 4.040

4.5.7 Left Thigh Skin Temperature Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:26:46 PM

Data source: Skin Temp LT Thigh Data in combined.JNB

General Linear Model

Dependent Variable: skin temp Lt thigh

Equal Variance Test: Passed (P = 0.929)

Source of Variation	**DF**	**SS**	**MS**	**F**	**P**
group	1	6.391	6.391	1.087	0.316
subject(group)	13	76.437	5.880		
treatment	3	2.213	0.738	0.241	0.867
group x treatment	3	11.641	3.880	1.266	0.300
Residual	39	119.573	3.066		
Total	59	215.591	3.654		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.316).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.867).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.300)

Power of performed test with alpha = 0.0500: for group : 0.0563
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.0943

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))

Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	31.916	0.495
2.000	31.250	0.404

Least square means for treatment :

Group	Mean
1.000	31.626
2.000	31.379
3.000	31.442
4.000	31.884

Std Err of LS Mean = 0.512

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	32.635	0.793
1.000 x 2.000	31.348	0.793
1.000 x 3.000	31.328	0.793
1.000 x 4.000	32.352	0.793
2.000 x 1.000	30.616	0.647
2.000 x 2.000	31.411	0.647
2.000 x 3.000	31.555	0.647
2.000 x 4.000	31.416	0.647

4.5.8 Left Calf Skin Temperature Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:27:33 PM

Data source: Skin Temp LT Calf Data in combined.JNB

General Linear Model

Dependent Variable: Lt calf skin temp

Equal Variance Test: Failed (P < 0.050)

Source of Variation	DF	SS	MS	F	P
group	1	56.478	56.478	7.674	0.016
subject(group)	13	95.676	7.360		
treatment	3	7.724	2.575	1.986	0.132
group x treatment	3	3.089	1.030	0.794	0.505
Residual	39	50.572	1.297		
Total	59	215.881	3.659		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.016). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.132).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.505)

Power of performed test with alpha = 0.0500: for group : 0.670
Power of performed test with alpha = 0.0500: for treatment : 0.241
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**
1.000	31.226	0.554
2.000	29.246	0.452

Least square means for treatment :

Group	**Mean**
1.000	29.900
2.000	30.126
3.000	30.064
4.000	30.854

Std Err of LS Mean = 0.442

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	31.181	0.685
1.000 x 2.000	31.042	0.685
1.000 x 3.000	31.171	0.685
1.000 x 4.000	31.511	0.685
2.000 x 1.000	28.619	0.559
2.000 x 2.000	29.209	0.559
2.000 x 3.000	28.958	0.559
2.000 x 4.000	30.197	0.559

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**

1.000 vs. 2.000	1.980	2	3.918	0.016	Yes

4.5.9 Left Foot Skin Temperature Between Groups

Two Way Repeated Measures ANOVA (One Factor Repetition) Monday, September 30, 2013, 4:28:03 PM

Data source: Skin Temp LT Foot Data in combined.JNB

General Linear Model

Dependent Variable: Lt foot skin temp

Equal Variance Test: Passed (P = 0.624)

Source of Variation	**DF**	**SS**	**MS**	**F**	**P**
group	1	8.369	8.369	0.839	0.376
subject(group)	13	129.653	9.973		
treatment	3	9.676	3.225	1.143	0.344
group x treatment	3	8.301	2.767	0.981	0.412
Residual	39	110.043	2.822		
Total	59	270.302	4.581		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.376).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.344).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.412)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.0727
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**

1.000	30.316	0.645
2.000	29.554	0.526

Least square means for treatment :

Group	**Mean**
1.000	29.370
2.000	29.719
3.000	30.293
4.000	30.357

Std Err of LS Mean = 0.566

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	30.363	0.877
1.000 x 2.000	30.092	0.877
1.000 x 3.000	30.476	0.877
1.000 x 4.000	30.334	0.877
2.000 x 1.000	28.378	0.716
2.000 x 2.000	29.347	0.716
2.000 x 3.000	30.111	0.716
2.000 x 4.000	30.380	0.716

4.5.10 Femoral Artery Diameter

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:08:21 PM

Data source: Delta Mean Diameter Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: Mean diameter

Normality Test: Failed (P < 0.050)

Equal Variance Test: Passed (P = 0.647)

Source of Variation	**DF**	**SS**	**MS**	**F**	**P**
group	1	0.0798	0.0798	0.215	0.651
subject(group)	13	4.827	0.371		
treatment	3	0.516	0.172	0.785	0.509
group x treatment	3	3.227	1.076	4.911	0.005
Residual	39	8.544	0.219		
Total	59	17.002	0.288		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.651).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.509).

The effect of different levels of group depends on what level of treatment is present. There is a statistically significant interaction between group and treatment. (P = 0.005)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.793

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**
1.000	0.121	0.124
2.000	0.0470	0.102

Least square means for treatment :

Group	**Mean**
1.000	0.126
2.000	-0.0788
3.000	0.135
4.000	0.155

Std Err of LS Mean = 0.123

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	-0.0669	0.191
1.000 x 2.000	-0.277	0.191
1.000 x 3.000	0.346	0.191
1.000 x 4.000	0.484	0.191
2.000 x 1.000	0.319	0.156
2.000 x 2.000	0.120	0.156
2.000 x 3.000	-0.0764	0.156
2.000 x 4.000	-0.175	0.156

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
1.000 vs. 2.000	0.0745	2	0.656	0.651	No

Comparisons for factor: **treatment**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
4.000 vs. 2.000	0.234	4	1.893	0.545	No
4.000 vs. 1.000	0.0286	4	0.232	0.998	Do Not Test
4.000 vs. 3.000	0.0199	4	0.162	1.000	Do Not Test

3.000 vs. 2.000	0.214	4	1.731	0.616	Do Not Test
3.000 vs. 1.000	0.00868	4	0.0703	1.000	Do Not Test
1.000 vs. 2.000	0.205	4	1.661	0.646	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
4.000 vs. 2.000	0.761	4	3.984	0.037	Yes
4.000 vs. 1.000	0.551	4	2.883	0.192	No
4.000 vs. 3.000	0.138	4	0.722	0.956	Do Not Test
3.000 vs. 2.000	0.623	4	3.262	0.114	No
3.000 vs. 1.000	0.413	4	2.161	0.431	Do Not Test
1.000 vs. 2.000	0.210	4	1.101	0.864	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 4.000	0.494	4	3.164	0.131	No
1.000 vs. 3.000	0.396	4	2.535	0.292	Do Not Test
1.000 vs. 2.000	0.199	4	1.278	0.803	Do Not Test
2.000 vs. 4.000	0.294	4	1.886	0.548	Do Not Test
2.000 vs. 3.000	0.196	4	1.257	0.811	Do Not Test
3.000 vs. 4.000	0.0981	4	0.629	0.970	Do Not Test

Comparisons for factor: **group within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	0.386	2	2.043	0.155	No

Comparisons for factor: **group within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	0.397	2	2.101	0.144	No

Comparisons for factor: **group within 3**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	0.422	2	2.235	0.121	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	0.658	2	3.484	0.017	Yes

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.11 Mean Blood Velocity

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:03:54 PM

Data source: Delta Mean Blood Velocity Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: MBV

Normality Test: Failed (P < 0.050)

Equal Variance Test: Failed (P < 0.050)

Source of Variation	DF	SS	MS	F	P
group	1	31.874	31.874	5.888	0.031
subject(group)	13	70.373	5.413		
treatment	3	11.135	3.712	0.676	0.572
group x treatment	3	10.015	3.338	0.608	0.614
Residual	39	214.141	5.491		
Total	59	342.039	5.797		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.031). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.572).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.614)

Power of performed test with alpha = 0.0500: for group : 0.529
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	-0.713	0.475
2.000	0.775	0.388

Least square means for treatment :

Group	Mean
1.000	-0.179
2.000	-0.575

3.000 0.562
4.000 0.315
Std Err of LS Mean = 0.617

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	-1.154	0.957
1.000 x 2.000	-0.613	0.957
1.000 x 3.000	-0.547	0.957
1.000 x 4.000	-0.538	0.957
2.000 x 1.000	0.796	0.781
2.000 x 2.000	-0.536	0.781
2.000 x 3.000	1.670	0.781
2.000 x 4.000	1.169	0.781

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	Diff of Means	p	q	P	P<0.050
2.000 vs. 1.000	1.488	2	3.432	0.031	Yes

Comparisons for factor: **treatment within 1**

Comparison	Diff of Means	p	q	P	P<0.05
4.000 vs. 1.000	0.615	4	0.643	0.968	No
4.000 vs. 2.000	0.0753	4	0.0787	1.000	Do Not Test
4.000 vs. 3.000	0.00865	4	0.00904	1.000	Do Not Test
3.000 vs. 1.000	0.607	4	0.634	0.970	Do Not Test
3.000 vs. 2.000	0.0666	4	0.0697	1.000	Do Not Test
2.000 vs. 1.000	0.540	4	0.565	0.978	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	Diff of Means	p	q	P	P<0.05
3.000 vs. 2.000	2.206	4	2.824	0.207	No
3.000 vs. 1.000	0.874	4	1.119	0.858	Do Not Test
3.000 vs. 4.000	0.501	4	0.642	0.969	Do Not Test
4.000 vs. 2.000	1.705	4	2.183	0.422	Do Not Test
4.000 vs. 1.000	0.373	4	0.477	0.987	Do Not Test
1.000 vs. 2.000	1.332	4	1.705	0.627	Do Not Test

Comparisons for factor: **group within 1**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	1.950	2	2.237	0.120	No

Comparisons for factor: **group within 2**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.0775	2	0.0889	0.950	No

Comparisons for factor: **group within 3**

Comparison	Diff of Means	p	q	P	P<0.05

2.000 vs. 1.000	2.217	2	2.543	0.078	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	1.707	2	1.958	0.172	No

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.12 Blood Flow

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 4:59:38 PM

Data source: Delta Blood Flow Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: blood flow

Normality Test: Passed (P = 0.065)

Equal Variance Test: Passed (P = 0.377)

Source of Variation	**DF**	**SS**	**MS**	**F**	**P**
group	1	0.0244	0.0244	5.283	0.039
subject(group)	13	0.0601	0.00462		
treatment	3	0.00700	0.00233	0.783	0.510
group x treatment	3	0.00560	0.00187	0.626	0.602
Residual	39	0.116	0.00298		
Total	59	0.215	0.00364		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.039). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.510).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.602)

Power of performed test with alpha = 0.0500: for group : 0.475

Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**
1.000	-0.0249	0.0139
2.000	0.0163	0.0113

Least square means for treatment :

Group	**Mean**
1.000	-0.00522
2.000	-0.0213
3.000	0.00884
4.000	0.000529

Std Err of LS Mean = 0.0144

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	-0.0417	0.0223
1.000 x 2.000	-0.0310	0.0223
1.000 x 3.000	-0.0109	0.0223
1.000 x 4.000	-0.0160	0.0223
2.000 x 1.000	0.0312	0.0182
2.000 x 2.000	-0.0117	0.0182
2.000 x 3.000	0.0286	0.0182
2.000 x 4.000	0.0170	0.0182

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
2.000 vs. 1.000	0.0412	2	3.250	0.039	Yes

Comparisons for factor: **treatment within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
3.000 vs. 1.000	0.0308	4	1.382	0.763	No
3.000 vs. 2.000	0.0201	4	0.902	0.919	Do Not Test
3.000 vs. 4.000	0.00510	4	0.229	0.999	Do Not Test
4.000 vs. 1.000	0.0257	4	1.153	0.847	Do Not Test
4.000 vs. 2.000	0.0150	4	0.673	0.964	Do Not Test
2.000 vs. 1.000	0.0107	4	0.481	0.986	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	Diff of Means	p	q	P	P<0.05
1.000 vs. 2.000	0.0429	4	2.357	0.355	No
1.000 vs. 4.000	0.0142	4	0.780	0.946	Do Not Test
1.000 vs. 3.000	0.00268	4	0.147	1.000	Do Not Test
3.000 vs. 2.000	0.0402	4	2.210	0.411	Do Not Test
3.000 vs. 4.000	0.0115	4	0.633	0.970	Do Not Test
4.000 vs. 2.000	0.0287	4	1.577	0.683	Do Not Test

Comparisons for factor: **group within 1**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.0729	2	3.361	0.021	Yes

Comparisons for factor: **group within 2**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.0193	2	0.890	0.532	No

Comparisons for factor: **group within 3**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.0394	2	1.817	0.205	No

Comparisons for factor: **group within 4**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.0330	2	1.522	0.287	No

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.13 Heart Rate

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:05:59 PM

Data source: Delta Heart Rate Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: HR

Normality Test: Passed (P = 0.129)

Equal Variance Test: Passed (P = 0.392)

Source of Variation	DF	SS	MS	F	P
group	1	55.195	55.195	0.907	0.358
subject(group)	13	791.208	60.862		

treatment	3	321.134	107.045	3.511	0.024
group x treatment	3	12.106	4.035	0.132	0.940
Residual	39	1189.047	30.488		
Total	59	2407.804	40.810		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.358).

The difference in the mean values among the different levels of treatment is greater than would be expected by chance after allowing for effects of differences in group. There is a statistically significant difference (P = 0.024). To isolate which group(s) differ from the others use a multiple comparison procedure.

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.940)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.572
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 13.000

Expected MS(group) = var(res) + 4.000 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 4.000 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	**Mean**	**SEM**
1.000	-2.598	1.592
2.000	-4.556	1.300

Least square means for treatment :

Group	**Mean**	**SEM**
1.000	0.239	1.455
2.000	-5.350	1.455
3.000	-5.718	1.455
4.000	-3.480	1.455

Least square means for group x treatment :

Group	**Mean**	**SEM**
1.000 x 1.000	0.566	2.254
1.000 x 2.000	-4.012	2.254
1.000 x 3.000	-4.243	2.254
1.000 x 4.000	-2.704	2.254
2.000 x 1.000	-0.0881	1.841
2.000 x 2.000	-6.688	1.841
2.000 x 3.000	-7.192	1.841
2.000 x 4.000	-4.255	1.841

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
1.000 vs. 2.000	1.958	2	1.347	0.358	No

Comparisons for factor: **treatment**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
1.000 vs. 3.000	5.957	4	4.094	0.030	Yes
1.000 vs. 2.000	5.590	4	3.841	0.046	Yes
1.000 vs. 4.000	3.719	4	2.556	0.286	No
4.000 vs. 3.000	2.238	4	1.538	0.699	No
4.000 vs. 2.000	1.871	4	1.286	0.800	Do Not Test
2.000 vs. 3.000	0.367	4	0.253	0.998	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 3.000	4.810	4	2.134	0.442	No
1.000 vs. 2.000	4.579	4	2.031	0.485	Do Not Test
1.000 vs. 4.000	3.270	4	1.451	0.736	Do Not Test
4.000 vs. 3.000	1.539	4	0.683	0.963	Do Not Test
4.000 vs. 2.000	1.308	4	0.580	0.976	Do Not Test
2.000 vs. 3.000	0.231	4	0.102	1.000	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 3.000	7.104	4	3.860	0.045	Yes
1.000 vs. 2.000	6.600	4	3.586	0.070	No
1.000 vs. 4.000	4.167	4	2.264	0.390	Do Not Test
4.000 vs. 3.000	2.937	4	1.596	0.675	No
4.000 vs. 2.000	2.433	4	1.322	0.786	Do Not Test
2.000 vs. 3.000	0.504	4	0.274	0.997	Do Not Test

Comparisons for factor: **group within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	0.655	2	0.285	0.841	No

Comparisons for factor: **group within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	2.676	2	1.164	0.415	No

Comparisons for factor: **group within 3**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	2.949	2	1.282	0.369	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	1.551	2	0.675	0.636	No

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.14 Systolic Blood Pressure

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:09:52 PM

Data source: Delta Systolic BP Data in master_analysis_notebook.SNB

Balanced Design

Dependent Variable: systolic BP

Normality Test: Failed (P < 0.050)

Equal Variance Test: Passed (P = 0.368)

Source of Variation	DF	SS	MS	F	P
group	1	288.447	288.447	7.173	0.023
subject(group)	10	402.134	40.213		
treatment	3	161.044	53.681	0.828	0.489
group x treatment	3	481.507	160.502	2.476	0.081
Residual	30	1944.921	64.831		
Total	47	3278.053	69.746		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.023). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.489).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.081)

Power of performed test with alpha = 0.0500: for group : 0.611
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.341

Least square means for group :

Group	Mean
1.000	-0.0833
2.000	4.819

Std Err of LS Mean = 1.294

Least square means for treatment :

Group	Mean
1.000	3.611
2.000	2.861
3.000	-0.750
4.000	3.750

Std Err of LS Mean = 2.324

Least square means for group x treatment :

Group	Mean
1.000 x 1.000	1.833
1.000 x 2.000	-4.611
1.000 x 3.000	0.556
1.000 x 4.000	1.889
2.000 x 1.000	5.389
2.000 x 2.000	10.333
2.000 x 3.000	-2.056
2.000 x 4.000	5.611

Std Err of LS Mean = 3.287

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	Diff of Means	p	q	P	P<0.050
2.000 vs. 1.000	4.903	2	3.788	0.023	Yes

Comparisons for factor: **treatment**

Comparison	Diff of Means	p	q	P	P<0.050
4.000 vs. 3.000	4.500	4	1.936	0.528	No
4.000 vs. 2.000	0.889	4	0.382	0.993	Do Not Test
4.000 vs. 1.000	0.139	4	0.0598	1.000	Do Not Test
1.000 vs. 3.000	4.361	4	1.876	0.554	Do Not Test
1.000 vs. 2.000	0.750	4	0.323	0.996	Do Not Test
2.000 vs. 3.000	3.611	4	1.554	0.693	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	Diff of Means	p	q	P	P<0.05
4.000 vs. 2.000	6.500	4	1.977	0.510	No
4.000 vs. 3.000	1.333	4	0.406	0.992	Do Not Test
4.000 vs. 1.000	0.0556	4	0.0169	1.000	Do Not Test
1.000 vs. 2.000	6.444	4	1.961	0.517	Do Not Test
1.000 vs. 3.000	1.278	4	0.389	0.993	Do Not Test
3.000 vs. 2.000	5.167	4	1.572	0.686	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 3.000	12.389	4	3.769	0.056	No
2.000 vs. 1.000	4.944	4	1.504	0.714	Do Not Test
2.000 vs. 4.000	4.722	4	1.437	0.742	Do Not Test
4.000 vs. 3.000	7.667	4	2.332	0.368	Do Not Test

4.000 vs. 1.000	0.222	4	0.0676	1.000	Do Not Test
1.000 vs. 3.000	7.444	4	2.265	0.393	Do Not Test

Comparisons for factor: **group within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	3.556	2	1.137	0.426	No

Comparisons for factor: **group within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	14.944	2	4.779	0.002	Yes

Comparisons for factor: **group within 3**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	2.611	2	0.835	0.558	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	3.722	2	1.190	0.405	No

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.15 Diastolic Blood Pressure

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:11:20 PM

Data source: Delta Diastolic BP Data in master_analysis_notebook.SNB

Balanced Design

Dependent Variable: diastolic BP

Normality Test: Passed (P = 0.053)

Equal Variance Test: Passed (P = 0.489)

Source of Variation	**DF**	**SS**	**MS**	**F**	**P**
group	1	12.336	12.336	0.480	0.504
subject(group)	10	257.134	25.713		
treatment	3	135.729	45.243	2.568	0.073
group x treatment	3	120.359	40.120	2.277	0.100
Residual	30	528.551	17.618		
Total	47	1054.109	22.428		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.504).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.073).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.100)

Power of performed test with alpha = 0.0500: for group : 0.0500
Power of performed test with alpha = 0.0500: for treatment : 0.362
Power of performed test with alpha = 0.0500: for group x treatment : 0.298

Least square means for group :

Group	**Mean**
1.000	0.944
2.000	1.958

Std Err of LS Mean = 1.035

Least square means for treatment :

Group	**Mean**
1.000	3.444
2.000	2.028
3.000	-1.194
4.000	1.528

Std Err of LS Mean = 1.212

Least square means for group x treatment :

Group	**Mean**
1.000 x 1.000	1.333
1.000 x 2.000	-3.849E-015
1.000 x 3.000	0.222
1.000 x 4.000	2.222
2.000 x 1.000	5.556
2.000 x 2.000	4.056
2.000 x 3.000	-2.611
2.000 x 4.000	0.833

Std Err of LS Mean = 1.714

4.5.16 Left Thigh Skin Temperature

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:28:41 PM

Data source: Delta Skin Temp LT Thigh Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: Lt thigh skin temp

Normality Test: Failed (P < 0.050)

Equal Variance Test: Passed (P = 0.595)

Source of Variation	DF	SS	MS	F	P
group	1	2.666	2.666	1.743	0.210
subject(group)	13	19.888	1.530		
treatment	3	6.678	2.226	1.199	0.323
group x treatment	3	13.154	4.385	2.362	0.087
Residual	38	70.553	1.857		
Total	58	110.564	1.906		

The difference in the mean values among the different levels of group is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in treatment. There is not a statistically significant difference (P = 0.210).

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.323).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.087)

Power of performed test with alpha = 0.0500: for group : 0.119
Power of performed test with alpha = 0.0500: for treatment : 0.0823
Power of performed test with alpha = 0.0500: for group x treatment : 0.324

Expected Mean Squares:
Approximate DF Residual for group = 12.909

Expected MS(group) = var(res) + 3.923 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 3.934 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	-0.939	0.252
2.000	-0.505	0.210

Least square means for treatment :

Group	Mean	SEM
1.000	-0.838	0.371
2.000	-1.136	0.359
3.000	-0.193	0.359
4.000	-0.722	0.359

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	-1.689	0.556
1.000 x 2.000	-1.237	0.556
1.000 x 3.000	0.290	0.556
1.000 x 4.000	-1.121	0.556

2.000 x 1.000	0.0130	0.491
2.000 x 2.000	-1.035	0.454
2.000 x 3.000	-0.676	0.454
2.000 x 4.000	-0.323	0.454

4.5.17 Left Calf Skin Temperature

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:31:24 PM

Data source: Delta Skin Temp LT Calf Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: Lt calf skin temp

Normality Test: Failed (P < 0.050)

Equal Variance Test: Passed (P = 0.223)

Source of Variation	DF	SS	MS	F	P
group	1	14.288	14.288	8.645	0.012
subject(group)	13	21.486	1.653		
treatment	3	5.341	1.780	1.099	0.361
group x treatment	3	1.357	0.452	0.279	0.840
Residual	38	61.533	1.619		
Total	58	104.202	1.797		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.012). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group . There is not a statistically significant difference (P = 0.361).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.840)

Power of performed test with alpha = 0.0500: for group : 0.731
Power of performed test with alpha = 0.0500: for treatment : 0.0653
Power of performed test with alpha = 0.0500: for group x treatment : 0.0500

Expected Mean Squares:
Approximate DF Residual for group = 12.927

Expected MS(group) = var(res) + 3.923 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 3.934 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)

Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	-1.063	0.262
2.000	-0.0587	0.219

Least square means for treatment :

Group	Mean	SEM
1.000	-0.569	0.346
2.000	-0.472	0.335
3.000	-0.177	0.335
4.000	-1.025	0.335

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	-1.121	0.520
1.000 x 2.000	-0.911	0.520
1.000 x 3.000	-0.896	0.520
1.000 x 4.000	-1.325	0.520
2.000 x 1.000	-0.0169	0.458
2.000 x 2.000	-0.0332	0.424
2.000 x 3.000	0.541	0.424
2.000 x 4.000	-0.726	0.424

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	Diff of Means	p	q	P	P<0.050
2.000 vs. 1.000	1.004	2	4.158	0.012	Yes

Comparisons for factor: **treatment**

Comparison	Diff of Means	p	q	P	P<0.050
3.000 vs. 4.000	0.848	4	2.529	0.295	No
3.000 vs. 1.000	0.392	4	1.149	0.848	Do Not Test
3.000 vs. 2.000	0.295	4	0.879	0.925	Do Not Test
2.000 vs. 4.000	0.553	4	1.650	0.651	Do Not Test
2.000 vs. 1.000	0.0968	4	0.284	0.997	Do Not Test
1.000 vs. 4.000	0.457	4	1.339	0.780	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	Diff of Means	p	q	P	P<0.05
3.000 vs. 4.000	0.429	4	0.826	0.936	No
3.000 vs. 1.000	0.225	4	0.433	0.990	Do Not Test
3.000 vs. 2.000	0.0150	4	0.0289	1.000	Do Not Test
2.000 vs. 4.000	0.414	4	0.797	0.942	Do Not Test
2.000 vs. 1.000	0.210	4	0.404	0.992	Do Not Test
1.000 vs. 4.000	0.204	4	0.393	0.992	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	Diff of Means	p	q	P	P<0.05
3.000 vs. 4.000	1.267	4	2.988	0.168	No
3.000 vs. 2.000	0.574	4	1.354	0.774	Do Not Test
3.000 vs. 1.000	0.558	4	1.264	0.808	Do Not Test
1.000 vs. 4.000	0.709	4	1.606	0.670	Do Not Test
1.000 vs. 2.000	0.0163	4	0.0370	1.000	Do Not Test
2.000 vs. 4.000	0.693	4	1.633	0.658	Do Not Test

Comparisons for factor: **group within 1**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	1.104	2	2.248	0.118	No

Comparisons for factor: **group within 2**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.878	2	1.846	0.198	No

Comparisons for factor: **group within 3**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	1.437	2	3.022	0.038	Yes

Comparisons for factor: **group within 4**

Comparison	Diff of Means	p	q	P	P<0.05
2.000 vs. 1.000	0.599	2	1.259	0.377	No

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.5.18 Left Foot Skin Temperature

Two Way Repeated Measures ANOVA (One Factor Repetition) Friday, December 09, 2011, 5:35:43 PM

Data source: Delta Skin Temp LT Foot Data in master_analysis_notebook.SNB

General Linear Model

Dependent Variable: Lt foot skin temp

Normality Test: Passed (P = 0.138)

Equal Variance Test: Passed (P = 0.597)

Source of Variation	DF	SS	MS	F	P
group	1	16.580	16.580	8.995	0.010
subject(group)	13	23.931	1.841		
treatment	3	2.245	0.748	0.758	0.525
group x treatment	3	4.047	1.349	1.366	0.268
Residual	38	37.513	0.987		
Total	58	83.443	1.439		

The difference in the mean values among the different levels of group is greater than would be expected by chance after allowing for effects of differences in treatment. There is a statistically significant difference (P = 0.010). To isolate which group(s) differ from the others use a multiple comparison procedure.

The difference in the mean values among the different levels of treatment is not great enough to exclude the possibility that the difference is just due to random sampling variability after allowing for the effects of differences in group. There is not a statistically significant difference (P = 0.525).

The effect of different levels of group does not depend on what level of treatment is present. There is not a statistically significant interaction between group and treatment. (P = 0.268)

Power of performed test with alpha = 0.0500: for group : 0.752
Power of performed test with alpha = 0.0500: for treatment : 0.0500
Power of performed test with alpha = 0.0500: for group x treatment : 0.113

Expected Mean Squares:
Approximate DF Residual for group = 12.960

Expected MS(group) = var(res) + 3.923 var(subject(group)) + var(group)
Expected MS(subject(group)) = var(res) + 3.934 var(subject(group))
Expected MS(treatment) = var(res) + var(treatment)
Expected MS(group x treatment) = var(res) + var(group x treatment)
Expected MS(Residual) = var(res)

Least square means for group :

Group	Mean	SEM
1.000	-1.771	0.277
2.000	-0.689	0.231

Least square means for treatment :

Group	Mean	SEM
1.000	-1.004	0.270
2.000	-1.374	0.262
3.000	-1.066	0.262
4.000	-1.476	0.262

Least square means for group x treatment :

Group	Mean	SEM
1.000 x 1.000	-1.890	0.406
1.000 x 2.000	-1.509	0.406
1.000 x 3.000	-1.597	0.406
1.000 x 4.000	-2.086	0.406
2.000 x 1.000	-0.117	0.358
2.000 x 2.000	-1.238	0.331
2.000 x 3.000	-0.534	0.331

2.000 x 4.000 -0.865 0.331

All Pairwise Multiple Comparison Procedures (Tukey Test):

Comparisons for factor: **group**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
2.000 vs. 1.000	1.082	2	4.244	0.010	Yes

Comparisons for factor: **treatment**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.050**
1.000 vs. 4.000	0.472	4	1.772	0.598	No
1.000 vs. 2.000	0.370	4	1.390	0.760	Do Not Test
1.000 vs. 3.000	0.0618	4	0.232	0.998	Do Not Test
3.000 vs. 4.000	0.410	4	1.566	0.687	Do Not Test
3.000 vs. 2.000	0.308	4	1.177	0.839	Do Not Test
2.000 vs. 4.000	0.102	4	0.389	0.993	Do Not Test

Comparisons for factor: **treatment within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 4.000	0.577	4	1.422	0.747	No
2.000 vs. 1.000	0.381	4	0.939	0.910	Do Not Test
2.000 vs. 3.000	0.0879	4	0.217	0.999	Do Not Test
3.000 vs. 4.000	0.489	4	1.205	0.829	Do Not Test
3.000 vs. 1.000	0.293	4	0.723	0.956	Do Not Test
1.000 vs. 4.000	0.196	4	0.482	0.986	Do Not Test

Comparisons for factor: **treatment within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
1.000 vs. 2.000	1.121	4	3.251	0.116	No
1.000 vs. 4.000	0.748	4	2.169	0.428	Do Not Test
1.000 vs. 3.000	0.417	4	1.209	0.828	Do Not Test
3.000 vs. 2.000	0.704	4	2.126	0.446	Do Not Test
3.000 vs. 4.000	0.331	4	1.000	0.894	Do Not Test
4.000 vs. 2.000	0.373	4	1.126	0.856	Do Not Test

Comparisons for factor: **group within 1**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	1.773	2	4.196	0.005	Yes

Comparisons for factor: **group within 2**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	0.271	2	0.663	0.642	No

Comparisons for factor: **group within 3**

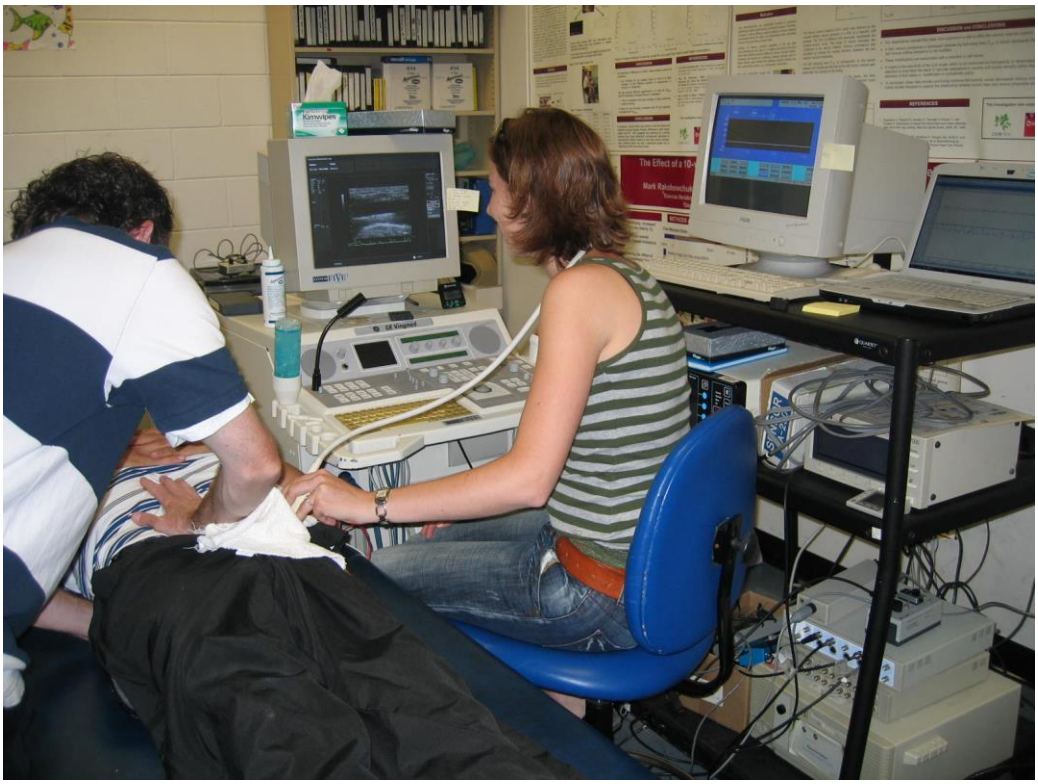
Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	1.063	2	2.599	0.073	No

Comparisons for factor: **group within 4**

Comparison	**Diff of Means**	**p**	**q**	**P**	**P<0.05**
2.000 vs. 1.000	1.221	2	2.984	0.040	Yes

A result of "Do Not Test" occurs for a comparison when no significant difference is found between two means that enclose that comparison. For example, if you had four means sorted in order, and found no difference between means 4 vs. 2, then you would not test 4 vs. 3 and 3 vs. 2, but still test 4 vs. 1 and 3 vs. 1 (4 vs. 3 and 3 vs. 2 are enclosed by 4 vs. 2: 4 3 2 1). Note that not testing the enclosed means is a procedural rule, and a result of Do Not Test should be treated as if there is no significant difference between the means, even though one may appear to exist.

4.6 Appendix E: Photograph Within the Vascular Dynamics Lab



4.7 Appendix F: Osteopathic Techniques

4.7.4 venous sinus technique – step 1 - Jugular Foreamen

Position of patient: Patient supine

Position of D.O.: Seated at head of patient
Ulnar borders of hands in contact with each other.
Fingers 4 and 5 are flexed at MCP and PIP, extended at DIP.
Fingers 2 and 3 are extended. The tips of the middle fingers of both hands are in contact.

Preparation: Middle fingers of both hands behind and are as close as possible to the occipital condyles.

Action: Contact PRM.
Lean thorax forward ever so slightly and bring hands down into table (increases presence).
Move hips and thorax posteriorly on chair (causes longitudinal traction).
Bring elbows together slightly (causes lateral translation between two middle fingers).

Comments: Technique is finished when:
Neutral point
Expansion
Heat
Feel increase in local vitality

Chin of patient must be up slightly when performing the technique.

4.7.5 Venous Sinus Technique – Step 2 - transverse sinus

Position of patient: Patient supine

Position of D.O.: Seated at head of patient.
Hands and arms supported on table.
Ulnar border of hands are in contact.
Fingers are slightly flexed at PIP, and flexed at DIP.
The tips of the fingers run lateral to the inion on both sides. That is, found between the two fifth fingers.
The head of the patient is being supported on the fingertips.

Action: Spread between fingers.

Comments: Technique is finished when:
Neutral point
Expansion
Heat
Feel increase in local vitality
Chin of patient must be up slightly when performing the technique.

4.7.6 Venous Sinus Technique – Step 3 – Lambda

Position of patient: Patient supine, legs straight, arms by side.
Position of D.O.: Seated at head of patient.
Wrists are extended and slightly radially deviated.
Thumbs of each hand are crossed at PIP.
Fifth Phalanx is flexed at PIP.
Fourth phalanx (ring finger) behind ear.
Third phalanx (middle finger) in front of ear.
Thumbs on parietals (external bevel), on either side of sagittal suture, distal to the occipital bone (internal bevel).
Action: The weight of the cranium will liberate the surface.
Comments: Technique finished when you feel liberation of suture.

4.7.7 Venous Sinus Technique – Step 4 – Straight Sinus

Position of patient: Patient supine, arms by side, legs extended.
Position of D.O.: Seated at head of patient.
Sides of both thumbs, medial borders of hands, and along the side of the fifth phalanx are in contact. The tip of the fifth phalanx is in contact with the inion. The tip of the thumbs are in contact as close to the vertex as possible.
Action: The therapist leans forward to increase tension between hands.
Comments: **W**ith cranial flexion the index and thumbs will come closer together.
The technique is finished when:
Neutral point
Warmth
Increased expansion and retraction (vitality) – feeling that the tips of the thumb and 5^{th} finger come closer (flexion) together and spread apart (extension)

4.7.8 Venous Sinus Technique – Step 5 – Obelion

Position of patient: Patient supine, legs extended, arms resting by side.
Position of D.O.: Seated at head of patient.
Forearms and wrists supported.
Thumbs crossed at PIP.
Thumbs in contact with the parietals on either side of the sagittal suture.
Action: Therapist leans thorax forward (this increases tension between thumbs).
Comments: The technique is finished when:
Neutral point.
Warmth.
Increased expansion and retraction (vitality).

Can perform this technique at as many points along the superior sagittal suture, as is necessary.

4.7.9 Venous Sinus Technique – Step 6 - Bregma

Position of patient:	Patient supine, legs extended, arms resting by side
Position of D.O.:	Seated at head of patient. Forearms and wrists supported. Thumbs crossed at PIP. Thumbs in contact with the parietals on either side of the sagittal suture at the Bregma
Action:	Spread 50-50 between fingers and lean forward to increase tension Between thumbs
Comments:	The technique is finished when: Neutral point. Warmth. Increased expansion and retraction (vitality).

4.7.10 Venous Sunus Technique – Step 7 – Metopic Suture

Position of patient:	Patient supine, arms resting at side, legs extended.
Position of D.O.:	D.O. seated at head of patient. Elbows rested on the side of the patient's head. The second to fifth phalanges are flexed at the PIP and DIP joints. The fingertips of each hand are on either side of the metopic suture, such that the nail beds of each hand are facing each other.
Action:	The Therapist leans forward slightly. A small traction
Comments:	The technique is finished when: Neutral point. Warmth. Increased expansion and retraction (vitality).

4.7.11 Venous Sinus Technique – Step 8 – Ethmoid ; Phillippe Druelle Variation

Position of patient:	Patient supine, arms resting at sides, legs extended.
Position of D.O.:	D.O. standing to side of patient. One hand is intra-oral, middle finger on cruciform, thumb is extra-bucal at base of the nasal bones just proximal to the articulation with the frontals. (a) The other hand is on the greater wings of the sphenoid. (b) The other hand is on the tips of the wings of the frontal bones.

The elbows are held out, away from the body. The forearms of both arms should almost be in line.

Action: The therapist performs a slight traction obliquely downward and forward of the intra-bucal hand.
The therapist performs a frontal lift with one hand (down towards the patients nose and up towards the ceiling). The therapist performs a slight traction obliquely downward and forward of the intra-bucal hand.

Comments: The technique is finished when:
Neutral point.
Warmth.
Increased expansion and retraction (vitality).

4.7.12 Compression Of The Fourth Ventricle

Position of patient: supine

Position of D.O.: Seated at the patient's head
Hands are cupped together, fingers flexed, hypothenars together, thumbs straight.
The hands are positioned low on the occiput, inferior to the tentorium cerebelli

Action: D.O. listens to the occiput**.** There may be a sort myofascial Stillpoint as the fasciae release.
Contact the expansion/retraction phase of the PRM
During the expansion phase, the D.O. will resist the expansion
Using a gentle contraction of the deep flexor digitorum muscles, bring the occiput down to the table and lean backward putting tension on the dural system.
Wait for the Stillpoint
At the end of the Stillpoint, palpate the expansion of the ventricle and follow the motion until it resumes an expansion/retraction cycle
Remove the hands on inspiration.

4.7.13 Basal Expansion

Position of patient: supine

Position of D.O.: Seated at head of patient
Find the base of the occiput, get the 4^{th} and 5^{th} fingers on either side of the inion (right and left)
Place tips of 3^{rd} fingers at SP of C1
Place tips of 2^{nd} fingers at SP of C2
Make sure not to push C1 anteriorly
The foreamen magnum should be in the hole

Action: Support the head with the thenars so not all the weight of the head is resting on your thumbs
Let the patient's head sink into your hands

May feel fascial torsions – want to balance out these torsions
Do the longitudinal distraction by separating fingertips and wait until a release of tension is felt.
Will feel warmth and a symmetrical movement of the straight sinus

Then do a lateral distraction of finger tips and wait for a symmetrical movement of the straight sinus.

Then put tension on the tentorium
Tighten up the thenars slightly to bring more pressure on the mastoids
Have now added a new membrane and a new tension
Wait for a release and a symmetrical movement

Dorsiflex feet to add tension on the dura
Wait for a release and a symmetrical movement

Stick tongue out to bring a new tension on the dural membranes
Wait for symmetrical movement

With each inspiration, release the parameters in reverse order, one at a time.

4.7.14 Decompaction Of The Sphenobasilar Joint

Position of patient: Supine

Position of D.O.: Seated at the head of the patient
Index fingers placed on greater wings and 3rd finger in front of ear and 4th finger behind ear

Action: Hands placed on the vault but thumbs stay off in order to become a fulcrum/point of reference.
D.O. separates fingers and leans forward in order to induce flexion.
Feel for presence of sphenobasilar joint.
Get patient to dorsiflex feet until movement within occiput is felt – this will force liquids to create more power.
Then have patient stick out tongue to increase fascial tension.
Wait for Stillpoint.
When increase of volume is felt, get patient to take a deep breath in and swallow 2-3x's while sticking tongue out – this will further increase tension to help free up compaction
When swallowing finished, patient breathes in and relaxes feet.

Comments: With expansion, fingers feel like they are spreading and moving caudally.

4.7.15 Correction Of Torsion Lesion Of Sphenoid

Position of patient: Supine

Position of D.O.: Seated at head of patient
Index fingers on greater wings and 3rd fingers in front of ear, 4th fingers behind ears

Action: Hands on the vault bones but thumbs stay off to become a fulcrum/point of reference.
D.O. turns head to the direction of the torsion to help exaggerate the lesion.
Patient then dorsiflexes foot of lesioned side and plantarflexes opposite foot – wait for Stillpoint and visualize axis.
At the end of the Stillpoint, patient inhales and holds to increase pressure in cranium.
Patient then exhales and switches direction of feet.
D.O. turns head to the other side following the sphenoid into the other torsion.
Patient inhales and D.O. turns head a little more to further increase range.
Patient then exhales.
Repeat process 2-3x's.
Integrate by dorsiflexing feet and assist flexion by leaning forward on breath in and then on exhalation, patient plantarflexes feet while D.O. assists extension by leaning back.

4.7.16 Correction Of Temporal Bone Using Opposite Physiological Motion

Position of patient: Supine
Position of D.O.: Seated at patient's head
One hand has classic hold of temporal and one hand has hand transverse across occiput

Test: Hold the occiput and induce IR/ER of the temporal.
Then hold the temporal and induce flex/ext of the occiput.
Determine which bone is in lesion and which bone is mobile

Action: D.O. takes the lesioned bone and holds it in it's lesion
D.O. then takes other bone and puts it in opposite movement
Patient then dorsiflexes foot until tension is palpated in the occiput
Wait for Stillpoint.
As motion returns, follow the lesioned bone into the opposite direction and hold the other bone in same direction.
Follow flex/ext for a few cycles

4.7.17 Release Of Om Suture Using V-Spread Technique

Position of patient: Supine
Position of D.O.: Seated at patient's head
One hand positioned with index and third fingers placed on either side of the OM suture
Third finger of other hand is placed on anterolateral aspect of head directly opposite to fingers surrounding OM suture – these two

hands should be placed in such a way so that the line between the two hands runs directly through the SBS.

Action: Direct a fluid movement from anterior cranium to OM suture such that axis of motion passes through the SBS.
When the fluid hits the suture, it forces it to separate.

4.7.18 Balance Of C1 In Relationship With The Dura

Position of patient: Supine
Position of D.O.: Seated at side of patient's head
Cephalic hand on frontal bone, with lift hold
Caudad hand on occiput
Action: Detranslate C1, hold, and then do a frontal lift
Contact the dura.
Wait for Stillpoint and then release of C1

4.7.19 Recipricol Membranous Tension Between Occiput And Sacrum – Release Of Spinal Cord Dura

Position of patient: Sidelying in fetal position
Position of D.O.: Seated behind patient
One hand cupping sacrum and one hand cupping occiput
Action: Assess motion of occiput and sacrum, feeling for flexion and extension of sacrum and occiput
When in contact with dura, apply a 50/50 tension between two hands and wait for Stillpoint.
Feel for release and follow the vitality.
Add tension through breathing
D.O. then leans forward to further increase the tension.
Perception is along the centre of the dura.
Wait for further Stillpoint and release.
Can work through many layers, Stillpoints and releases
by leaning further forward to further increase the tension
released when sacrum and occiput move synchronously

4.7.20 Recipricol Equilibrium Of Tentorium Cerebelli – Cranial Diaphragm

Position of patient: Supine
Position of D.O.: Seated at patient's head
Hands cradle the occiput with thumbs on the mastoids
Action: Hands transverse pressure across the occiput while feeling the volume in the hands.
During flexion, the tentorium should flatten and the mastoids should go in.
Place tension on the mastoid processes bilaterally tightening up the 'tent'.

If one side won't go in, the tent could be in an extension lesion, while if one mastoid goes in and the other goes out, there could be a torsion.
Find the fulcrum between your two hands, remembering that it may not always be centered.
Wait for a Stillpoint and release.
Respiration can also be used to increase Stillpoint potential.

Comments: **The tentorium must be released before the three diaphragms can be balanced.**

4.7.21 Diaphragm Lift Supine – Thoracic Diaphragm

Position of patient: Supine
Generally, knees are bent and arms are around D.O.'s waist – this, however, is not possible due to loss of motor control. Therefore this position was modified so that legs were straight and arms remained at side

Position of D.O.: Standing at head of patient with hands placed on bilateral antero-lateral thorax.

Action: On inhalation, D.O. leans back and on exhalation, D.O. holds.
Repeat for 3-4 repetitions
On last exhalation, D.O. guides the rib cage inferiorly while leaning body backwards.

Comments: **Thoracic Diaphragm must be released before balancing 3 diaphragms**
This technique was used if supported sitting was not possible or too uncomfortable

4.7.22 Thoracic Diaphragm Release

Position of Patient: Sitting

Position of D.O.: Standing behind patient with pillow placed between the two
Both hands reach around the patient from behind and are placed under the costal ribs.

Action: **Evaluation of the diaphragm**:
Test inspiration (does it drop down) and expiration (does it rise)
When it stays down - inspiration lesion and when it stays up – expiration lesion.
Test rotation/SB/A?P and find which side moves easier – ease
Combine movements into ease and wait for Stillpoint and release
Then breathe holding lesion direction.
Afterwards, move in opposite direction and finish with circumductions both ways of thorax
Retest all positions to see what released

Note: for some SCI individuals, sitting in this position, even with support, is too difficult and a Diaphragm Lift must be used instead

4.7.23 Inspiration And Expiration Of Pelvic Floor –Release Of Pelvic Diaphragm

Position of patient: Supine
Position of D.O.: Standing on affected side of patient
Caudad Hand follows from ischial tuberosity up to pelvic floor
Action: Find the pelvic floor and if it is stuck down (inspiration lesion and if it is stuck up (expiration lesion)
For inspiration lesion, have patient inhale while D.O. resists expansion.
On exhalation, D.O follows diaphragm inward. Continue several times until release is felt.
Coughing may also break the lesion at the end of holding breath.
For expiration lesion, breathe in and out, following into pelvic floor as far as restriction.
Continue with breathing until D.O can start to feel the diaphragm coming into fingers.
Offer the floor a bit of resistance and then move down with it (caudally) – this activates the stretch reflex of the fibres (contraction). Breathe again and recheck restriction of floor.
May need to stimulate several times – invite it to come down

4.7.24 BALANCING Of The THREE DIAPHRAGMS

1. Cranial and Thoracic Diaphragm

Position of patient: Supine with C-spine in neutral
Position of D.O.: Sitting at the head of the patient, slightly to the contralateral side to the temporal and hemi-diaphragm to be treated.
Forearms resting against the table and patient.
- cephalic hand in temporal classical hold with focus or attention on the excursion of the tentorium
- caudal hand in relation to the diaphragm leaf, under the costal margin. It is also possible to be on the thorax at the level of the 5^{th} or 6^{th} rib to contact the leaf and perceive its excursion

Action: Contact the hemi-tentorium and hemi-diaphragm to be treated, assess by listening or breathing, induce their lesion tendencies and prioritize.
Choose the breathing parameter corresponding to the lesion tendency of the most affected party while the D.O. follows the tissues of both diaphragms to reach a point of balance, Stillpoint, release, return to PRM expression and normality
Follow for a few cycles
Repeat the correction process for the other sid**e.**

Comments: Balancing can be done at the PRM expression level or the breathing mechanical level.

2. Thoracic and Pelvic Diaphragms

Position of patient: Supine

Position of D.O.: Standing at the side of the hemi-diaphragms to be treated, body resting against the table.
- one hand in relation to the thoracic diaphragm leaf under the costal margin
- other hand in classical hemi-pelvic floor contact

Action: Contact the excursions of the thoracic and pelvic hemi-diaphragms, assess by listening or breathing, induce their lesion tendency and priority.
Choose the breathing parameter corresponding to the most affected hemi-diaphragm, while you follow the tissues to reach a point of balance, Stillpoint, release, return to PRM expression and normality.
Follow for a few cycles the excursions
Repeat the correction process for the other side

Comments: The balancing can be done at the PRM level or the breathing mechanical level

4.7.25 Decompaction Of C0/C1/C2

Position of patient: Supine, chin up in slight axial extension

Position of D.O.: Standing at head of table
One hand cups the occiput while the 2nd and 3rd fingers of the opposite hand are across the posterior arch of C1, well behind the TPs on the lateral masses.

Action: **Decompaction of C0/C1:**
Test for compaction by fixing C1 and leaning back with body to distract the occiput.
D.O. uses abdomen to compact by leaning forward with chest without compressing the vertex – move the volume of the occiput with your hand and abdomen together.
Approximate the occipital condyles onto the concave surfaces of C1 just until they contact the surfaces
It is a specific action to the articular surfaces
Wait for Stillpoint and at the end of the Stillpoint, you will feel a driving force of occiput coming towards you.
Hold C1, follow the occiput and hold it in correction with a slight traction (50/50) for a few breathing cycles to balance the ligaments between occiput and C1 and the short muscles of the neck posteriorly.

Decompaction of C0/C1 on C2:
Hold C0/C1 as a unit in one hand and C2 in a pinch hold with the other hand.
Traction C0/C1 from C2 to test for compaction at level of C1/C2.
To treat, compact C0/C1 (convex surfaces) onto the convex surfaces of C2.

With release, follow in the direction of the correction and hold for a few breathing cycles to balance and release the muscles

4.7.26 Scar Tissue Release

Position of patient: Generally dependent upon the location of the scar but, in the case of the individuals with SCI, less rolling is better and, as a result, these individuals remained supine.

Position of D.O.: For C-spine scar, D.O. remained at patient's head
Fingertips of both hands along the scar

Action: Fingers placed along the scar, starting superficially.
As tension eases Fingers can go deeper.
Usually scar wants to go in longitudinal direction – take it perpendicular to this in order to exaggerate it.
Now follow it myofascially and wait for Stillpoint
Initially pain will be felt but, once it frees up, pain will exit.
If one area remains dense, stay longer in this area.

4.7.27 Inhibition Of Superior Cervical Fascias

Position of patient: Supine

Position of D.O.: Seated at head of patient
Fingers are placed low along the occiput in the suboccipital muscles
Fingers are pointed up towards the ceiling

Action: With fingers in place, come into contact with suboccipital muscle tension.
- Spread between fingers and then between the 2 hands
- D.O. leans back to contact all the posterior fascias
- Wait for release of fascias

4.7.28 Normalization Of C3 And Infrahyoid Fascias – Cervical Fascia

Position of patient: Supine

Position of D.O.: Seated at head of patient
One hand on C3 (pinch hold with C3 between the thumb and index finger).
Palm of other hand at level of manubrium

Action: Lift C3 to ceiling until you feel it register in the palm of the manubrium.
In palm hand, first contact is superficial cervical fascia tension
Observe the direction of tension and follow it with balanced membranous tension
Will have a Stillpoint and release
Drop down to the next fascial level (middle cervical fascia) and repeat technique.
Will have a Stillpoint and release

Drop down to layers of deep cervical fascia and repeat technique.
At end of technique, C3 will have increased mobility in upward direction (anterior movement of vertebra into postflexion)

4.7.29 Sacral Decompaction

Position of Patient: Supine
Position of D.O.: Standing on right side of patient
Right hand placed on lower segment of sacrum and left hand placed at on upper segment of sacrum, or at L5
Action: Feel each segment for mobility/resilience/vitality all the way down to the coccyx.
If no vitality, compact the segment to the segment above by bringing fingers together.
Hoover and wait for Stillpoint and release. Retest for vitality
Test at level of L5-S1 and at the sacral coccygeal joints
Apply procedure (Hoover) at any level, where compactions exist.

4.7.30 Normalization Of A Liver Expansion Lesion

Position of patient: Crook lying
Position of D.O.: Standing at patient's right side
Hands stacked over right anterior aspect of liver
Action: D.O. directly takes liver into retraction with each exhalation
Holds on inhalation, repeat until you feel you cannot retract anymore
Reevaluate
Hands are step-moved slowly on inspirations

4.7.31 Normalization Of A Liver Compaction – (Wake Up Technique)

Position of patient: Crook lying
Position of D.O.: Standing at patient's right side
Hands stacked on right lateral aspect of ribs over the liver
Action: D.O. evaluates the expansion/retraction on the anterior surface
Interpretation: If liver feels sucked in: Retraction state
If liver feels like it is pushing out: Expansion
D.O. then evaluates for a soft or hard endfeel.

To Treat: D.O. pushes into the lateral aspect of the liver to the depth of the parenchyma and then creates 2 shakes within the spring on exhalation in order to awaken it – repeat 3x's

4.7.32 Normalization Of Lesser Omentum

Position of patient: Crook lying
Position of D.O.: Standing on right side of patient

Cephalad hand along lesser curve of stomach
Caudad hand stabilizes the inferior border of liver with thenar eminence

Action: D.O. must visualize lesser curve of stomach
D.O. leans back to separate hands – use a 50/50 tension to address:
- Hepatogastric Ligament – oblique direction
- Hepatoduodenal Ligament – caudal direction
- Hepatoesophageal Ligament – lateral/transverse direction

Apply tension until release is felt

4.7.33 Recentering The Mesenteric Mass

Position of Patient: Supine with pillow under knees (SCI specific)
Position of D.O.: Standing at patient's side
Cup the mesenteric mass with palm of dominant hand

Action: **To Evaluate:**
1. D.O. listens for the PRM movement – Inspiration – counterclockwise
2. D.O. moves the mass in the direction of the 4 quadrants to locate adherences (sup./inf., L/R SB, L/R Rot., compress/decompress)

To Treat:
Direct: D.O. takes it into correction and has patient cough to break adherences.
Hoover: stack in midpoints of available range and await release
Functional: take into ease and await release
SCI population: Functional was most effective to extreme tension

4.7.34 Superior Mesenteric Artery Technique – Philippe Druelle, D.O.

Position of patient: Crook lying
Position of D.O.: Standing at patient's side
Dominant hand cups mesenteric mass

Action: **To evaluate:**
D.O. brings the mass up over the navel such that the D.O.'s 3rd MCP sits on the navel
Evaluate the PRM – Inspiration = Counterclockwise rotation
To treat:
Either functional or direct technique can be used

4.7.35 Normalization Of The Fascia Iliaca

Position of patient: Supine
Leg remains extended with pillow under knee – this is modified as leg is generally bent
Position of D.O.: Standing on side of patient opposite to the side being treated

Action: Evaluate fascia iliaca by cupping your hands inside the iliac crest and leaning backwards towards patient's opposite shoulder in an oblique direction.
Test for superior restrictions by turning your body towards patient's feet and inferior restrictions by turning your body towards patient's head.
If the patient is sensitive, go into the ease and wait for the fascia to start unwinding until a Stillpoint is reached.
If the patient is not sensitive, go directly into the restriction

4.7.36 Normalization Of The Fascia Iliaca, Si And Psoas

Position of patient: Supine
Leg remains extended with pillow under knee – this is modified as leg is generally bent
Position of D.O.: Standing on side of patient ipsilateral to the side being treated
Action: Place posterior hand in the sulcus of the SI joint and apply a lateral traction.
Place the other hand inside the iliac, moving it up towards the shoulder.
D.O. can lean back and draw leg slightly inferior to address psoas

4.7.37 Evaluation And Normalization Of The Cecum

Position of patient: Crook lying
Position of D.O.: Standing on opposite side relative to structure being treated
Fingertips bilaterally sensing, halfway between umbilicus and ASIS of right iliac.
Action: **To Evaluate in Relation to Iliac Fascia:**
D.O sinks fingers along the lateral border of the cecum and gently pulls medially and lifts their head to test for appropriate roll response (internal rotation).
To Evaluate in Relation to Mesentery Proper:
D.O. sinks fingers along the medial border of the cecum, lifts their head to test for appropriate roll response (external rotation).
To Treat:
D.O. applies 50/50 reciprocal tension technique and/or has the patient cough to break adherences.

4.7.38 Evaluation And Normalization Of The Sigmoid Colon

Position of patient: Crook lying
Position of D.O.: Standing at the patient's right side relative to the sigmoid colon
Fingertips of both hands sensing
Action: **Evaluating the Left Iliac Fascia** (standing on patient's right)

- D.O. pulls the mesenteric mass aside and comes down the ilium until hitting the sigmoid colon
- D.O. lifts head to test if the sigmoid colon dissociates from the iliac fascia (internal rotation)

To Treat:
D.O. applies 50/50 reciprocal membranous tension technique and/or has the patient cough to break adherences.

Evaluating the Sigmoid Mesocolon (standing on patient's left)
- D.O. rolls his/her fingers down the medial side of the sigmoid to locate.
- D.O lifts his/her head to test sigmoid mesocolon's response (external rotation of the sigmoid colon).

To Treat:
D.O. applies 50/50 reciprocal tension technique and/or has patient cough to break adherences.

4.7.39 Femoral Artery Technique

Position of patient: Supine

Position of D.O.: Seated at patient's side with elbows on the table
Hands are placed on either side of the patient's thigh
Unwind first with palms, then sensing artery PRM with palms and fingers

Action: **To Evaluate:**
1. unwind the fascia of the leg using a palm contact
2. D.O. then visualizes the femoral artery and feels it as an axis between the hands adding the finger contact also.
3. D.O. then listens to see if artery is being pulled up or down.

If artery is being pulled up or down, a restriction is present

To Treat:
Direct correction is applied using intention. With return of leg PRM, D.O. backs out slowly to the fascial layer and then comes off on an inhalation

4.7.40 Technique For Improving Circulation To The Lower Extremities

- As described by Edward Brown, D.O., The Academy of Applied Osteopathy, Yearbook 1946.

Position of Patient: Supine

Position of D.O.: Standing at side of patient on side being treated

Action: D.O hooks the fingers of one hand over the ischial tuberosity.
The palm of the other hand is placed along the antero-lateral side of the ilium.
Pressure is exerted by pulling on the tuberosity and pushing on the upper part of the ilium.

The pressure is held until the patient feels a distinct sense of warmth radiating down into the knee and the foot – this is very difficult for SCI individuals due to a lack of neurological supply to the lower extremities. Therefore, D.O. must be aware of any temperature or skin colour changes – SCI individuals may be able to sense slight changes, or alterations in sensation, however.

4.7.41 Interosseous Membrane Release – Anterior And Posterior

Position of patient: Supine

Position of D.O.: Seated at the side of the patient

Posterior - One hand has fingertips along posterior membrane while top hand Hoovers/myofascial work

Anterior – Thumb pads dig into anterior membrane while finger pads separate membrane from behind.

Action:

Posterior – Weight of leg rests on finger tips while top hand Hoovers from anterior surface.

Lift leg at the foot to reposition your bottom hand

Do this all the way down the leg

Anterior – thumb pads dig into anterior membrane, one above the other in order to cover more area.

Patient's leg is bent off the table and footed is rested, in slight dorsiflexion, on the chair you are sitting

Wait for release and continue down the leg

Reference: unless otherwise indicated, all techniques are taken from the Canadian College of Osteopathy Techniques Manual, 2005.

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